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SYSTEMS ONCOLOGY

Integrated Approaches to Understand and Cure Cancer

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THE JOURNEY OF ONCOLOGY AS A FIELD, FROM A FIELD TO STUDY TUMORS OF UNKNOWN ETIOLOGY AND CHARACTERISTICS, HAS BEEN VERY EVENTFUL FOR THE HUMAN RACE, BUT SEEMS TO BE HIJACKED BY THE COMPULSIONS OF **ONCONOMICS**, A TERM I SUGGEST TO PARTLY DESCRIBE THE ECONOMICS OF ONCOLOGY DRUG DISCOVERY AND DEVELOPMENT AND THE PAYER DYNAMICS

-Dr. Gopala Kovvali, Editor-in-Chief,
Journal of Carcinogenesis

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-Dr. Gopala Kovvali, Editor-in-Chief,
Journal of Carcinogenesis

Journal of Carcinogenesis

Editorial

Systems oncology: A new paradigm in cancer research

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Published: 11 March, 2014
Journal of Carcinogenesis 2014,13:6
This article is available from: http://www.carcinogenesis.com/content/13/1/6

Received: 09 March, 2014
Accepted: 09 March, 2014

Since the time the word oncology was coined in 1857, the field has expanded exponentially metamorphosing the original connotation and intent of the word (Roman word "oncos" (swelling) in relation to the tumors). The word oncology should, then, literally mean the study of swelling or tumors. In a premolecular or pregenomic era, oncology was confined to diagnosing and treating the solid tumors, which was later expanded to include hematological malignancies, which are now referred to as liquid tumors. The word liquid tumor is a misnomer, in that context, but it is a topic for another discussion on another day. The advent of DNA era has focused on seeking answers to the origin of tumors in the genetics under the genetics paradigm or genetics-only paradigm. The rapidly evolved disciplines of molecular biology, biotechnology and related disciplines have enormously contributed to the understanding of tumors and tumorigenesis. The genetic paradigm has recently been sharing its prime spot with the epigenetic phenomenon that could explain the tumorigenesis and has a promise for reversibility of the process. The most recent and exciting paradigm of tumorigenic process relates to cancer stem cells. Therefore, the concepts and models of tumorigenesis are still evolving and the field seems to be far from fully explored.

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Access this article online

Quick Response Code:

Website: www.carcinogenesis.com

DOI: 10.4103/1477-3163.128641

So, I ponder, if cancer is a disease or a phenomenon? I tend to believe that cancer is a phenomenon. The conceptual frameworks used so far to understand cancer, from its origin to the development of therapeutics to treat, are based on the deep-rooted notion that cancer is a single disease with diverse molecular manifestations in different organ sites. This notion seems to be strongly subscribed to and is used for diagnostics and therapeutic development as it offers an opportunity for clinical intervention. Interestingly, a general framework for oncology drug discovery is based on the ability to target an up-regulated molecule, in many cases a protein. A critical gap in this approach is the missing knowledge about the cause of events leading to up-regulation. Expression of a protein resulting from a gene fusion, like BCR-ABL, is easy to address by inhibitors, but they represent a rare genetic phenomenon leading to cancers. Even in those cases where the drugs prove effective, how sure are we that the underlying causes of molecular dysregulation are re-balanced by the therapy?

The Journey of Oncology as a field, from a field to study tumors of unknown etiology and characteristics, has been very eventful for the human race, but seems to be hijacked by the compulsions of **onconomics**, a term I suggest to partly describe the economics of oncology drug discovery and development and the payer dynamics. The major casualty of onconomic considerations seems to be the incentive to address cancer as a phenomenon rather than as a disease in need of desperate treatment. The governmental attitude, around the world, to the need for robust, long term and

sustainable basic research has in fact resulted in diminished interest to seriously look for the cause of the malady.

Carcinogenesis as a process is not expected to start overnight, not even in a few weeks. It has been estimated that it would take decades for cancer to manifest after exposure to carcinogens. This duration between the exposure and the manifestation of cancer, assuming direct correlation, seems to be shortening as can be seen by the lower age of onset of somatic cancers. Population and demographic differences in the incidence of cancers and the outcomes of treatment suggest a gap in our core understanding of the carcinogenesis process. The noncanonical and nonstochastic events and outcomes in the carcinogenic pathway alert us to the need to look at cancer as an end point of a series of nonlinear, systemic imbalances rather than as a result of an isolated molecular assault. In a simplistic view, a tumor is an accumulation of camaraderie of dysregulated, dysfunctional or mis-functional cells resulting from the colonization of a single renegade cell. How does one look at the trajectory of this renegade cell? From the time a cell has been subjected to molecular insult to the stage it becomes fully committed nonconformistic member of the normal colony, the cell is a part of a series of voluntary and involuntary events. In a well-developed species such as Homo sapiens, all carcinogenic exposures, both exogenous and endogenous, do not result in mutagenesis; all mutagens do not produce cancer-prone cellular lineage. What happens between the deleterious encounter with harmful exogenous agents and the manifestation or lack thereof, of the ill-effects of the assaulting agent? Humans are not simple machines that treat the incoming materials and messages as static inputs. Human systems are biologically evolved to intelligently metabolize or purge through the secretory system. Innate and adaptive immune systems are at the core of protecting human cellular integrity. Often, the power of human immune machinery is overlooked, while discussing the carcinogenic potential of agents originating in the environment and diet. Cellular memory following microbial and viral infections is another concept that needs to be integrated into the framework of understanding carcinogenesis and in the drug discovery process. The tools and technology to decipher the molecular and cellular footprints involved in the carcinogenic process are yet to be fully developed and perfected. In my opinion, this gap is mostly due to lack of comprehensive phenomenological framework to understand cancer and carcinogenic processes.

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Where is the field of oncology going? Does the long pipeline of potential drugs and the list of drugs in use that extend the life a few months indicate the accomplishments of oncology as a filed? The pipeline of drugs in the industry should not be misread as a measure of success against cancer or as an indication of mastery of **carcinome,** a term I propose to describe a complex system that runs the kingdom of renegade cells. Nor should we expect that the molecular profiling of a "whole genome" or a "whole proteome" results in clear messages about the culprits and the Samaritans.

I have provided arguments to drive the point that cancer and the carcinogenesis processes are complex and efforts to delineate them need to be more sophisticated than are currently employed. Looking at cancer from a systems oncology perspective will enable us to investigate the pathways from normal to tumor cells, behavior of pretumor and tumor cells, interactions and adaptability of normal and tumor cells, and in fact, the differences in survival motives of normal and tumor cells.

It may be tempting to draw comparisons between the proposed systems oncology and the systems biology. At the outset, the major difference is that systems oncology, enunciated in this editorial, encompasses the study of a disease or a phenomenon, from the perspectives of the multitude of disciplines such as immunology, cell biology, and molecular biology and so on. It proposes to investigate cancer in an integrated fashion utilizing the tools and methods of individual disciplines. Systems oncology opens a new way to look at treatment of cancers, therapeutic development, and understanding of the genesis of cancers at a deeper level. Journal of Carcinogenesis has already moved in this direction by introducing therapeutics as a part of its scope and is geared to be at the forefront of this new field by publishing excellent articles that represent the spirit of Systems Oncology.

How to cite this article: Kovvali G. Systems oncology: A new paradigm in cancer research. J Carcinog 2014;13:6.

AUTHOR'S PROFILE

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Publish in the Journal of Carcinogenesis

Journal of Carcinogenesis (www.carcinogenesis.com), published by Wolters Kluwer, is inviting participants of ACOS to publish manuscripts. The manuscripts can be of 1500 words and less than 20 references. High quality manuscripts will receive consideration for special nominal page charges or waivers.

Journal of Carcinogenesis is also soliciting articles for a special issue on Celebrating Cancer Research in Asia.

Please send your inquiries to manager@carcinogenesis.com, along with name and institutional affiliation of corresponding author.

Scope of the journal

Journal of Carcinogenesis publishes research articles from diverse fields of oncology and Chemoprevention. Primary areas of interest to the journal include: physical and chemical carcinogenesis and mutagenesis; processes influencing or modulating carcinogenesis, such as DNA repair; genetics, nutrition, and metabolism of carcinogens; the mechanism of action of carcinogens and modulating agents; epidemiological studies; and, the formation, detection, identification, and quantification of environmental carcinogens. Manuscripts that contribute to the understanding of cancer prevention are especially encouraged for submission.

Journal of Carcinogenesis has special interest to publish articles related to pre-clinical and translational oncology research.

Journal of Carcinogenesis publishes special supplements on focused topics related to cellular, molecular and clinical oncology. The editors of the journal welcome proposals from researchers who may be interested to bring out special issues in the field of their expertise. Write to editor@carcinogenesis.com with details of the proposal.

Publish in CARCINOMICS® and Clinical Communications

CARCINOMICS and Clinical Communications (www.Carcinomics.org) publishes outcomes of research from the fields of RNaOmics, proteomics, metabolomics, genomics, epigenomics, pharmacogenomics, etc. related to Oncology and closely related subjects. The word Carcinome™ was coined in a recent editorial by Dr. Gopala Kovvali (Kovvali G. Systems oncology: A new paradigm in cancer research. Journal of Carcinogenesis. 2014;13:6. doi:10.4103/1477-3163.128641) to describe an ensemble of molecular entities that is likely to regulate carcinogenesis process in a cell. The word CARCINOMICS is proposed to describe the methods and technologies used to investigate to understand the functions of the Carcinome™ and cancer as a systemic disease in the context of carcinogenesis, tumorigenesis and oncogenesis.

CARCINOMICS® and Clinical Communications encourages publications that describe new techniques as well as the modification of the existing ones that promote various aspects of cancer research. The journal especially encourages manuscripts that deal with concepts related to emerging and yet to invented technologies. CARCINOMICS® and Clinical Communications also publishes techniques and technologies that have a promise in Oncology drug discovery and development; these techniques include but not limited to structural oncology techniques as performed in the crystal, solution and in-silico environments, conjugation of drugs to antibodies and other carrier molecular vehicles, and emerging technologies that help deliver cancer drugs to the target cells. Articles related to diagnostic techniques like mammography, CT scans and other radiological and surgical techniques used in oncology will be considered.

Biomarkers are becoming an integral part of oncology drug development and have a strong impact on the diagnosis and treatment of cancers in the rapidly emerging era of personalized medicine. CARCINOMICS® and Clinical Communications has a special interest in publishing articles related to oncology biomarkers.

Articles related to pharmacokinetics, pharmacodynamics, pharmacogenomics and pharmacovigilance of oncology drugs will be considered.

As the development of cancer diagnostics and therapeutics is cost and time intensive, their use in the clinical practice is a huge burden to the payers. Therefore, there is a need for discussions on the economics of development of diagnostics, discovery and development of oncology drugs as well as the economics of treatment. Articles related to these topics will be solicited and published under a special section ONCONOMICS®.

The journal will also cover technical and clinical studies related to health, ethical and social issues in field of Oncology and closely related fields. Articles with clinical interest and implications will be given preference. Case reports, commentary of historical cases reports will also be considered.

Focused and insightful articles that shed light on oncology clinical trials will be considered expeditiously.

Please write to editor@carcinomics.org for details.

12th International Conference of The Asian Clinical Oncology Society
CANCER IN ASIA: BRIDGING THE GAPS

ABOUT ACOS

The Asian Clinical Oncology Society (ACOS) was established in Osaka, Japan, on 16 October 1991, for an unlimited period by representative doctors from several Asian countries. The inaugural meeting of ACOS was held in Osaka, Japan on October 16, 1991, and was chaired by Dr. Tetsuo Taguchi. ACOS will be devoted to the care of cancer patients and to the development of scientific knowledge through research in oncology and promoting the recruitment of facilities for oncology services. The first Constitution of ACOS was recognized by the executive committee members and then the ACOS was established. After the first meeting, it shall be held every two years for a business meeting and/or a scientific meeting. ACOS have successfully organized ten meetings, Osaka Japan, Bangkok Thailand, Kunming China, Bali Indonesia, Taipei Taiwan, Seoul Korea, Beijing China, Manila Philippines, Gifu Japan and Seoul Korea.

Mission

ACOS aims to ensure the current best practice for Asian cancer patients by implementing multidisciplinary treatments. To achieve this mission, ACOS holds the following core values:

1. To make a difference in Asian oncology through translational research and expert techniques.
2. To rethink cancer therapy from palliative to curative.
3. To highly motivate both of doctors and patients.
4. To identify the best practices and do it at good timing.
5. To develop less invasive and less expensive therapies.
6. To bolster cancer prevention through education and early diagnosis.

The Successive Presidents

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Chronicle of Presidents & The Conference Site

1st	1991, Osaka, Japan	by Prof. Tetsuo Taguchi
2nd	1993, Bangkok, Thailand	by Dr. S. Puribhat
3rd	1996, Kunming, China	by Prof. Yan Sun
4th	1999, Bali, Indonesia	by Evert D.C. Poetiray
5th	2001, Taipei, Taiwan	by Prof. Jacqueline Whang-Peng
6th	2003, Seoul, Korea	by Prof. Jin-Pok.Kim
7th	2006, Beijing, China	by Prof. Yan Sun
8th	2008, Manila, Philippine	by Prof. Antonio H. Villalon
9th	2010, Gifu, Japan	by Prof. Shigetoyo Saji
10th	2012, Seoul, Korea	by Prof. Kyung Sam Cho
11th	2014, Taipei, Taiwan	by Prof. Tsang-Wu Liu
12th	2016, New Delhi, India	by Dr. Sanjeev Misra
13th	2018, Thailand	by Dr. Sumitra Thongprasert

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Viet Nam	Dang Huy Quoc Thinh, Nguyen Chan Hung

INVITED SPEAKERS' ABSTRACTS

The emerging role of chemotherapy in endometrial cancer

Dr. Robert Woolas

MD FRCS

Endometrial cancer is now the commonest gynaecological malignancy in the Western world. Although the overall prognosis from the increasingly large cohort of patients remains optimistic, 30% of patients succumb to their disease despite adequate primary surgery and adjuvant pelvic radiotherapy. In resected patients found to have advanced disease, survival may be prolonged by approximately 25% following platinum, doxorubicin and or taxane based chemotherapy regimens. Among women found to have high risk surgical pathological features, potentially cured by surgery alone, the addition of chemotherapy to the treatment strategy appears to confer a small benefit toward overall survival in the order of 5%. The manner in which these cytotoxic drug protocols integrate with radiotherapy or novel Robert Woolas molecular therapeutic strategies awaits further elucidation.

Strategies for screening of cervical cancer in developing countries

Dr. Partha Basu

Screening Group (SCR), Early Detection and Prevention Section (EDP), International Agency for Research on Cancer (IARC),World Health Organization (WHO), France

Cervical cancer is the fourth most common cancer in women causing estimated 266,000 deaths globally every year. Large majority (85%) of the deaths occur in the less developed regions of the world with limited resources. Cervical cancer screening is effective if the services are delivered through population based organized programs. It is necessary for the screening programs to have definite policies regarding the public financing of the program, program management, test to be used, the target

Pratha Basu population, screening interval etc. A system of data collection across different levels of services is MD FRCS essential to implement program monitoring and quality control. Achieving high coverage of the target population and ensuring robust linkage between screening, diagnostic and treatment services are the most crucial components of the effective screening programs. The latest guidance document from the World Health Organization (WHO) recommended HPV test as the screening test of choice provided the programs can afford and sustain HPV detection based screening. VIA is the next best alternative to HPV test for the developing country programs though the subjective nature of the test leads to highly variable performance across the programs. Ideally the screen positive women need further evaluation with colposcopy. However, the HPV or VIA positive women may be directly treated by ablative or excisional techniques if organizing good quality colposcopy services is a challenge in a particular setting. Implementing cryotherapy is diffcult in many countries as the supply of the refrigerant gas is inadequate and irregular. Thermo-coagulation (also known as cold coagulation) as an alternative to cryotherapy is being evaluated in different studies. The developing countries also need to invest their resources into improving the cervical cancer diagnostic and therapeutic services so that the women with early symptoms have access to appropriate diagnosis and prompt treatment. Many of the countries in the less developed parts of the world will not be able to implement population based screening. Improving public awareness about early symptoms and augmenting the cancer early diagnosis and treatment services will lead to downstaging of the disease and higher possibilities of cure from the eminently treatable cervical cancer.

Role of Cyclin-Dependent Kinase 4/6 inhibitors in Endocrine Therapy for Metastatic Breast Cancer (MBC)

Dr. Adam Brufsky

MD, PhD, Professor of Medicine, University of Pittsburgh School of Medicine, Pittsburgh, PA, USA

Inhibition of the cyclin dependent kinases 4 and 6 through small molecule agents has the potential to change the natural history of estrogen receptor (ER) positive metastatic breast cancer (MBC). The rationale for the use of these agents in ER positive MBC will be reviewed. Clinical trial data from palbociclib in the first line MBC treatment setting with letrozole (PALOMA-1) and the second line and beyond treatment setting with fulvestrant (PALOMA-3) will also be reviewed. Indications for the use of these agents in MBC will be discussed. Finally, novel CDK 4/6 inhibitors such as abemaciclib and ribociclib will also be discussed.

Management of Her2 + Breast Cancer: Beyond Traztuzumab

Dr. Adam Brufsky

The introduction of traztuzumab into the therapy of Her2 positive metastatic breast cancer (MBC) changed the natural history of this disease. Current combinations of traztuzumab with cytotoxic chemotherapy such as taxanes and platinum agents when used as first line therapy results in progression free survival in excess of 12 months and overall survival in excess of 36 months. While these figures represent a major step forward, further advances beyond traztuzumab have the potential to substantially improve on this initial success. This presentation will review current clinical trial results in Her2 positive MBC therapy beyond traztuzumab with (a) anti-Her3 antibodies such as pertuzumab; (b) antibody-traztuzumab conjugates such as traztuzumab-emtansine; and (c) novel Her2 tyrosine kinase inhibitors such as neratinib. Novel agents such as MM-302 (Her2 targeted anthracycline liposomes), margetuximab (Her2 Fc fragment), and ONT-380 (pure Her2 tyrosine kinase inhibitor) will also be discussed.

Debate Early lung Cancer Surgery Versus SBRT: Surgery

Dr. Chien-Sheng Huang

MD, Bilng-Shiun Huang, MD, Phd

Anatomic surgical resection with mediastinal lymph node dissection remains the gold standard of care for early-stage non-small cell lung cancer (NSCLC). For medically inoperable patients, no doubt, stereotactic body radiotherapy (SBRT) has become an effective modality for compromised treatment. Nowadays, interest has emerged in this non- operative therapy for patients with early-stage NSCLC. Recent studies relevant to SBRT for inoperable stage I NSCLC has shown promising results including good local tumor control, low treatment-related morbidity, acceptable survival rates, and most importantly, a better quality of life when compared to surgical intervention. It comes as no surprise that this wave of alternative has moved even from inoperable to operable cases – although two independent, randomized phase-three trials of SBRT in patients with operable stage I NSCLC (STARS and ROSEL) closed early due to slow accrual.

However, from surgeons' perspective, with the improvement of postoperative care, and the development of techniques for Video-Assisted Thoracoscopic

Surgery (VATS), such as single-port and non-intubated approaches, so-called high risk (or medically inoperable) classification should be re-defined for patients undergoing surgical intervention for lung resection. In addition, other factors that may affect the outcomes of "early" stage lung cancer should be re-considered. For example, a new classification proposed by International Association for the Study of Lung Cancer/American Thoracic Society/ European Respiratory Society (IASLC/ATS/ ERS) for lung cancer, radiological appearance and pathological predominate patterns of treated tumor, regardless of pleural invasion…etc. These prognostic factors should also be considered when comparing these two modalities of treatment of early-stage lung cancer.

Stereotactic body radiation therapy for early stage non-small cell

Katsuyuki Karasawa M.D. Phd.

Dept. of Radiology, Tokyo Metro. Cancer and Infectious Diseases Center Komagome Hospital

Stereotactic body radiation therapy (SBRT) can deliver a high enough dose to ablate the tumor while sparing the surrounding tissues. For early stage non-small cell lung cancer (NSCLC), SBRT has been successfully used and many studies demonstrated its superiority over the conventional radiation therapy. Many series reported their 3-year local control rate around 80 to 100% and 3-year overall survival around 50 to 80%, which are not much worse than those of surgical series, with minimal toxicity. Furthermore, several studies are going on to raise the therapeutic ratio. Recently-published report on phase III trials comparing surgery and SBRT revealed that SBRT was superior to surgery for Stage I NSCLC in spite of limited number of the cases. At present, with the development of new techniques, SBRT has, at least, been recommended for elderly and / or high-risk operable patients with Stage I NSCLC.

Immuno-Oncology: New Developments in Solid Tumour therapy

Stefan Glück MD PhD FRCPC

Professor of Medicine,Vice President Global Medical Affairs, Breast, Ovarian, Bladder Cancer and Immuno-Oncology Celgene Corporation, USA

The idea of using the immune system to fight cancer is over 100 years old (Paul Ehrlich's "Magic Bullet") but immunotherapy in solid tumors has been disappointing over the last several decades; new molecular approach led to a better understanding of the immune system. Check point regulation, understanding roles of Tregs, Th1 and Th2, development of CAR-T cells, as well as regulation of DC and Macrophages, led to discovery of inhibitors and modulators that are currently used in studies of several solid tumors. Effcacy in melanoma and lung cancer led to the US FDA approval of a few of these compounds); moreover, interesting and promising results in ovarian cancer and breast cancer (that were previously thought to be less immunogenic) were demonstrated and a number of large clinical trials in many solid tumors and in all phases are underway. We will discuss the MoA, its impact on solid tumors, and some of the early results.

Immuno-oncology: KEY not so far away - Focus on H&N and other emerging indications for immunotherapy

Dr Tanguy Seiwert, USA

Immunotherapy utilizing checkpoint blockade has shown preliminary activity in a wide range of cancers. In this presentation we will examine the effcacy of PD-1 checkpoint blockade in head and neck cancer, including HPV(+) tumors and EBV(+) nasopharyngeal cancers as examples of virally associated cancers, as well as HPV(-) head and neck tumors as an example of activity in many solid tumors. The characteristics of responses to immunotherapy, likely impact on survival, and unique side effect profile will be discussed. Finally I will discuss implications for other cancers, and summarize key characteristics of this emerging treatment modality.

Improving Lung Cancer Outcome in The era of Immunotherapy

Dr. Sumitra Thongprasert

Bangkok Hospital Chiang Mai (BDMS Group) Chiang Mai,Thailand

Immunotherapy destroy cancer cells via the activation of patients' immune system. PD-1(Programmed cell death-1) and the PD-L1(Programmed Death Ligand 1) are the targets of immune treatment to block the tumor via T lymphocytes. Recently FDA had approved two immunotherapy drugs: Nivolumab and Pembrolizumab for the treatment of advanced non- small cell lung cancer. Nivolumab was approved initially for patients with squamous non- small cell lung cancer (NSCLC) who had failed first line chemotherapy and later the approval was expanded to non-squamous NSCLC. Pembrolizumab was also approved to both squamous and non-squamous NSCLC patients with tumors test positive for PD-L1.

Review of the immune mechanism and clinical trials data will be presented.

Checkpoint Inhibition Immunotherapy For Mbladder Cancer:

Dr Fairooz Kabbanivar MD, FACP

Professor of Medicine and Urologic Oncology,

Henry Alvin and Carrie L. Meinhardt Endowed Chair in Kidney Cancer Research, Medical Director GU Oncology Program, In an expanded phase 1 trial with an adaptive design, the safety and activity of atezolizumab, an anti-programmed death-ligand 1 (PD-L1) inhibitor, in metastatic bladder cancer has been reported. Sixty eight patients were treated with an overall response rate of 43 percent for tumors with PD-L1-positive expression on the tumor-infiltrating immune cell.

The potential role of these agents in urothelial carcinoma has been confirmed by the results of a phase II study (Imvigor210), in which 429 patients with metastatic urothelial cancer were treated with atezolizumab. All cohort 2 patients (310 pts) had progressed during or after prior platinum-based chemotherapy. There were 12 complete and 35 partial responses confirmed by central review (objective response rate 15 percent), and an additional 15 unconfirmed responses. The median duration of response had not been reached with a minimum follow-up of 11.7 months, and 38 of 45 responses were ongoing at data cutoff. The response rate was higher in those with increased expression of PD-L1.

Treatment is associated with immune-related adverse events (irAEs) that typically are transient, but occasionally can be severe or fatal. The most common and important irAEs are dermatologic, diarrhea/colitis, hepatotoxicity, and endocrinopathies, although other sites can also be affected.

The current data also underscores the fact that PD-L1 expression is an imperfect surrogate for an "immunogenic" tumor microenvironment that has higher rates of functionally exhausted T cells infiltrating the tumor. At present, PD-L1 and all other candidate biomarkers remain investigational. No patient with an advanced cancer and an established clinical rationale for use of an immune therapy agent should be refused immune therapy on the basis of a lack of PD-L1 expression or any other investigational biomarker

ROLE OF IMMUNOTHERAPY IN mRCC

Dr Fairooz Kabbanivar MD, FACP

Professor of Medicine and Urologic Oncology, Henry Alvin and Carrie L. Meinhardt Endowed Chair in Kidney Cancer Research, Medical Director GU Oncology Program,

The first immunologic intervention in oncology happened in 1891, when the surgeon William Coley reported that an injection of killed bacteria into sites of sarcoma could lead to tumor shrinkage. Since that time, understanding of immune surveillance and tumor growth has led to broad therapeutic advances in treatment strategies of cancers. A number of therapeutic approaches are being studied to harness and redirect the immune system to control malignancy. These approaches include cytokines, T cells (checkpoint inhibitors, agonism of costimulatory receptors), manipulation of T cells, oncolytic viruses, therapies directed at other cell types, and vaccines. Examples of targeting "immune checkpoint" molecules include cytotoxic T-lymphocyte-associated protein 4 (CTLA-4), programmed cell death-1 (PD-1), PD ligand 1 (PDL1) etc. Chronic recognition of an antigen in a malignant state may lead to feedback inhibition of effector T cell function, resulting in a phenotype termed "exhaustion". Tumors can upregulate the expression of immune checkpoint molecules such as PD-1 and PD ligand 1 (PD-L1) that promote peripheral T cell exhaustion. A variety of PD1 And PDL1 inhibitors are in clinics either as FDA approved therapy or in clinical trials. Some examples of anti-PD1 agents are- Nivolumumab, Pembrolizumab and an example of anti- PDL1 drug is Atezolizumab. Yervoy targets the CTLA-4 molecule.

NIVOLUMAB AND CHECKPOINT INHIBITION — Nivolumab is an anti-programmed cell death-1 (PD-1) antibody that has received regulatory approval for patients with advanced melanoma and non-small cell lung cancer based upon a demonstration of improved overall survival. nivolumab improved overall survival compared with everolimus in patients with advanced clear cell renal cell carcinoma who had progressed after prior anti-angiogenic therapy.

In a phase III CheckMate 025 trial, open-label randomized trial of 821 patients with advanced RCC whose disease progressed following prior antiangiogenic therapy, median overall survival (OS) within the intent-to-treat population reached 25.0 months among patients treated with single-agent nivolumab, as compared with 19.6 months among patients treated with single-agent everolimus (hazard ratio [HR] 0.73, 98.5% CI [0.57, 0.93]; $p = 0.0018$). Moreover, the ORR reached 25% with nivolumab versus only 5% with everolimus (odds ratio 5.98, 95% CI [3.68, 9.72]; $p < 0.0001$).

A prespecified analysis of OS and ORR by subgroup revealed that nivolumab confers its benefits across prognostic risk categories, the number and sites of metastases, and prior therapies, consistent with the benefit observed in the overall population of CheckMate 025. Fewer patients had grade 3 or 4 toxicity with nivolumab compared with everolimus (19 versus 37 percent).

Expression of the PD-1 ligand 1 (PD-L1) on tumor cells was not associated with overall survival benefit to nivolumab, and those with ≥1 percent expression and those with <1 percent expression had a similar survival benefit compared with everolimus.

Other anti-PD1/PDL1 agents are also being tested either alone or in combination. Results are pending.

Function preservation Surgery for Hypopharyngeal cancer: State of Art

Dr. Min Sik Kim

Min Sik Kim M.D., Ph.D. Department of Otolaryngology-HNS, The Catholic University of Korea

Usually locally advanced hypopharyngeal cancer needs to take a aggressive treatment such as total laryngopharynectomy followed by chemo-radiation therapy. Especially hypopharyngeal cancer is an aggressive cancer that is generally diagnosed at advanced stages and consequently has a poor prognosis and a low survival rate.

Nowadays the goal of the treatment of these tumors is to cure the patient of the cancer and to preserve or restore useful laryngeal and hypopharyngeal function. However, the need for extensive ablative surgery often coupled with radiotherapy renders many patients incapable of performing the basic human functions of swallowing and speech. Loss of such integral Functions has a dramatically negative effect on a patient's quality of life, which is already Threatened by the aggressive nature of this disease. Therefore, it is imperative to use a reliable reconstructive strategy with low morbidity that will allow the expedient restoration of speech and swallowing.

Pharyngolaryngeal reconstruction remains a challenge for the head and neck surgeon. The most challenging problem in all partial laryngopharyngectomies is glottic insuffciency resulting from partial or subtotal removal of the laryngeal sphincter.

Conservation surgery is rarely considered suitable in locally advanced hypopharyngeal cancer for either oncologic reasons or patient factors, such as inadequate pulmonary reserve and postoperative swallowing disorders. And chemo-radiotherapy takes the role of replacing surgery for the purpose of organ preservation.

Recently new surgical procedures to solve these problems is developed to this stubborn enemy. Extended supracricoid partial laryngectomy and vertical partial laryngopharyngectomy could be an answer for the surgeons for the successful treatment of locally advanced layngopharyngeal cancer. We can revise and introduce the surgical procedures for locally advanced layngopharyngeal cancer with satisfactory oncologic and functional results.

Key word: conservation . surgery. hypopharyngeal cancer

Robotic Surgery for Head and Neck Cancer.

Eun Chang Choi, MD, Ph.D.

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Head and neck tumor is characterized by its diverse origin of tissue with rarity and serious impacts of its treatment on vital function such as breathing, speaking, chewing and swallowing. Third peculiarity is that surgery in this area leaves inevitable disfiguring scar. Although cultural perception of it is different between countries, many efforts of hiding or minimizing unsightly scar on exposed area has long been made.

Recently surgical robot with 3D close-up view and robust harmonic scalpel came into the market. Many head and neck surgeons tried this robot on resection of oral cavity cancer. Trans-oral robotic surgery is widely and rapidly propagating worldwide, but not all esthetic

problem was solved yet, because neck dissection is done separately or simultaneously with classic open surgery. Nodal metastasis is single most important adverse prognostic factor in management of head and neck squamous cell carcinoma.

We designed various approaches of neck dissection with robot. Depending on the neck levels of nodal metastasis, we used modified facelift incision or retro auricular incision. We could extirpate primary tumor and neck node simultaneously without any notable scar in face and neck area. We think this type of neck dissection is technically feasible. This approach was quite useful not only to the young head and neck cancer patients but also to the oral cancer patients who needs microvascular free flap reconstruction

With accumulation of the cases with robot assisted head neck surgery, we hereby suggest the concept of Esthetic Head and Neck Surgery which will be the first step of pulling quality of life of head and neck cancer patients upwards.

Early stage pharyngeal Ca — How to choose appropriate patients?

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Recent advances in technology has urged the introduction of surgical robotics in the field of head and neck surgery and changed the indefinitely. Major applications of robotics in head and neck surgery were transoral robotic surgery (TORS) in laryngopharyngeal cancer, especially oropharyngeal and selected hypopharyngeal and laryngeal cancer. However, TORS would not be indicated in cases with poor exposure of laryngopahryngeal area. Inevitably, other approach such as lateral pharyngotomy should be needed after conventional neck dissection. Recently, we developed and verified the feasibility of the lateral pharyngotomy approach to address the hypopharyngeal/ laryngeal area even after robotic neck dissection via RA approach.

Most lesions in the neck requiring surgical removal, benign or malignant, have traditionally been operated leaving an inevitable scar in the area where it can easily be noticed by others. This could develop displeasing cosmetic results, especially if the operated patient is relatively young, female, or is an active member of his/her society. The social impact may be even worse if a large incisional scar has been created due to neck dissection from cervical metastasis of head and neck cancer. What is more, conventional transcervical operations frequently require large amount of normal tissue dissection just for the purpose of surgical approach which could lead to prolonged postoperative recovery and various degree of functional deterioration.

Therefore, in order to reduce the extent of surgical trauma and consequently reduce associated morbidities including disfiguring large scars, many operative techniques of minimally invasive surgery have been developed and reported. Minimally invasive surgeries incorporating the endoscopy was primarily adopted and popularized in surgical specialties working in natural body cavities such as general, gynecological, urological, orthopedic, and cardiac surgery. The application of endoscopic surgery in the neck was more challenging since the neck is a relatively restricted area bearing intense network of vital neurovascular structures. The robotic thyroidectomy has a distinct difference to other minimally invasive surgeries since it adopts a gasless transaxillary (TA) technique. Conversely, robotic applications to other neck surgeries such as SMG resection or neck dissection via a retroauricular (RA) approach were still in its infancy stage. Based on the initial reports of Terris on robotic facelift thyroidectomy and our extensive surgical experience on TA endoscopic thyroidectomy, we have actively utilized the retroauricular (RA) approach in head and neck surgery and developed many operative techniques of robotic head and neck surgery. We have shown promising results of the universal application of the RA approach. This session will discuss in detail the indication and surgical techniques of lateral pharyngotomy with robotic neck dissection via RA approach as well as TORS in early pharyngeal cancer.

Management of the Carotid Artery in Advanced Head and Neck Cancer

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The carotid artery is invaded in 5% to 10% of advanced head and neck cancer with cervical lymph node metastasis. The management of patients who have advanced head and neck cancer with persistent or recurrent cervical metastasis involving the carotid artery has been controversial and treatment dilemma to the surgeon, given that historically the local control and survival has been dismal and the complications of surgery are high.

Carotid artery invasion is usually assessed by clinical examination, and various imaging modalities have been used to predict tumor attachment to the carotid artery. The height in contact between the adenopathy and CA , the deformity , the circumferential encasement of the CA in degrees, and the obliteration of the fascial plane are radiological features used to predict tumor invasion. When invasion of the CA is suspicious in the imaging modalities, we should evaluate collateral cerebral circulation before surgery.

Previously untreated squamous cell carcinoma with cervical metastasis and carotid involvement may be treated with neoadjuvant chemotherapy or curative chemo radiation before any attempt at surgical extirpation. Frequently, there is a suffcient response to obviate the need for carotid resection and sacrifice of the adjacent structures such as vagus, hypoglossal, or sympathetic nerves. Cancers less responsive to chemotherapy or chemoradiation and nonepithelial origin carcinomas such as adenocarcinoma, adenoid cystic carcinoma, or melanomas are best treated with surgical resection, intraoperative radiotherapy, and/or postoperative radiation or chemoradiation. The heavy burden of deciding to resect the carotid artery involved with advanced or recurrent cancer should be balanced against the natural history of the disease process if not it is treated. It is not only a heavy burden for the head and neck surgeons but also for the patients and the families, so it requires detailed understanding by the patient and family. And it is also dependent on the surgeon's philosophy and skills as well as the patient's desire and fortitude.

If surgical resection is contemplated, careful planning by the surgeon to determine the collateral cerebral perfusion as well as coordination among the interventional radiologist, anesthesiologist, and radiation oncologist are essential to provide the patient the optimal chance of survival without cerebrovascular complications.

This presentation will review recent reports of the surgical management of the carotid artery when cancer is adherent to it and will highlight the author's experience at the Hallym University, College of Medicine.

Key word: conservation . surgery. hypopharyngeal cancer

Gastric Cancer in Asian Countries : Epidemiology and Challenges

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Despite its declining incidence, gastric cancer remains the fourth most common cancer worldwide. The epidemiologic studies reported that there is ethnic difference in tumor biology, behavior, and host-tumor interaction. As a consequence, there was difference in mortality, effcacy and safety of treatment, and survival outcome.

From several epidemiologic studies, gastric cancer in Asian ethnicity compared to non-Asian counterpart showed under mentioned findings on clinical manifestations of gastric cancer. Asian patients were younger and had a greater proportion of signet ring cell histology and diffuse type histology according to Lauren classification. Many Asian trials also reported a lower percentage of gastroesophageal junctional carcinoma. Asian-specific Helicobacter pylori and genetic polymorphisms may play a role in unique characteristics of Asian gastric cancer.

Difference in effcacy and safety of treatment and survival was reported previously. Survival outcome was superior in Asian patient with gastric cancer. The choice of treatment modalities differs significantly between Asian and non-Asian trials. A meta-analysis reviewed the impact of potential difference in patient characteristics and treatment patterns on safety and effcacy reported by gastric cancer clinical trials. Effcacy of each chemotherapeutic regimen was different from ethnic group. Asian trials reported significantly more common use of second line chemotherapy and lower incidence of grade 3-4 toxicity. Pharmacogenetic differences in drug targets and drug-metabolizing enzyme may be found to explain the different results according to ethnicity.

Consequently, future clinical trials of gastric cancer should consider the ethnicity as a stratification factor to control potential bias. It is needed that future international clinical trials should incorporate more detailed biomarker and pharmacogenetic studies to explore the optimal regimens for different ethnic groups.

Keywords: Ethnicity, Gastric cancer, Pharmacogenomics

New targeted Therapies in Gastric Cancers

Dr. Yeul Hong KIM

It is increasingly recognized that gastric cancer is a heterogeneous disease which may be divided into subgroups based on histological, anatomical, epidemiological and molecular classifications. Distinct molecular drivers and tumor biology, and thus different treatment targets and predictive biomarkers, may be implicated in each subtype.

For patients with advanced gastric cancer, traditional double or triplet cytotoxic chemotherapy regimens result in a median survival of 9-11 months. As combination therapy is associated with increased survival, but also increased toxicity in a patient population whose performance status often compromised by their malignancy, development of more effective and less toxic treatment choices is mandated. Emerging data from gene expression profiling suggests that differences in pathological appearance and clinical behavior may be due the presence of unique molecular phenotypes. Treatment of HER2 positive gastric cancer with trastuzumab has led to significant gains in overall survival, and further manipulation of this pathway using the novel anti-HER2 directed agent's pertuzumab and T-DM1. In contrast, targeting of the EGFR pathway in combination with chemotherapy in unselected patients has not been fruitful to date, with no significant gains over standard chemotherapy yet demonstrated. Similarly, use of the anti-angiogenic monoclonal antibody bevacizumab was not successful in a large global randomized trial; however selective inhibition of VEGFR2 with ramucirumab was beneficial either alone or combined with paclitaxel in 2nd line setting. Careful selection of patient subsets will become a key factor in future clinical trials, as novel targeted agents such as those targeting the MET/HGF and FGFR

Non-operative strategies for HCC: Improvement of Therapeutic Outcome by Multimodal Approach Involving Radiotherapy

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Management of hepatocellular carcinoma (HCC) has been complex and much varied by new emerging treatment modalities. However, main stream of therapeutic decision is relatively well kept according to the HCC treatment guidelines. While the guidelines from Barcelona Liver Cancer Clinic (BCLC) as well as from National Comprehensive Cancer Network (NCCN) are serving as main ones, Korean Liver Cancer Study Group has made Korean HCC guideline with recent update in 2014.

BCLC system clearly defines treatment modality that can be recommended in each stage; potentially curative therapies for HCC are well established for early stages and sorafenib for advanced stage. Radiotherapy is not included in this guideline. However, there are a plenty of occasion, in which clinical outcome can be further improved with radiotherapy in each subset of BCLC stages. Radiotherapy can either be complementary to weakness of BCLC-recommended treatment or be effective as alone. This notion is well reflected in other guidelines. In NCCN guideline, combination treatment of RT and chemotherapy is recommended either in unresectable but not a transplant candidate or in inoperable local disease. According to the Korean Liver Cancer Study Group (KLCSG) practice guidelines, radiation therapy is considered for unresectable, locally advanced HCC without extrahepatic metastasis, Child-Pugh class A or B, tumors occupying less than two-thirds of the total liver volume, and V30Gy (percentage of liver volume that received a dose of 30 Gy or more) of less than 60% of whole liver.

Current radiotherapy technology has evolved remarkably during the past decade. It can be precisely delivered, thereby permitting higher doses to the tumor and reduced doses to surrounding normal tissues. Based on accumulated experiences and evidences, importance of radiotherapy is recognized more widely and increasing number of institutes apply radiotherapy in clinic. Radiotherapeutic strategies will be further discussed according to each clinical setting for patients with HCC.

Key Words: Radiotherapy, Hepatocellular carcinoma

Intensity-modulated radiation therapy for Squamous Cell Carcinoma of the Anal Canal

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Squamous cell carcinoma of the anal canalll!has been reported to be radiosensitive as well as chemosensitive. Old study demonstrated that high pathological complete response rate of the resected specimen would be expected when concurrent chemoradiotherapy (CCRT) was used preoperatively. Because the loss of anus would highly jeopardize the patient's quality of life, CCRT has become the standard of care in western countries. And the standard chemotherapeutic regimen has been 5-FU and mitomycin C. To draw the target volumes, it is important to include inguinal regions as the clinical target volume as well as pelvic lymph nodes because of the lymph drainage in the anal region. As the results, the planning target volume becomes concave shape requiring intensity-modulated radiation therapy (IMRT) to decrease the intestinal dose within the pelvis. By using IMRT technique, RTOG-0529 study revealed the less intestinal toxicity compared with the previous study using only 3-dimensional conformal radiation therapy.

Comparative cancer CAM Modalities, Interventions and Analysis in Asia

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Traditional medicine (TM) is widely used in the countries of Southeast Asia including India, China, Japan and Korea. Southeast Asian CAM therapies in different countries have many commonalities and share similar practices, botanical sources, remedies and medical applications. The program on Comparative Cancer CAM Modalities, Interventions and Analysis in Asia will bring together scientists and clinicians from India, China, Japan, Korea and the U.S. to discuss their work and share their experience.

The program: The program includes several sessions.

The first, Analytical Approaches and Challenges for CAM Material Analysis, will feature discussions about bio-analytical approaches for complex natural materials, research resources to promote cancer research with CAM, and DNA-based identification of TM material. These topics are important to chemical characterization, validation and annotation of herbal mixtures with the goal of improving their safety, consistency and standardization.

The second session, Comparative Cancer CAM Modalities and Interventions, aims to compare traditional medicine approaches, philosophies and practices in India, China, Korea and Japan. The session includes talks on molecular mechanisms, formulation of TM material for cancer treatment, symptom control and prognosis improvement, and combination TM therapy and Western medicine.

Goals: The goal of this program is to foster regional cooperation and exchange of knowledge, through the developing of research collaborations, training opportunities, and access to botanical sources, with the aim of improving public health in the region.

Funding opportunity: A funding opportunity (RFA-CA-15-007) to support the planning of regional cooperation efforts and the establishment of Centers of Research Excellence in Non-Communicable Diseases in Low and Middle Income Countries was recently issued by the U.S. National Cancer Institute http://grants.nih.gov/grants/guide/rfa-files/RFA-CA-15-007.html

NCI Developmental Therapeutics Program: Providing resources to promote cancer research worldwide

Min He*, Jerry M. Collins

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The Developmental Therapeutics Program (DTP) at National Cancer Institute provides resources to the academic and private-sector research communities worldwide to facilitate the discovery and pre-clinical development of new cancer therapeutics. Since its inception in 1955 by the US Congress, DTP has contributed to the development of more than 40 FDA-approved anti-cancer agents through extensive collaborations with academic and industrial researchers, including some well-known natural product agents such as Paclitaxel, Romidepsin and Eribulin. This presentation will focus on the unique research materials, tools and services provided by DTP to the cancer researchers around the world, as well as the various routes to access different categories of resources. Successful stories of the development of several anti-cancer agents will also be presented to highlight the indispensable roles of DTP in advancing candidate therapeutics into clinical evaluation, particularly the drug leads derived from natural sources.

Bio-analytical Approaches for Complex Natural Materials

Prof James B McAlpine

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Herbal preparations are widely used in Europe and the Americas and make up the bulk of Ayurvedic, Kampo and Traditional Chinese Medicines. However standardization and quality control of these represents a major problem. Even if it starts with a correct definition of the species used, the content can vary significantly depending on the geographic and geologic specific collection site and on the seasonal climatic variation. Hence, as well as identifying the species, and collecting information on its traceability, it is necessary to standardize the extraction procedure and then analyze, both qualitatively and quantitatively, the metabolites in the produced extracts, and in the final products. The biosynthetic nature of secondary metabolites assures that even heavily purified extracts will comprise considerable residual complexity, moreover the preparations of most Traditional Medicines does not encompass extensive purification to individual constituents. These factors make epidemiological studies of the true effcacy of herbal preparations almost impossible. Two top-selling herbals in the US will be examined in detail and exemplify the variety of bio-analytical procedures that are necessary to obtain scientifically sound characterization.

Korean medicine: Molecular targeting and mechanisms in The Development of New Anticancer herbal medicinal product (Sh003)

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Cancer inflammation promotes cancer progression, resulting in a high risk of cancer and tumor angiogenesis is a key feature of cancer progression, because a tumor requires abundant oxygen and nutrition to grow. Here, we demonstrate that our new herbal extract, SH003, suppresses both tumor growth and metastasis of MDA-MB-231 breast cancer cells via inhibiting STAT3-IL-6 signaling path and represses VEGF-induced tumor angiogenesis both in vitro and in vivo. Our new herbal formula, SH003, suppressed MDA-MB-231 tumor growth and lung metastasis in vivo and reduced the viability and metastatic abilities of MDA-MB-231 cells in vitro. Furthermore, SH003 inhibited STAT3 activation, which resulted in a reduction of IL-6 production. SH003 inhibited VEGF-induced migration, invasion and tube formation in human umbilical vein endothelial cells (HUVEC) with no effect on the proliferation. SH003 reduced CD31-positive vessel numbers in tumor tissues and retarded tumor growth in our xenograft mouse tumor model, while SH003 did not affect pancreatic tumor cell viability. Consistently, SH003 inhibited VEGF-stimulated vascular permeability in ears and back skins. Moreover, SH003 inhibited VEGF-induced VEGFR2-dependent signaling by blocking VEGF binding to VEGFR2. Therefore, our data conclude that SH003 suppresses highly metastatic breast cancer growth and metastasis by inhibiting STAT3-IL-6 signaling path and represses tumor angiogenesis by inhibiting VEGF-induced VEGFR2 activation, and suggest that SH003 may be useful for treating cancer.

High sensitivity assessment of tumor response using a novel functional assay

Dr. Eric K. Rowinsky, M.D

Chief Medical Officer, Mitra Biotech, Executive Chairman and President of RGenix, Inc., Board of Directors of Navidea, Fortress Biotech, and Biogen Inc., Ex. CMO & Head of Development at ImClone Systems, Inc., Ex. CMO & Head of Research & Development at Stemline Therapeutics, Inc

Predicting clinical response to anticancer drugs remains a major challenge in the management of cancer. Recent advances show that tumor microenvironment (TME) and heterogeneity impact therapy outcomes; indicating the limitations of biomarker-guided strategies for personalizing therapy. There is a need for platforms that can predict treatment outcome with high fidelity by contextually integrating tumor heterogeneity and phenocopying the TME.

Methods: Tumor grade-matched matrix support and autologous sera from individual patients were used to engineer personalized Tumor Ecosystems (CANScript™) in head and neck, breast and colorectal cancers. We evaluated functional outcomes as a measure of response to a panel of anticancer drugs in this platform. In the training data set obtained from a cohort of patients. CANScript™ read-outs were integrated with their corresponding clinical outcomes for generation of a machine learning (M-score) algorithm to predict clinical response to these drugs. This algorithm was further validated in a test group of new patients.

Results: Histopathological and molecular characterization of the tumor slices cultured in CANScript™ revealed a close approximation to the parental tumor at baseline as confirmed by Ki-67 and critical phosphoproteomic status, global transcriptomic profiles and balance in active components of tumor and stromal phenotypes. The M-score algorithm when applied to the test cohort of more than 100 patient tumors assessed in the functional CANScript™ achieved 100% sensitivity while keeping specificity in a desired high range for predicting short term clinical outcome.

Recent Trends in the Management of Childhood Acute Lymphoblastic Leukaemia Li Chi-kong, Prince of Wales Hospital

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There is marked improvement in the treatment outcome of childhood acute lymphoblastic leukaemia (ALL) in the past few decades, the survival rates reported by various western collaborative groups are in the range of 90%. The

improvement is contributed by better stratification according to biological features and the optimal treatment intensity of chemotherapy regimens. Treatment related morbidity still happens in some survivors including cardiac, skeletal and neurological sequelae. Second malignancy is an emerging problem with longer follow-up of the survivors. Reducing treatment burden in low risk patients can now be achieved by identification of good early responders who have excellent prognosis with less intensive treatment. Genetic markers such as hyperdiploidy and TEL/AML1 are well known to have good prognosis and happened in about 40-45% of ALL. Minimal residual disease (MRD) monitoring is found to be another powerful tool to differentiate good and poor outcome after initial treatment for first 1-2 months. Patients with rapid clearance of MRD can be managed with less intensive protocol, while less favourable responders require upstage of treatment intensity to prevent relapse. Neurological complication is not uncommon in ALL survivors especially those who received cranial irradiation. The effective systemic chemotherapy and intrathecal chemotherapy can virtually eliminate irradiation in nearly all ALL patients. The late complication of brain tumour is now markedly reduced after avoidance of cranial irradiation, and the neurocognitive function of non-irradiated survivors also appears improved. Pharmacogenomics also plays important role in management of treatment complication, the recently identified NUDT15 mutation causing more severe marrow suppression after chemotherapy is more common in Asia population. The 10-20% of poor prognostic subgroups included infant ALL with MLL rearrangement, the Ph-like positive patients and high MRD after initial treatment. Ph chromosome positive patients can now be treated with TKI in combination with chemotherapy, and the result appears encouraging. The Ph-like ALL may benefit from target therapy of kinase inhibitor such as dasatinib and JAK2 inhibitor. Allogeneic stem cell transplant is now much less frequently applied to ALL in first complete remission. Relapsed ALL may also be salvaged with second course of chemotherapy. However very early relapse ALL (less than 30 months from diagnosis) still fares poorly with chemotherapy and allogeneic SCT is indicated. With high cure rate and more long term survivors, the objective of treatment of ALL is now to achieve a high cure rate with normal quality of life in the survivors.

Current Concepts in Radiotherapy for Pediatric Medulloblastoma and Ependymoma

Yavuz Anacak

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From the view of a radiation oncologist medulloblastoma and ependymoma in children are among the most challenging malignancies to deal with. Unlike other CNS tumors ependymoma and especially medulloblastoma has a strong potential to disseminate through CSF, and in some cases distant metastases to other organs can occur as well. Medulloblastoma cells are quite sensitive to radiation. Long-term survival after surgery and postoperative radiotherapy is higher than 80% in those without CSF dissemination. The risk for CSF dissemination necessitates treatment with craniospinal irradiation (CSI) in all patients with a diagnosis of medulloblastoma which is absolutely one of the most sophisticated radiotherapy techniques. CSI is the irradiation of the all CSF bearing areas including brain, whole spine and retroorbital structures. Irradiating such a long field with variable thickness is extremely diffcult and needs meticulous planning. Multiple neighboring fields are required to cover the whole CSF volume, which creates hot and cold spots along the irradiation volume. Patient stabilization during the treatment is extremely important and since many patients are younger than 5 years old daily anesthesia or sedation is required to keep the child stable during the treatment, thus a good coordination with the anesthesiology department is essential. Radiation is toxic to living tissues, radiation doses of higher than 60 Gy to brain and 45 Gy to spinal cord may result in irreversible damage to neurological tissues. All efforts should be spent to keep the radiation doses lower than the limits while keeping the prescribed target doses which are 54 Gy to posterior fossa, 36 Gy to whole cranium and 23.4 Gy to spinal cord if chemotherapy is used. Spinal cord dose should be 36 Gy in case of disseminated disease and in those patients in whom no chemotherapy was given. Serious neurological problems are rare with these doses however growth retardation due to irradiation of hypophysis and vertebral bodies is frequent, which is presented by short stature. Almost all kind of endocrine insuffciency may develop. Current research in the radiotherapy of medulloblastoma focuses on reducing the late effects of radiotherapy by keeping the spinal cord dose to down to 18 Gy and using smaller fields to cover primary tumor of the posterior fossa.

Ependymoma is another interesting tumor which behaves unpredictable in many cases. Ependymomas have a range of histologic variations ranging from rather benign spinal myxopapillary ependymoma to highly aggressive anaplastic ependymoma. Once all ependymomas were treated with CSI, however currently typical ependymomas are irradiated only to cover the posterior fossa and CSI is reserved for anaplastic ependymomas and in case of CSF dissemination. Long-term survival with surgery followed by posterior fossa irradiation is higher than 80% in ependymomas confined to posterior fossa unfortunately survival is much lower in anaplastic histology despite CSI.

Advanced treatment techniques using intensity modulated radiation therapy (IMRT), volumetric arc therapy (VMAT) proton therapy, stereotactic radiotherapy (SBRT) and radiosurgery may further reduce the radiation doses to brain and spinal cord, and help to reduce the frequency and intensity of the late radiation effects.

Pancreatic Cancer: Challenging the Status Quo

Sushovan Guha, MD, PhD

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Pancreatic ductal adenocarcinoma (PDAC) or pancreatic cancer is one of the rarest gastrointestinal (GI) cancers not only in US but also worldwide. The estimated new cases of PDAC that will be diagnosed in US this year is approximately 53,070 (out of a total 1,685,210 new cancers; 3%). Compared to this the incidence of PDAC in India is very low. The age- standardized incidence rates of PDAC in India were 0.8-1.4 (1993-1997) and 0.5-2.4 (1988- 1992). However, the trend of identifying new PDAC in India is slowly going up. Despite the fact that it is one of the most uncommon cancers detected, the mortality rate is one of the highest. PDAC is one of the deadliest cancers with 5-year survival rate around 8% in US (2005-2011). In this year, estimated 41,780 deaths (out of total 595,690; 7%) will be reported from PDAC in US. One of the major reasons for this devastating statistics is that the cancer is rarely detected at an early (and possible resectable) stage. There are no early symptoms or signs in majority of patients who are diagnosed with PDAC. Also, environmental risk factors including smoking and chronic alcohol intake account for only a small fraction of patients diagnosed with PDAC. A strong family history of PDAC is identified in <10% of cases. Certain clinical conditions including chronic pancreatitis, hereditary pancreatitis and other genetic syndromes including Peutz-Jeghers can promote development of PDAC but these conditions are extremely uncommon. Hence majority of PDAC develop from sporadic genetic mutations in elderly individuals with age being considered as a major risk factor. Recently, Bailey et al as part of ICGC (International Cancer Genome Consortium) published (Nature, 2016) a detailed molecular subtypes of PDAC (squamous, ADEX, pancreatic progenitor and immunogenic) that expanded on earlier phenotypes proposed by Collison et al (Nature Medicine, 2011). One of the major reasons for poor survival of PDAC patients even after late diagnosis is intransigence to conventional chemotherapy or radiotherapy. The latter is most likely due to significant heterogeneity of PDAC at the molecular level as noted in these studies. Based on recent findings, hopefully personalized clinical trials can be instituted to target variegated molecular phenotypes of PDAC. But to create a dent to the dismal survival rate of PDAC, one needs to diagnose it early. Only 10-20% of PDAC cases are deemed resectable and 5-year survival rate has been 30% or higher in some centers in US. This presentation will touch upon the latest algorithm to diagnose early PDAC with special emphasis given to the high-risk groups. Our goal is to learn the benefits and risks of imaging-based screening high-risk individuals for PDAC so that it can be applied to general population. However, for population- based screening individuals >50 years of age, one needs to develop biomarkers-based simple diagnostic tests that can be used as an initial filter before proceeding with more invasive imaging studies. In this presentation, few of these diagnostic tests will be emphasized. In conclusion, this presentation will highlight that although PDAC is an uncommon deadly GI cancer, quite heterogeneous at molecular level and refractory to chemotherapy and radiotherapy yet recent imaging techniques coupled with advanced biomarker studies offer a ray of hope for early diagnosis and personalized cancer therapy for this disease.

Journal of Carcinogenesis

INVITED LECTURES ABSTRACTS

35th Annual Convention of Indian Association for Cancer Research Cancer in Asia: Bridging The Gaps

Insights into Novel Oncogenic Mechanisms of Human Papillomavirus

Dr. Alo Nag

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High risk-Human Papillomavirusis acclaimed to be the major causative agent of cervical cancer, a devastating disease with significant morbidity worldwide. In India, cervical cancer remains the major cause of cancer mortality among women. Till date, there exists no specific treatment for curing HPV infections. Lack of mechanism-based treatment strategies due to poor understanding of the HPV-induced malignant transformation machinery is a matter of great concern and utmost importance. Our study aims at catering to the need of the time by revealingsome of the key molecular mechanisms that contributes to HPV oncogenesis that can be utilized to discover promising anti-cancer molecules. We explored some of the novel targets of E6 and E7 and delineated the oncogenic connections.Our study proposes a possible mechanistic basis for HPV pathogenesis by identifying HPV16E6 mediated SUMOylation of hADA3 (a transcriptional coactivator) as the most likely cause of its downregulation in cervical cancer cells and thus, leading to oncogenesis.

In another study, we investigated the mechanism for aberrant expression of the oncogenic transcription factor, FoxM1 cervical cancer. In this work, we report that SUMOylation contributes to destabilization and nucleocytoplasmic shuttling of FOXM1b protein. We highlighted the biochemical mechanism that HPV employs to induce malignancy.Our work also shows how HPV oncoproteins attack the cellular SUMO machinery and wins the battle by manipulating key enzymes. Altogether, these studies shed light on mechanistic aspects of HPV pathogenesis and are important for development of more rationalized anti-cancer modalities.

Nuclear Receptors and Cancer Pharmacology

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Resistance to chemotherapy offers limitations to the treatment of breast cancer. This has generated an increased interest in identifying new biomarkers to better predict drug responses among patients. Gene expression analysis and immuno-histochemistry profiling of patient samples, randomized to a combination of docetaxel and doxorubicin, revealed a chemotherapy induced decrease in DP103 expression among responders, and an increase among non-responders. These clinical findings were also validated in-vitro, using representative cell lines to mimic responders, and their corresponding drug resistant subtypes as non-responders. Upon stratification by the receptor status, the predictive value of DP103 was only observed in patient samples and cell lines with ERα-positive status and not with ERα-negative status. The observed changes in DP103 expression was well correlated to a similar drug induced change in the expression of ERα; raising a possibility of a cross-talk between DP103 and ERα. ChIP-Seq analysis and estradiol-stimulation studies validated DP103 to be an estrogen-inducible gene. Interestingly, DP103 was also indentified as a potential modulator of ERα transcriptional activity. Silencing DP103 inhibited estradiol- induced ERα DNA-binding activity, expression of ERα target genes, cell growth and colony forming ability. These findings summarise a novel role of DP103 in acquired drug resistance; presenting a potential surrogate biomarker for predicting drug response in breast cancer. In addition, we have also uncovered a positive feed-forward loop between DP103 and ERα that could regulate the activity of the latter in ERα positive breast cancer.

HPV Viral Oncoproteins: Role beyond Cervical Cancer Initiation and Progression

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Persistent infection of high risk HPV is causally linked to the development of cervical cancer.Several molecular clinico-epidemiological studies demonstrate presence of the virus all stages of disease progression irrespective of is clinical stage. E6 and E7 oncoproteins encoded by HPV are essential for the transformation of cells in initial stage of cervical cancer. However, the pathophysiological relevance of the HPV infection in advance stage of cervical cancer remained poorly understood. Using established cervical cancer cell lines that differed with respect to their HPV status, we investigated the functional contribution of HPV in maintenance of a subset of tumorigenic cancer stem-like cells and associated signaling that contribute to chemoresistance and is eventually responsible for tumor recurrence. We identified and isolated cervical cancer stem-like cells (CaCxSLC) from HPV-positive cervical cancer cells using sequential gating strategies. Our findings indicate differential expression of E6in CaCxSLC is essential for their maintenance. Further, a 5-FU resistant chemoresistance cell lines, SiHaCR was developed whichdemonstrated differentially higher expression of HPV oncoproteins E6.Our data suggest an important functional contribution from HPVE6 in manifestation of EMT, a key event that promotechemoresistance. Moreover, HPV oncoprotein E6 showed cooperative interaction with the hedgehog signaling, by coactivating GLI1. Inhibition of both HPV E6 and GLI showed strong additive anti-cancer effects which can specifically targeted cancer stem-like cells. Overall, studies conducted by our group demonstrate a key role of viral oncoprotein E6 in behavior of tumors in advance stages of cervical cancer progression.

Potential Diagnostic Biomarkers for the early detection of Urothelial Carcinoma of Bladder

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Urothelial carcinoma of bladder (UBC) is the fourth most common cancer in men and ninth most common cancer in women. Currently the gold standard for detecting bladder cancer is cystoscopic examination, but this analysis is costly, causes discomfort to the patient (invasive method) and has variable sensitivity especially in cases of low-grade carcinoma. Identification of key non-invasive biomarkers from the plethora of molecules, intra-cellular and/or inter-cellular is one of the major areas of research worldwide. Interactions between tumor cells and the extracellular matrix (ECM) are found to be associated with promotion of cell motility, adhesion, migration and metastasis. Our lab is actively engaged in defining potential candidate biomarkers that include ECM molecules, cytoplasmic elements as well as key immunological factors that is linked with tumor growth and metastasis in UBC.

We have evaluated the usefulness of some important molecule as a diagnostic marker in UBC, such as, CD147, a transmembrane glycoprotein that triggers the production or release of matrix metalloproteinases for tumor invasion. BIGH3, an ECM protein that binds to type I, II and IV collagen and helps in cell growth and differentiation. Stathmin, an important cytosolic protein that regulates microtubule dynamics. Correlation with tumor grade has been done for CD147, BIGH3 and Stathmin and it has been found that the urinary levels of CD147 and serum STMN1 concentration showed a specific increase as compared to the controls, while BIGH3 was elevated in both serum and urine samples. Molecular (mRNA) expression was elevated in the high grade (Muscle Invasive) stage of the disease for all these molecules, with a significant 3-fold increase that correlated with disease severity being observed for STMN1. To observe the anti-tumor effects of Small Leucine Rich Proteoglycans (SLRPs), expression study of Decorin, Biglycan and Lumican has been done in UBC and it has been found that circulatory levels of biglycan and lumican were significantly higher in the patient group whereas it was reduced in case of decorin. Molecular expression and IHC (Immunohistochemistry) showed significantly higher biglycan expression and significantly reduced decorin expression in patients. Elevated expression of ECM proteins Laminin (a proteoglycan and class II member of the SLRPs that is involved in collagen fibril organization) and Nidogen (a matrix protein of basement membrane) have also been observed in UBC patients that might indicate the interplay between these molecules with tumor development & metastasis and could be utilized as potential biomarker.

We are also studying the potential members of immune microenvironment of tumor for the prognostic signature cells during tumor growth. Disproportion of Th1/Th2 cytokines with the predominance of Th2 cytokines has been observed in UBC patients. Our recent observation shows involvement of Th17 cells in immunopathogenesis of UBC patients where increased circulatory levels and tissue specific expression of Th17 related cytokines (i.e. IL-17, IL-22, IL- 23 & IL-6) and transcription factor (RORγt)was observed.

An important observation indicated that urinary CYFRA 21-1 (a cytokeratin-19 fragment that is soluble in serum and may be a useful circulating non-invasive tumor marker) provides a high value of overall sensitivity for UC of bladder and is also useful even for detection of low grade tumors that might indicate possible earlier detection and treatment administration.

A bridge from bench-to-bedside: Development of cancer therapy for Reproductive tract cancer

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Women's reproductive health is challenged by several problems, such as unwanted pregnancies, communicable diseases and gynaecological malignancies. Cervical cancer is one of the world's deadliest forms of cancer in women, responsible for more than 2.5 million deaths annually, 85% of which occur in developing countries (WHO report, 2014). Cervical cancer is one of the major concerns especially in developing countries like India because of lack of proper medical infrastructure and limited awareness associated with low socio- economic status. As part of the comprehensive approach to improve the women's reproductive health, cervical cancer effective therapy is of utmost importance. Our aim is to advance in cancer medical research and improve patient outcomes by discovering novel biomarkers (for early detection and diagnosis, prediction, and prognosis) and immunotherapeutic targets for reproductive tract cancer. In this context, past one decade we have extensively worked on a tumour associated antigen designated as Sperm associated antigen 9 (SPAG9) and shown its association with reproductive tract malignancies and various other cancers. On the basis of SPAG9 expression profile and immunogenic nature, recombinant SPAG9 protein will be used in Phase II clinical trial study: "Cancer immunotherapy dendritic cell vaccine based immunotherapy in cervical cancer-A phase II, double blind, randomized, three arm study to evaluate the efficacy of dendritic cell vaccine in stage IIB cervical cancer (n=54 patients)" to improve the women's reproductive health. "Our work would thus help in improving overall public health and economic benefit across countries. Our findings have opened up new avenues for novel treatment modalities in battling with this deadly disease worldwide for treating cervical cancer patients for better Reproductive Health". If successful, this will be the first molecule identified from India and will be an example of Translational Medicine Research of clinical relevance for "global reproductive health for all".

Acknowledgement: Contribution, Linkages with Hospitals and partnership with research

organizations: Dr. T. Rajkumar, Head Medical Oncologist, Cancer Instiute (WIA), Chennai, Dr. P.K. Julka, Head, Department of Radiotherapy, IRCH, Dr. G.K. Rath, Director, IRCH, Dr.Rajive Kumar, Head, Hematology oncology Laboratory IRCH, Dr. D. Pandey, Surgical Oncologist, AIIMS, Dr. Amlesh Seth, Onco-Urology, AIIMS, Dr. AlokThakar, Otolaryngology (Head and Neck) AIIMS, Dr. GovindMakharia, Department of Gastroenterology and Human Nutriton, AIIMS, Dr.Vaishali Suri, Department of Pathology, AIIMS, Dr. Ashish Suri, Department of Neurosurgery, AIIMS,Dr. Arvind Chaturvedi, Department of Neurosurgery, AIIMS, Dr. Anju Gupta, Head of Pathology, VIMHANS Hospital, Dr. Amar Bhatnagar, Surgical Oncologist, Safdarjung Hospital, Dr.ArunaBatra, Head, Obstetrics and Gynecology, Safdarjung Hospital, Dr. T. C. Sadasukhi, Department of Urology, Mahatma Gandhi Hospital, Jaipur, Prof. N. K. Lohiya, Centre for Advanced Studies, Jaipur.

Funding; Grant support from Cancer Research Program, Centre of Molecular Medicine,

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Precocious anaphase and expression of Securin and p53 genes as candidate biomarkers for the early detection in areca-nut induced carcinogenesis

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Research over the years has generated enough evidence to implicate areca-nut, as a carcinogen in humans. Besides oral, significant rise in the incidence of cancers of the esophagous, liver and stomach were seen among areca-nut-chewers, although associated genomic changes remain unclear. Early-stage of these cancers is highly curable and therefore, early diagnosis seems key. In North-East India,betel-quid contains raw areca-nut (RAN), lime and small portion of betel-leaf without any other

constituents.This study was not intended to isolate any active ingredients from the RAN and to look its action. The present objectiveis to validate the screening of precocious anaphase and analysis of expression of Securin and p53 in non-target cells like human peripheral blood lymphocytes (PBL) and mouse bone marrow cells (BMC) as early indicative parameters ofRAN+lime induced cancers and also see the involvement of CDKN2A and Rb1 genes in oral and esophageal cancers. The data indicate that the disruption of 9p21 where CDKN2A gene resides, is the most frequent critical genetic event in RAN-associated carcinogenesis. The involvement of 9p23as well as 13q14.2 could be required in later stages in RAN-associated carcinogenesis. A total of 35 mice were examined at different time points for following ad libitum administration of RAN-extract in drinking water with lime. Peripheral blood was collected from 32 human donors of which, 24 were RAN+lime heavy-chewers. Expression of genes was assessed by immunoblotting and/or by immuno-histochemistry. Histological preparation of stomach tissue of mice revealed that RAN+lime induced stomach cancer. A gradual increase in the frequency of precocious anaphases and aneuploid cells was observed in both RAN+lime treated mouse BMC and human PBL of RAN heavy-chewers. Levels of p53 and Securin were increased in these cells during early days of RAN+lime exposure. The level of Securin was significantly higher in human tumor samples than their adjacent normal counterpart. The expression of Securin was increased significantly in RAN+lime administered mice as well as in stomach tumor. Present study revealed that precocious anaphase and expression of p53 and Securin in non-target cells are significantly associated with an increased risk of RAN-induced cancer and thus these parameters can be of early diagnostic value.

Assessment of mitochondrial genome copy numbers and integrity in pediatric leukemias

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ONCOTARGETING: Molecular Strategies for Inhibiting Growth and Metastasis of Breast Cancer

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Tumor angiogenesis and dysregulation of apoptosis contributes to the pathophysiology of breast cancer.Neo angiogenesis “feed” growing tumors with oxygen and nutrients, allowing the cancer metastases. A variety of defects in the apoptotic machinery contribute to avoidance of apoptosis by tumor cells throughout the entire carcinogenic process. In breast cancer, tumor regression induced by chemotherapy, radiotherapy, and hormone therapy depends to a large extent on the induction of apoptosis. To block tumor angiogenesis and induce tumor cell apoptosis, we have developed immunoliposomes targeting breast cancer cells that overexpress VEGF and angiopoietin receptors. We havecloned and expressed human recombinant Flt-1 and Tie-2, the soluble receptors for VEGF and angiopoietin ligands and have validated their anti angiogenic activity using pre- clinical in vivo and xenograft model systems. Using polarity –based fractionation and activity guided purification, T1 and A1 molecules from T.cordifolia and A.occidentale were purified and structurally characterized. Both T1 and A1 had antiangiogenic and pro apoptotic activity as assessed by in vitro, cell-based and in vivo assays. Further these novel plant derived molecules sensitized radio or chemo, or TRAIL-resistant cells to TRAIL-induced apoptotic death. Recombinant sFlt-1 and/or TRAIL and sTie2 and/or TRAIL weretagged to PEG- maleimide liposomes encapsulated with either T1 or A1. Anti-angiogenic and pro-apoptotic activity of these liposomes were evaluated both in cell based and xenograft models using triple negative breast cancer cells. These imunoliposomes will have immense application in targeted therapy of breast and other cancers in clinics.

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Tumor angiogenesis and dysregulation of apoptosis contributes to the pathophysiology of breast cancer.Neo angiogenesis “feed” growing tumors with oxygen and nutrients, allowing the cancer metastases. A variety of defects in the apoptotic machinery contribute to avoidance of apoptosis by tumor cells throughout the entire carcinogenic process. In breast cancer, tumor regression induced by chemotherapy, radiotherapy, and hormone therapy depends to a large extent on the induction of apoptosis. To block tumor angiogenesis and induce tumor cell apoptosis, we have developed immunoliposomes targeting breast cancer cells that overexpress VEGF and angiopoietin receptors. We havecloned and expressed human recombinant Flt-1 and Tie-2, the soluble receptors for VEGF and angiopoietin ligands and have validated their anti angiogenic activity using pre- clinical in vivo and xenograft model systems. Using polarity –based fractionation and activity guided purification, T1 and A1 molecules from T.cordifolia and A.occidentale were purified and structurally characterized. Both T1 and A1 had antiangiogenic and pro apoptotic activity as assessed by in vitro, cell-based and in vivo assays. Further these novel plant derived molecules sensitized radio or chemo, or TRAIL-resistant cells to TRAIL-induced apoptotic death. Recombinant sFlt-1 and/or TRAIL and sTie2 and/or TRAIL weretagged to PEG- maleimide liposomes encapsulated with either T1 or A1. Anti-angiogenic and pro-apoptotic activity of these liposomes were evaluated both in cell based and xenograft models using triple negative breast cancer cells. These imunoliposomes will have immense application in targeted therapy of breast and other cancers in clinics.

Is there atie between risk factors cold environment and high cholesterol for cancer?

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Introduction: After cardiovascular diseases, cancer is the second-leading cause of morbidity and mortality of patients.Many extrinsic and intrinsic factors might increase the risk of cancer incidence and/or death. For example, some factors such as smoking, high fat diet, environmental toxin exposure, etc., have been connected positively with tumorigenesis. This is assumed to be by promoting oncogenic signals and/or altering epigenetic changes of cancer cells. This could be by either directly influencing the tumor cells or by favoring the tissue microenvironment. This study was planned to find out the potential risk factor(s) linked with cancer incidence and/or death. **Methods:**Average annualtemperature (AAT), cancer mortality rate (CMR), cancer incidencerate (CIR), meat-, alcohol-consumption, gross domestic product, body weight, physical inactivity, smoking, obesity,CO2 emission and serum total cholesterol of a country were collected.Statistical softwarewas used for data analysis. MTT and cell count assays were performed to see the effect of cold exposure on cancer cell proliferation. **Results:** Statistical analysis found that the AAT of a country may have a most potential Contribution in regulating CMR, when compared to other factors such as alcohol and meat consumption. CMR is low in those countries situated near to the Torrid Zone, but it is high for those countries situated away from this zone. This indicated that cold temperature may have a contribution in increasing the risk of cancer. Furthermore, statistical analysis found a positive relationship between serum total cholesterol (ATC) and overall CMR. A similar correlation was found between ATC and different anatomical site-specific CMRs, including lung, bladder, ovarian, breast, and pancreatic cancers. Our analysis further found a negative association between AAT and ATC, similar to that of AAT and CMR. It was also observed that the result patterns of univariate analysis between AAT and CMR are very much similar with AAT and ATC. Moreover, geographic location of the top 50

countries having the highest CMR is very similar to top 50 countries having the highest ATC. Similarly, the least 50 countries having the lowest CMR are located in the same geographic region, similar to least 50 countries having the lowest ATC. Moreover, multiple linear model depicts that the behavior of CMR in presence of other these two regreesors (AAT and ATC) can be observed easily. **Conclusion:** This study, for the first time, documents that a relationship exists among AAT and CMR for overall, as well as, many specific cancers such as lung, bladder, ovarian, breast, etc. This epidemiological studynot only proposes that cold-induced brown fat activation could be an inducer of cholesterol, for increasing risk of tumorigenesis, but also unravels a novel area for cancer research. Cell culture based studies indicate that cold exposure might augment cancer growth and migration.

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Post-transcriptional gene regulatory mechanisms in B-lymphoblastic leukemia

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Decoding metabolic programming in glioblastoma

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Tumor cells possess altered metabolic phenotype and heavily rely on the Warburg effect, to maintain unrestrained cellular proliferation and survival. Glioblastoma multiforme (GBM) - the most malignant of brain cancers is characterized by altered metabolic profile. Along with deranged metabolism, inflammation - an essential hallmark of tumor cells; also serves as an indispensable participant in glioma progression. As there is considerable overlap between the signaling mediators/transcriptional circuitries in metabolic adaptation and inflammation, we investigated whether inflammation regulates expression of metabolic regulators. Another notable feature that characterizes GBM is its obstinate resistance to current therapeutic regimen. Importantly, dysregulated metabolism is linked to therapeutic resistance in GBM. TERT promoter mutation that enhances expression of telomerase is remarkably high in adult GBMs; and telomeric proteins have been linked with metabolic reprogramming. Given the importance of telomere maintenance in glioma cell survival, we also investigated the importance of telomerase on metabolic adaptation and therapeutic resistance. By decoding metabolic reprogramming in glioma cells, this study attempts to provide valuable insights towards mechanisms that support glioma progression.

Intratumoral immune landscape: Immunogenicity to tolerogenicity

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Immune system possesses distinct innate and adaptive branches which act in a collaborative way to eliminate neoplastic transformation. In spite of the presence of immune response, tumors develop spontaneously through different immune escape strategies. It has been demonstrated that dysfunction of the host's immune system is one of the major mechanisms by which immunogenic immune system becomes tolerogenic. This dysfunction includes but not limited to loss of effector-/memory-T cells, Th2 cell bias and T-regulatory (Treg) cell expansion. However, the molecules involved in these processes were not fully understood. We observed that tumor-shed various soluble factors play critical role in suppression of anti- tumor immunity. Adding to the knowledge of abundant T cell plasticity in terms of cytokine production our study identifies an IL10-producing FOXP3+ Treg cell population that contributes to IL10-dependent type-2 cytokine bias in breast cancer patients. The master transcription factor FOXP3 associates with multiple interatomic partners which include tolerance partners, epigenetic modifiers, and differentiation factors to execute Treg- mediated immunosuppression. Targeting FoxP3-interatomic partners by micro-RNA would be promising approach to prevent the Treg-mediated tumor immune evasion. In recent findings we have identified miR-325 that regulates Treg development and function by interfering 3'-UTR region of FOXP3 and FOXP3-associated interactome partners. Lentiviral- mediated miR-325 over-expression hindered Treg augmentation and substantially reduced tumor progression in tumor-bearing mice. Hence targeting miR-325 may boost anti-tumor immunity.

Potential role of novel pharmacological STAT3 inhibitors in cancer therapy

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Introduction: Signal transducers and activators of transcription (STATs) comprise a family of cytoplasmic transcription factors that transmit signals, mediate intracellular signaling that is usually generated at cell surface receptors and then transmitted to the nucleus. Numerous studies have demonstrated constitutive activation of STAT3 in a wide variety of human tumors, including hematological malignancies (leukemias, lymphomas, and multiple myeloma) as well as solid tumors (such as head and neck, breast, lung, gastric, hepatocellular, colorectal and prostate cancers). There is strong evidence to suggest that aberrant STAT3 signaling promotes development and progression of human cancers by either inhibiting apoptosis or inducing cell proliferation, angiogenesis, invasion, and metastasis. However, the development of novel drugs for the targeting STAT3 that are both safe and efficacious remains an important scientific and clinical challenge. **Objectives:** To test the potential STAT3 modulatory effects of emodin and garcinol in hepatocellular carcinoma. **Material and Methods:** The effect of emodin and garcinol on STAT3 activation, associated protein kinases, and apoptosis was investigated using various HCC cell lines. Additionally, the in vivo effect of these drugs on the orthotopic/xenograft mouse models was also examined. Results: We will present recent data from our group that shows that novel small molecule inhibitors (garcinol/butein) can suppress STAT3 activation through diverse molecular mechanisms and modulate the expression of genes involved in cancer progression. Conclusions: Our findings have identified two novel STAT3 inhibitors with promising anticancer effects.

Therapeutic and Diagnostic Significance of Osteopontin and Associated Genesin Breast and Other Cancers

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Significant advances in breast cancer treatments have resulted in a substantial decrease in mortality. However, existing breast cancer therapies often result

in high toxicity and nonspecific side effects. Therefore, better targeted delivery and increased efficacy of drugs are crucial to overcome these effects. Osteopontin (OPN), a chemokine like protein plays crucial role in regulating the oncogenic and angiogenic potential of various cancers. Several groups have demonstrated the role of OPN in regulating the cell signaling that ultimately controls tumor progression and metastasis covering all the hallmarks of cancer. During last several years, we have demonstrated that both tumor and stroma-derived OPN regulate tumor growth and angiogenesis through induction of COX-2, uPA and VEGF expressions and activation of matrix metalloproteinase (MMP) in breastand other cancers. Our studies revealed that OPN regulates p70S6 kinase dependent ICAM-1 expression and JAK/STAT3 signaling leading to tumor growth in breast cancer. Our recent data showed that OPN controls HIF-1alpha dependent VEGF expression and breast tumor angiogenesis. Thus targeting OPN and its regulated signaling network could be novel therapeutic strategy for the management of cancers.

Tumor-stroma interaction in gliomathrough proteomic approaches

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During the last two decades, the neuro-oncology community is witnessing an explosion of knowledge about these extremely complex brain tumors. However, the median life expectancy of glioblastoma (the most common primary adult tumor) patients remains at 15-17 months. Hence, there is a pressing need to develop more comprehensive approaches to understand the biology of glioma in order to develop markers that could help diagnose glioma early, molecular stratification with respect to patient prognostication and treatment response prediction and in developing novel therapeutic methods. We have a comprehensive approach covering various aspects like genetic and epigenetic alterations in glioma, serum biomarkers using high-throughput proteomics, genome-wide shRNA screening for temozolomide sensitivity and exome sequencing to understand the glioma biology.

While the role of genetic and epigenetic alterations in tumor cells have been investigated extensively, the importance of the tumor stromal components in GBM development and progression has only been recognized recently. Since the interaction between tumor cells and stromal cells is more likely to involve secreted proteins and the fact that secreted proteins are more likely to be present in serum, we chose to analyze the glioma patient serum to begin with. We used various proteomic platforms like 2-DE, 2-DE DIGE, antibody microarrays, bead arrays and iTRAQ-LC MS/MS to answer some of the above questions.

In this presentation,I will present our recent work on identification and validation of a serum cytokine signature for distinguishing glioma patient sera from normal healthy individual sera. I will also present data related to validation and functional characterization of one of the cytokines, Macrophage ColonyStimulating Factor 1 (MCSF1). Unlike what is known in the literature, we found tumor secreted MCSF1 did not have effect either on tumor cells in an autocrine fashion or a role in M2 polarization of microglial cells in a paracrine fashion even though we found a huge infiltration of M2 polarized macrophages in the glioma stroma. MCSF1 induced angiogenesis through its action on macrophages. SILAC experiment based investigation of macrophage/microglial secretome identified several novel factors as mediators of MCSF1-induced angiogenesis. These results are particularly intersecting as bevacizumab, a VEGF targeting antibody approved by FDA, failed to show any significant improvement in overall and progression free survival in the recently conducted trails. These studies point to the possible presence of factors other than VEGF that may promote angiogenesis and cancer stem cell derived endothelial cells through transdifferentiation. In conclusion, our study identified a cytokine signature for distinguishing glioma sera from that of healthy individuals and identified novel proteins in the microglia secretome as novel mediator of MCSF-induced tumor angiogenesis with a potential of developing a targeted therapy.

Diversity Oriented Synthesis :: New Era in Creating Library of Molecules

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Synthetic chemists thriving to develop new methodologies there by creating library of organic molecules. Synthetic methods that allow rapid access to large number of diverse structural arrays is growing constantly, which served as a new driving force for the advancement. In order to synthesize large number of molecules with high level of diversity and complexity, In addition to developing new synthetic techniques and reagents, organic chemists are looking for exploring new methods to design and to evolve new molecules, strategies for new molecules leading to new source of diversity and improving the quality of compound libraries. This diverse new methodologies that will create many structurally diverse compounds efficiently in high yields and with excellent purity and with wide range of functional groups as handles to expand them further. One of the richest source of diversity in drug discovery are small molecule heterocycles, which in addition to exhibiting biological activity, also serve as rapid scaffolds for further display of broad range of functionalities. For several years Prof. M.V. Basaveswara Rao1 and his research group has been engaged in design and development of new efficient methodologies for a wide variety of heterocycles, displaying a range of skeletal and functional group diversity. The biological properties of heterocycles in general make them one of the prime interests of the pharmaceutical industry, biotechnology industry and as well as for opto-electronic industry. Our group initiated work on the synthesis of heterocycles with an aim to understand their properties towards bioactivity like, antibacterial, anti-malarial, antifungal, anti cancer, free radical scavenger, etc. and also towards Non Linear Optic materials. We have synthesized various heterocyclic skeletons initially and utilized them for making other heterocycles. All the synthetic methodologies reported by us are simple efficient and does not involve hitherto costlier chemicals, circuitous reaction pathways, drastic reaction conditions and corrosive molecules. Our aromatic and heteroaromatic annulation strategies are highly efficient, simple and results in variety of molecules with quantitative yields.

Metabolic Disorders: An Unexpected Role in Cancers

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Recent studies have suggested that metabolic disorders like diabetes and obesity alter the risk of developing variety of cancers and the associations are biologically plausible. Obesity is now recognized as one of the most important public health problem in developed as well as developing countries. It has been identified as a risk factor for breast, colon, pancreatic, cervical cancers as well as melanomas. Obesity is also associated with late-stage disease, poor prognosis and cancers chemotherapy has turned out to be increasingly complicated and the anticipated success rate is much below than expected. We demonstrate that obesity induced metabolic alterations directly affect the transcriptional regulation of important mediators of proliferation in melanoma. These factors may be explored for developing newer approaches towards preventing rapid progression of melanoma in obese individuals. Thus, it is likely that a better understanding of the relationship(s) between metabolic disorders and cancer will lead to innovative avenues of pharmaceutical intervention and improvement in cancer therapeutic

Transcriptome analysis of oral tongue cancer reveals novel insights into wild type and mutant TP53 transcription program

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Tp53 is the most frequently mutated gene in human cancers and majority of mutations are located in the region encoding the DNA binding domain compromising thereby its transcription activation ability and resulting in loss of tumor suppressor function. Recent studies have revealed certain mutant p53 proteins to exhibit an 'oncogenic' gain of function activity. Specific p53 missense mutations can result in an altered transcription program causing positive regulation of cell proliferation, metastasis and chemoresistance. In our previous studies, we performed comprehensive characterization of squamous cell carcinoma of the oral tongue (SCCOT) with respect to p53, EGFR, Wnt, MSI, LoH of several tumor suppressor loci and HPV status. Mutant p53 was a significant predictor of overall survival and theTP53 codon 72 Proline allele was significantly associated with SCCOT. In order to analyse a possible gain of function role of mutant p53 in tongue cancer, we performed genome wide DNA and RNA profiling of SCCOT samples stratified for p53 status. Both mutant and wild type tumour samples appeared to exhibit comparable levels of DNA copy number alterations. Computational analysis of transcriptome data generated from the same samples surprisingly identified only two genes to be differentially up-regulated in p53 mutant samples namely TP53 itself and SMARCD1; the latter a member of the SWI/SNF chromatin remodelling complex. Elevated levels ofTP53 transcript in tumours harbouring mutant p53 significantly correlated with levels of ZMAT3, itself known to be transcriptionally induced by p53 to stabilize the TP53 transcript. In addition, the analysis revealed several known (ATF3 and others) and novel (GCHFRand others) targets of wild type p53. Differential expression of all targets was validated in additional tongue cancer samples. Ectopic expression of certain (but not all) p53 mutant proteins in p53 null cells induced SMARCD1 (but not canonical wild type p53 targets) while expression of wild type p53 induced GCHFR, ATF3, CDKN1A, etc. (but not SMARCD1). In contrast, p53 stabilization in cells harbouring wild type p53 caused elevation of GCHFR, ATF3, CDKN1A, etc., but not of SMARCD1. Validation of novel targets using promoter-luciferase constructs, chromatin immunoprecipitation PCR and a tongue cancer tissue microarray is currently underway. This is perhaps the first evidence from Head and Neck tumour samples for the presence of a distinct transcription program supported by wild type and mutant p53.

Lupeol hinders aggressive tumor growth by inhibiting Vasculogenic Mimicry

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Introduction: All aggressive cancers possess a novel mechanism called Vasculogenic Mimicry (VM) by which cancer stem-like cells create pseudo-vascular channels in order to promote tumor growth and metastasis. It has been a field of vast interest nowadays as rupture of these channels can actually be a useful tool to control aggressive tumor growth. **Objectives:** Our main objective was to evaluate the effect of phytochemical Lupeol on VM present in aggressive murine melanoma and in tumor tissues of head and neck cancer patients' sample. **Material and Methods :** Highly aggressive melanoma cell line B16-F12 was treated with different doses of Lupeol alone and combination with Dacarbazine for 24 hr. After incubation, the cells were inoculated sub-cutaneously into C57BL/6J mice. Scratch assay, PAS staining, flow cytometry, matrigel tube formation assay, immunofluorescence staining, western blot and mRNA analysis was performed to check the effect of Lupeol on tumor VM. In another set of experiments, Ex-vivo explant culture followed by PAS staining was performed in head and neck tumor tissues using the novel CANScript technology. **Results :** Lupeol treated Melanoma tumors demonstrated inhibition of growth, very less amount of VM and a low percentage of cancer stem-like cells whereas Dacarbazine treated tumors had higher tumor growth compared to Lupeol treatment. Head and neck tissues in ex vivo explants culture model showed similar kind of response. **Conclusions :** Together, these findings are indicative of a promising anticancer function of Lupeol as novel strategies that potentially effect maximum benefit in a clinically challenging scenario against aggressive tumors.

microRNAs as therapeutics for Breast Cancer.

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Introduction: Despite substantial progress in understanding the breast cancer signaling network, effective therapies remain scarce due to tumor heterogeneity, insufficient disruption of oncogenic pathways, drug resistance and drug-induced toxicity. Hence new and additional approaches are required for the treatment of breast cancer. Role of Bcl-2 in carcinogenesis and progression makes this gene worthy of investigation **Objective:** Identifying miRNA (s) that target bcl-2, and functionally characterize their targets, and possible new functions guided by these small regulators of gene expression so that they can be used as therapeutics for breast cancer. **Material and Methods :** Using experimental and computational approaches we identified several miRNAs(has-miR-195 etc) that can regulate the anti-apoptotic protein BCL2. Gene expression profilingetc was done to functionally characterize the role of hsa-miR-195, **Results:** Our findings revealed that hsa-miR-195 targets genes of de novo lipogenesis, inhibits cell proliferation, migration, and invasion which potentially opens new avenues for the treatment of breast cancer. Further it is believed that resistance to apoptosis and epithelial- to-mesenchymal-transition(EMT) facilitates metastasis via over-expression of anti-apoptotic Bcl-2. We observed that over expression of hsa-miR-195 modulatesMesenchymaland Epithelial markers. **Conclusion :** The role of pro-apoptotic hsa-miR-195 in inhibiting de novo lipogenesis via targeting genes overexpressed in breast cancer (BCL-2, FASN, ACACA, HMGCR, CYP27B1) makes hsa-miR-195 an effective anticancer molecule for breast cancer.

Multispecific macromolecules increase efficiency of targeting tumor cells

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Role of Insulin like Growth Factor Binding Protien-2 in the progression of Glioblastoma

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Insulin Like Growth Factor Binding Protein 2 (IGFBP-2) is often over expressed in aggressive glioblastoma (GBM) and contributes to poor prognosis of GBM patients. Earlier, we showed regulation of β-catenin by IGFBP-2 in breast cancer and its association with the lymph node metastasis. Previous reports suggest a role for β-catenin pathway in glioma invasion, proliferation and maintenance of glioma stem cells. However, the mechanism of regulation of β-catenin by IGFBP-2 and its role in GBM prognosis has not been elucidated. In this study by over expression and knockdown of IGFBP2 expression, we show stabilization of β-catenin and regulation of its nuclear functions involving integrin mediated inactivation of GSK3β independent of IGF signaling. In order to identify the domain (s) in IGFBP2 that causes this, we over expressed the various domains (C-, N-, and Full

length) in glioma cells. The results suggest C-terminal domain of IGFBP-2 being as potent as the full length protein. Subcutaneous xenograft tumors in immunocompromised mice over-expressing either full length or C- terminal domain of IGFBP-2 showed larger tumor volumes compared to controls. Furthermore, co-expression of IGFBP2 and β-catenin revealed poorer prognosis of GBM patients in Cox regression and Kaplan Meier survival analysis in a cohort of GBM patients. All these data suggest potentiation of GBM tumor growth by IGFBP-2 by the activation of β- catenin pathway through its C-terminal domain. By using a single chain monoclonal anti IGFBP2 antibody, we show reversal of pro tumorigenic properties of glioma cells. Therefore, inhibition of IGFBP2 could be a potential therapeutic target in the management of GBM.

Glycosylation Networking: Role in oral cancer Progression & Metastasi

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India ranks number one in the prevalence of oral cancer in the world. Disappointingly, no considerable improvement in outcome of oral cancer patients is observed in recent decades because of frequent development of loco-regional recurrences, distant metastases and second primary tumours. Moreover, there is no significant change in treatment modalities over the past few decades. There is a need for development of molecular markers for early screening, detection, monitoring disease progression and better treatments outcomes.

Our laboratory is working on glycosylation networking in various cancers. We have reported a progressive increase in glycosylation pattern from healthy individuals to patients with oral precancerous lesions to oral cancer patients. Recent data from our laboratory also indicated that the glycosylation alterations are observed in saliva as well. The alterations in saliva/serum/tissue glycosylation pattern, along with other molecular markers like MMPs, VEGFA isoforms expression, EGFR, E-cadherin, c-Jun, p53 polymorphisms/mutations play a significant role in oral cancer development and progression. Most of the molecules reported in our recent studies are focused for targeted therapy. Therefore, our research efforts in oral cancer may provide better understanding of the molecular and biological profile of oral cancer to facilitate more efficient targeted therapies.

Our data indicate that the methodical understanding of oral cancer biology will certainly improve oral cancer screening, diagnostics and treatment modalities of tomorrow, which is an anticipated remedy to strengthen the fight against oral cancer.

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Non-coding genetic aberrations in breast and ovarian cancers

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DNA copy number aberrations (CNA) drive tumorigenesis in a number of cancer lineages. Thus identification of drivers of CNA offers an opportunity to treat several novel therapeutic targets. Although some CNA are narrow targeting a discrete set of genes, others such as the 3q26.2 amplicon is large and present in ~35% of high-grade serous ovarian cancer (HGSOC) and ~15% of breast cancer. Since 3q26.2 locusis large and structurally complex, suggesting that multiple coding genes and non-coding RNAs in the 3q26.2 amplicon contribute to tumor initiation and progression either alone or through cooperative activity. In contrast to the coding regions, the effects of genomic aberrations on non-coding RNAs and microRNAs have not been well characterized. Our high-resolution SNP array mapping of 3q26.2 amplicon identified several microRNAs amplified and overexpressed in breast and ovarian cancers as part of 3q26.2 CNA. Our results demonstrate that microRNAs miR569 and miR551b, are overexpressed in a subset of ovarian and breast cancers due to the 3q26.2 amplicon. Using target based analysis, AGO-CLIP methods, cellular and molecular approaches, we have demonstrated that 3q26 microRNAs altered the expressionof several genes including TP53INP1, P53AIP1, and STAT3 are critical regulators of survival and proliferation of cancer cells. Furthermore, targeting mature microRNAs using anti-miRs encapsulated in nano- liposomes reduced the tumor growth and metastasis of breast and ovarian cancer cells in vivo. Thus our results employing the microRNA therapy, further warrants exploration to use/target miRs to treat breastand ovarian cancers.

Genomic Background and Cellular Metabolism status Tunes Cells towards Pro-Cancerous State

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We have observed a combined effect of the genomic background of DDR-Apoptotic and Immune regulatory pathway genes with diverse genotype combinations and epigenetic regulation both at methylation (Mol Cancer. 2010 Nov 23;9:303) and microRNA levels (Breast Cancer Res. 2011 Apr4;13(2):R39; PLoS One. 2014 Oct 29;9(10):e111177 ; GENE 567 (2015) (217–224), providing risk/protection to the sporadic breast cancer patients. Extending similar studies to whole mitochondrial genome has shown a strong association with 10398 G>A germline variation (in the ND3 gene) in these patients (Cancer Lett. 2007 May 8;249(2):249-55; Int J Cancer. 2008 Dec 1;123 (11) :2580-6). An experimental approach adopted to understand the biological relevance of the specific mitochondrial genomic background in generating elevated ROS and regulating epigenetically the apoptotic pathway in vitro, favoured the appearance of pro-cancerous metabolic features (Singh et al, Sci Rep.2014 Oct 10;4:6571), suggesting the vulnerability of mitochondrial status and response to both cellular and environmental insults in favouring promotion of cancer. The observations bring out a complex collective role of genotype status and regulation of cellular metabolism (J Biol Chem. 2010 May28;285(22):16864-73; Protein Sci. 2010 Nov;19(11):2031-44; PLoS One. 2012;7(5) : e36764; Mol Cancer. 2013 Jul9;12:72; FEBS Lett. 2014 Apr 18. pii: S0014-5793(14)00297-X; J Biol Chem. 2014 289: 8098-8105) to facilitate a cell towards tumour development. The understanding of metabolic tuners in cancer cell metabolism has facilitated designing therapeutic interventions accordingly. [All students, collaborators and funding agencies, appearing in the published work quoted, are acknowledged].

Radio Frequency Radiations (RFR) and Cancer

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DNA copy number aberrations (CNA) drive tumorigenesis in a number of cancer lineages. Thus identification of drivers of CNA offers an opportunity to treat several novel therapeutic targets. Although some CNA are narrow targeting a discrete set of genes, others such as the 3q26.2 amplicon is large and present in ~35% of high-grade serous ovarian cancer (HGSOC) and ~15% of breast cancer.Since 3q26.2 locusis large and structurally complex, suggesting that multiple coding genes and non-coding RNAs in the 3q26.2 amplicon contribute to tumor initiation and progression either alone or through cooperative activity. In contrast to the coding regions, the effects of genomic aberrations on non-coding RNAs and microRNAs have not been well characterized. Our high-resolution SNP array mapping of 3q26.2 amplicon identified several microRNAs amplified and overexpressed in breast and ovarian cancers as part of 3q26.2 CNA. Our results demonstrate that microRNAs miR569 and miR551b, are overexpressed in a subset of ovarian and breast cancers due to the 3q26.2 amplicon.Using target based analysis, AGO-CLIP methods, cellular and molecular approaches, we have demonstrated that 3q26 microRNAs altered the expressionof several genes including TP53INP1, P53AIP1, and STAT3 are critical regulators of survival and proliferation of cancer cells. Furthermore, targeting mature microRNAs using anti-miRs encapsulated in nano- liposomes reduced the tumor growth and metastasis of breast and ovarian cancer cells in vivo. Thus our results employing the microRNA therapy, further warrants exploration to use/target miRs to treat breastand ovarian cancers.

Hypomethylation in the promoter region of E-cadherin gene provides a rationale for lesser predisposition of cancer in diabetes patients undergoing metformin treatment

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Epithelial-mesenchymal transition (EMT) is the key biological phenomenon behind tissue fibrosis and cancer. Clinical studies suggest that patients undergoing metformin therapy are less predisposed to cancer but the underlying mechanism is not known. Moreover metformin also acts as TGF-beta inhibitor. Therefore in this study we explore whether and how metformin could modulate EMT in a cancer like microenvironment.

Our data using human cell lines revealed that metformin induced a distinct change from stromal-shaped mesenchymal cells to cuboidal-shaped epithelial cells with sharp boundaries accompanied with upregulation of epithelial markers and mitigation of their invasive property. One of the key regulatory pathways, which intersect tumorigenesis and metformin activity, is AMPK. We demonstrated that metformin attenuates ERK signaling by activating AMPK pathway that leads to suppression of Snail and Slug resulting in upregulation of crucial tumor suppressor gene E-cadherin in both cell types. ChIP assay then confirmed insufficient binding of repressors like Slug to the E-cadherin promoter. Further, our data revealed reduction in HDAC activity prompting hypomethylation of E-cadherin promoter thus reflecting an epigenetic modification. The active state of E-cadherin promoter was confirmed by lesser recruitment of H3K27me2 and corresponding increase in the acetylation markers. In pursuit to expand the translational significance of the study we verified these findings in diabetic patients undergoing metformin treatment. This is the first report presenting an inverse relationship of AMPK and ERK signaling axis in promoting mesenchymal to epithelial transition (MET) via re-expression of E-cadherin upon metformin treatment. Taken together, these findings may help rationalizing lower incidence of cancer in metformin-administered patients.

Alternate therapy for cancer treatment – "Experimental Studies with Homoeopathic medicines

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Homoeopathic medicines are frequently given for several ailments including cancer. Homoeopathic medicines which use ultra diluted preparations are found to be effective but their mechanism of action cannot be explained by modern scientific methods. Reports on the efficacy of homoeopathic medicines in animal models are limited and there are only very few reports on the in vitro action of these dynamized preparations in cultured cells. We have evaluated the cytotoxic activity of ten dynamized medicines (30C and 200C) against Dalton's Lymphoma Ascites (DLA) , Ehrlich's Ascites Carcinoma, lung fibroblast (L929) and Chinese Hamster Ovary (CHO) cell lines and compared activity with their undiluted mother tinctures using short term and long-term cell culture. Mother tinctures as well as some dynamized medicines showed significant cytotoxicity to cells to cultured cells. Potentiated alcohol control did not produce any cytotoxicity at concentrations studied. The dynamized medicines were found to inhibit CHO cell colony formation and thymidine uptake in L929 cells. Potentiated preparations were found to reduce animal tumours when given orally and in fact were found to reduce already developed solid tumours in mice. Moreover these preparations were found to inhibit chemical carcinogenesis induced by 3-methyl cholanthrene and nitrosodiethylamine. The effect of dynamized medicines to induce apoptosis was also evaluated and we studied how dynamized medicines affected gene expression during apoptosis. Potentiated preparation of Thuja, Hydrastis and Carcinosinum were found to induce apoptosis in DLA cells. Carcinosinum was found to induce the expression of p53 gene and inhibited anti- apoptotic BCl2 gene expression. Dynamized Thuja produced characteristic laddering pattern of apoptosis during agarose gel electrophoresis of DNA. Micro array analysis of the exposed cells indicated that several enzymes related to apoptosis and cell proliferation were altered by homoeopathic medicines. These results indicated that ultra diluted preparation in homoeopathy behave like their undiluted preparation in their biological effectiveness.

Key words : Homoeopathic medicines - Apoptosis

A dual regulation of immune evasion and angiogenesis for anti-carcinogenesis by neem leaf glycoprotein having human hemoglobin b-chain like sequence

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Apart from conventional therapies, effective cancer management requires additional considerations on two important hallmark criterions for carcinogenesis, i.e., immune evasion and angiogenesis. We have already reported that neem leaf glycoprotein (NLGP) mediates sustained tumor growth restriction by modulating the dysregulated anti-tumor immune responses of tumor host. Our recent works suggested that NLGP regulates angiogenesis too within tumor microenvironment and peri-tumoral areas in CD8+ T cell dependent manner to obtain vascular normalization in murine melanoma and carcinoma models. NLGP treatment-associated immune modulation, particularly CD8+ T cell activation, facilitates downregulation of VEGF-VEGFR2 signalling in CD31+ vascular endothelial cells and promotes pericy te stabilization to prevent aberrant neovascularization within tumor microenvironment. Additionally, NLGP

can directly downregulates VEGF in melanoma cells by targeting the binding between HIF1a and its associate co-factors to prevent ultimate binding of HIF1a to HRE region of VEGF promoter. Considering the well synthronized effects of NLGP on immune cells and tumor cells to restrain murine malignant growth surely suggests its clinical translation for cancer management. Furthermore, current proteomic analysis provided evidences for existence of human hemoglobin beta chain like sequence in this novel glycoprotein, NLGP, and such understanding on NLGP conformation will help to explain the structural basis of NLGP functionality. Exploration of this essential step further will pave the way to bring this molecule from bench to bedside.

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Insights from Integrated Molecular Analysis of Gliomas

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Transcriptional regulation of dipeptidyl peptidase expression by IL-6 in human glioblastoma cells

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Interplay between mitochondria and nucleus to maintain genome integrity

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Germline mutations in the nuclear RECQL4 helicase are associated with Rothmund Thomson syndrome (RTS). A subset of RTS patients is predisposed towards cancer. It has been shown that RECQL4 localizes to the mitochondrial nucleoid where it enhances the 5' to 3'polymerization and 3' to 5'exonuclease activities of Polymerase γ, thereby acting as an accessory factor during mitochondrial DNA replication. Mitochondrial genome sequencing in RTS patient cells have revealed incorporation of somatic mutations and polymorphisms in the mitochondrial genes coding for oxidative phosphorylation, tRNA, rRNA and the D-loop, which potentially can alter mitochondrial functions in the RTS patient cells. To understand the mitochondrial functions that might be perturbed in the absence of functional RECQL4, we have studied the ultra structure of mitochondria, mitochondrial membrane permeability, mitochondrial ROS, mitochondrial mass, structure and functions of electron transport chain which subsequently effect the ATP production in the RTS patient cells and its complemented counterparts. Interstingly the loss of the mitochondrial functions of RECQL4increases aerobic glycolysis which in turn led to an increased invasive capability in these cells. Altogether these studies will help to understand the functions of RECQL4 in the mitochondria and provide evidence about the interplay between the nucleus and mitochondria in the maintenance of genomic integrity.

Metronomics in Cancer Therapy

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Altered E2F5/p38/SMAD3 axis reinforces the pro-tumorigenic switch of TGFβ signaling in prostate cancer

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Introduction: Transforming growth factor-β signaling exerts divergent impact on normal cells and cancer including prostate adenocarcinoma. Mechanism underlying this differential behaviour remains unclear. **Objectives:** The present study aims to identify the precise genes/protein components of deregulated TGFβ signaling pathway with the expectation that the information accrued will be a helpful addition to prostate cancer management. **Material and Methods:** Methods used in the study include quantitative Real Time-PCR, Western Blot analyses, immunohistochemistry, immunocytochemistry, confocal microscopy, siRNA mediated gene knockdown and cell cycle analysis. **Results:** E2F5 was identified as the most dysregulated molecule in the TGFβ pathway in prostate cancer tissues, predominantly in samples with Gleason score 6. E2F5 over-expression was accompanied by significantly higher phosphorylation of p38 MAPK and SMAD3 at the linker-region (pSMAD3L). The pattern of SMAD3 phosphorylation was strikingly different in tumor (Ser 208) and benign tissues (Ser 423 and 425). Co-localization of E2F5 with pSMAD3L in the nuclei of tumor and PC3 cell line indicated a cross-talk between the proteins. Down- regulation of E2F5 resulted in marked reduction in the abundance of pSMAD3L and phospho- p38, and perturbation of cell cycle. **Conclusions:** Our findings demonstrated that E2F5/p38 MAPK axis played a cardinal role in mediating pro-tumorigenic switch in prostate cancer through pSMAD3L activation. It also underscores a strong potential for E2F5 to be incorporated in the screening tool to improve the diagnostic accuracy of prostatic lesions.

A Novel Inhibitor of BCL2, Disarib Binds to its Bh1 Domain and Disrupts BCL2-BAK Interaction to Promote Apoptosis

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The antiapoptotic protein, BCL2 is overexpressed in several cancers and contributes to prolonged cell survival and chemoresistance, lending itself as an excellent target for therapy. Here we report the design, synthesis and characterization of Disarib, a novel BCL2 inhibitor. BCL2 knockdown in cells rendered remarkable resistance to Disarib, while sensitivity was regained upon its ectopic expression, establishing target specificity. Unlike other known BCL2 inhibitors, Disarib binds predominantly to BH1 domain of BCL2 and does not interact with its homologues, significantly. Disarib specifically disrupted the BCL2-BAK interaction both in vitro and inside cells, but not those of BCL2-BAX, BCL2-BIM or BCL2- PUMA. Importantly, Disarib activated intrinsic pathway of apoptosis in both, BCL2 'high' cancer cell lines and primary cells from chronic lymphocytic leukemia patients. Further, Disarib administration led to tumor regression in three mouse models, exhibited

platelet sparing property and was devoid of significant side effects. Interestingly, Disarib synergises with paclitaxel, suggesting potential for combination therapy especially in chemoresistant cancers. Thus, we report a novel BCL2 inhibitor, characterize its mechanism of action and demonstrate efficacy.

'Regulatory T cells in oral cancer

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Loss of 14-3-3σ leads to the induction of an Epithelial Mesenchymal Transition.

Challenges and promises of identifying cancer stem-like cells in solid tumors: Implications in cancer therapy

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Many questions about cancer remain unanswered. More studies are needed to determine precisely how different cancers grow and how they resist medical therapy. Recent evidences on cancer biology suggest that a subset of cells called cancer stem cells are present within the tumor mass which possess tumorigenic capacity. These are the cells responsible for propagation, relapse and metastatic dissemination. These cells have certain stem cell-like properties, e.g. quiescence, self-renewal, asymmetric division, and multidrug resistance which allow them to drive tumor growth and evade conventional therapies. The idea that many cancers are organized as hierarchies sustained by cancer stem cells (CSCs) at their apex has generated a lot of excitement in many quarters of the cancer research community. From our studies, we concluded that a small portion of cells in the tumors may have characteristics of CSC and these cells could be an attractive source for CSC research. However, very little is known about the regulation of cancer stem cell (CSC) maintenance pathways in cancer and how these are affected by cancer-specific genetic alterations and by treatment. Treatments targeted at cancer stem cells could eliminate recurrences of the disease. In this context,we have identified the CSCs from the bulk population by characteristic features like increased migration, invasiveness, drug resistance, tumor formation alongwith phenotypic markers. However, the main stumbling block is isolation of sufficient number of CSCs for in vitro studies. We have generated some *invitro* models for enriching the CSC population. We have also identified autophagy as one of the mechanisms that contribute to the ability of the CSCs in to survive conventional chemotherapy and regenerate a cancer population, leading to relapse especially in bladder cancer model. We demonstrated that the chemotherapeutic agents; gemcitabine (GC) and mitomycin (MM) led to increase in autophagy and combination of autophagy inhibitors with GC and MM synergistically inhibited bladder cancer cell growth. Inhibition of JAK2 also reduced the proportion of CSC enriched side population, tumor sphere forming ability and led to decrease in expression of Oct-4 and Nanog in both low and high grade of cisplatin resistant primary cultured cells. Destroying cancer stem cells in the original tumor by targeting their survival pathways could reduce the risk of deadly metastasis.

Metastasis suppression and telomerase function – emerging connecti between two important pathways in cancer progression and spread

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India $ supported by Wellcome Trust / DBT India Alliance Senior Research Fellowship While investigating mechanisms underlying metastasis control by the metastasis suppressor Non Metastatic 2 (NME2) we found that NME2 localizes at telomere ends. This was a result of our analysis that used de novo mapping next generation sequencing reads obtained from multiple cell lines following chromatin immunoprecipitation (ChIP-seq) using antibodies specific to NME2. Furthermore, our results demonstrate that NME2 associates with the ribonucleoprotein telomerase and suggest that NME2 could control telomerase activity through this interaction. These findings not only demonstrate novel telomere/telomerase related functions of NME2 but also present an opportunity to investigate this new role of NME2 to gain mechanistic understanding of the potent but poorly understood mechanisms behind metastases suppressor activities of NME2

The interplay between E7 and non-coding RNAs in the manifestation of HPV16 related cervical cancer pathogenesis

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Cervical cancer (CaCx) is the second most common cancer in women worldwide and the leading cause of cancer deaths in women from developing countries. About 70% of CaCx cases harbour Human Papillomavirus (HPV) type 16 infection. HPV16oncoprotein E7 plays a major role in cervical carcinogenesis by interacting with and functionally inactivating various host regulatory molecules. Long noncoding RNA (lncRNA) HOTAIR is one such regulator that recruits chromatin remodelling complex PRC2, creating gene silencing H3K27me3 marks, a hallmark of HPV16 E7 expressing cells. Hence, we hypothesized that HOTAIR could be a potential target of E7, in HPV16 related CaCx. We identified HOTAIR as an important marker of disease progression with a significant linear trend of progressive HOTAIR down-regulation through HPV negative controls, HPV16 positive non-malignants and CaCx samples, which correlated positively with E7. HOTAIR expression levels also served as a marker for patient stratification with low HOTAIR (LH) expressingCaCx samples showing an enrichment of cell proliferative pathways and high HOTAIR (HH) expressing CaCx samples, harboring high E7 expression and enrichment of metastatic pathways. Such enrichment of cancer related pathways could be attributed to global reduction of H3K27me3 gene silencing marks, despite E7-mediated enhanced expression of PRC2-complex members, EZH2 and SUZ12. This could be due to loss of HOTAIR function, either due to decreased HOTAIR expression ordirect physical interaction between HOTAIR and E7. Moreover, a SNP rs2366152C was found to be significantly associated with LH CaCx samples and either singly or collectivelywith the two SNPs, rs17720428C and rs12312094C (all in linkage disequilibrium),altered the HOTAIR secondary structure. rs2366152C also provided a gain of miR-22-5p binding site on HOTAIR, which was significantly up-regulated among the LH CaCx cases only and correlated negatively with HOTAIR and E7 expression, indicating towards a miR-22-5p mediated regulation of HOTAIR through E7. HPV16 E7 therefore seems to be a master regulatory molecule, facilitating CaCx development through its interplay with non-coding RNAs. Overall, the study holds potential of providing guidelines for the development of prevention and therapeutic strategies for combating such cancers.

Loss of 14-3-3σ leads to the induction of an Epithelial Mesenchymal Transition.

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The role of 14-3-3 proteins has been well established in regulation of cell cycle, DNA damage, regulation of gene expression, cytoskeletal dynamics and regulation of cell to cell adhesion and tumor progression. Our previous results suggested that 14-3-3γ regulates desmosome formation in HCT116 cells. To determine if this is true of other 14-3-3 isoforms, we examined desmosome function in cells lacking both copies of 14-3-3σ (σ-/-). To our surprise and in contrast to the results observed with 14-3-3γ loss, Western blots, reverse transcriptase P C R as well as Q P C R and immunofluorescence studies clearly demonstratedthat 14-3-3σ loss lead to a decrease in the levels of epithelial markers and the expression of mesenchymal markers, suggesting that loss of 14-3-3σ leads to an Epithelial Mesenchymal Transition (EMT). 14-3-3σ loss leads to an increase in cell migration,invasion and a decrease in cell to cell adhesion and cell-ECM adhesion. The levels of the EMT transcription factors, Slug and ZEB1, were increasedin the σ-/- cells. Re-expression of 14-3-3σ in these cells led to a reversal of the phenotype, suggesting that the observed phenotypes are due to loss of 14-3-3σ. Our results suggest that 14-3-3σ, which is silenced in multiple epithelial tumor types, is required to induce EMT, which might lead to the formation of invasive and metastatic tumors. The mechanism by which 14-3-3σ loss leads to an increase in Slug levels is currently being investigated and will be presented at the meeting.

Up regulation of neuronal specific RNA binding protein PTBP2 in CML potentiates proliferation of cells

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Alternative splicing, a process mediated by spliceosome machinery and splicing factors is the key mechanism that leads to the proteome diversity. Altered or aberrant expression of several splicing factors has been reported in the progression of different cancers. Although several RNA binding proteins have been implicated in chronic myeloid leukemia (CML) disease progression, ours is the first report to show the up regulation of neuronal specific splicing regulator, polypyrimidine tract binding protein 2 (PTBP2) in CML disease progression. PTBP2 expression was found to be more in KCL22, a granulocytic CML- blast crisis (BC) cell line when compared to other erythropoietic or megakaryocytic CML-BC cell lines. In contrast, there was a decreased expression of its ubiquitously expressed homolog PTBP1 in KCL22 cell line. Analysis of publicly available CML microarray dataset clearly showed a positive correlation between PTBP2 and the blast count. We also observed, an increase in PTBP2 expression in a set of progressed cases (CP to BC) and in CML-BC cases when compared to CML-CP cases. Increased PTBP2 exon 10 inclusion was observed in KCL22 cell line in comparison to other CML cell lines. Furthermore, analysis of publically available CML Rseq dataset confirmed increased PTBP2 exon 10 inclusion in BC cases than in CP cases. Decreased PTBP2 protein expression in imatinib treated KCL22 cells and increased PTBP2 exon 10 inclusion in BCR/ABL transduced 32Dcl3 myeloid cells compared to the parental 32Dcl3 cells confirmed that PTBP2 expression is BCR/ABL kinase dependent. Knockdown of PTBP2 in KCL22 cells showed reduced growth rate, increased apoptosis and increased G2/M cell cycle arrest. Thus our study portrays PTBP2 as a novel target in CML and it might play an important role in the splicing of genes involved in CML disease progression.

Cell subpopulations and chromatin states in cervical cancer cell migration

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Previous studies from our lab have identified a subset of cells in cervical cancer marked by the expression of cell surface marker CEACAM/CD66. These cells show enhanced invasion and migration properties and greater tumour initiation capacity in vivo (Bajaj et al., 2011, Pattabiraman et al., 2014). Further we have attempted to add resolution to this population by the addition of a basal cell surface marker, alpha 6 integrin/ CD49f(Ammothumkandy, A., et al., manuscript under review). We observed that CD66 and CD49f subsets can be segregated into distinct cellular entities in the trailing and leading edge of collectively invading cells with striking correlation with EMT (Epithelial to mesenchymal transition) and proliferation respectively.TGFβ1 a well known regulator of EMT positively co-related with CD66 expression concomitant with enhanced cell migration and block in cell proliferation. TGFβ1+ve and CD66+ tumors correlated with a positive therapeutic outcome compared to TGFβ1-ve and CD66-ve tumours.There is a paradoxical association of TGFβ1+ve and CD66+CD49f+ tumors with metastasis. Our study suggests that functionally distinct CD66 and CD49f subsets, contribute differently to overall poor survival due to local-recurrences and metastasis in human cervical cancer. This makes it a clinically compelling challenge to identify master regulators which regulate such context dependent cellular functions.Given the plastic nature of these subpopulations, we sought to examine whether changes in chromatin states are associated with these phenotypes. Cells sorted on the basis of migratory ability showed visibly changed nuclear shape and global reductions of the repression associated histone modification H3K9me3. These cells also show a distinct transcriptional profile- a gain in cell migration and wound healing signatures, and a loss of apoptosis signatures.A candidate H3K9me3 writer, Suv39H1, was also downregulated in the migrated fraction. Knocking down Suv39H1 resulted in enhanced anoikis resistance, invasion, migration and clonogenic potential. Data analyzed from The Cancer Genome Atlas (TCGA) revealed that patients expressing low levels of Suv39H1 show poorer survival over a period of time. Interestingly, these Suv39H1 low patient samples show expression signatures of cell- cell adhesion, but also cell migration and TGF-B signaling.Current directions seek to determine the mechanisms by which Suv39H1 regulates cell migration.

Integrated Genomic and Epigenomic Approaches to Identify Biomarkers for Esophageal Cancer in North East India

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Mutant p53: one name, many functions

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Identification of radioresistance related markers through profiling of established radiation resistant oral cancer cells

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Contribution of cancer stem cells to acquired chemo-resistance of breast cancer and its reversal by aspirin

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Acquired chemo-resistance has curtailed cancer survival since the dawn of the chemotherapy. Accumulating evidence suggests a major role for cancer stem cells (CSCs) in chemo- resistance, though their involvement in acquired resistance is still unknown. In this study, we investigated the contribution of CSCs to acquired chemo-resistance of breast cancer and the avenues for reversing such effects with aspirin. We observed that the residual risk of recurrence was higher in breast cancer patients who had acquired chemo-resistance. In breast cancer cell line, a small population of cells always failed to surrender even at the lethal doses of chemotherapeutic drugs. These drug-spared cells not only displayed self-renewal, tumorigenic, angiogenic and differentiation properties, but also exhibited 'stemness signature' - thereby confirming their identity as CSCs, and even trans-differentiated into endothelial-like cells to initiate VEGF-independent angiogenesis. These in vitro results are in line with those in chemotherapy-treated breast cancer patients, where enrichment of aggressive CSC repertoire in resected breast cancer tissue is observed when compared with matched-pairs of un-treated patients. A search for the underlying mechanisms revealed that treatment of pre-existing CSCs with a genotoxic drug combination generated an NFκB-IL6-dependent inflammatory environment that imparted stemness to non-stem cancer cells, induced multi-drug resistance, and enhanced the migration potential of CSCs. The use of aspirin has been associated with reduced cancer risk and recurrence, suggesting that the anti- inflammatory drug may exert effects on CSCs. Our results showed that treatment with aspirin prior to chemotherapy suppressed the acquisition of chemo-resistance by perturbing the nuclear translocation of NFκB in pre-existing CSCs. Such disruption of the NFκB-IL6 feedback loop prevented (i) CSC induction and (ii) sensitized pre-existing CSCs to chemotherapy. Collectively, our findings suggest that combining aspirin and conventional chemotherapy may offer a new treatment strategy to improve recurrence-free survival of breast cancer patients.

Role of histone interacting proteins in transcription regulation & chromatin dynamics: Implications in cancer manifestation

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Multifunctional histone interacting proteins play important roles in the regulation of chromatin dynamics and thereby fine-tune the underlying gene expression. We found that, multifunctional nucleolar protein Nucleophosmin (NPM1), a histone chaperone and a potent regulator of RNA pol II driven transcription is overexpressed in oral tumors. Interestingly, we found that NPM1 is acetylated by histone acetyltransferase p300 and the acetylated form is significantly higher in the oral tumor tissues as compared to the adjacent normal tissues. Further, we found that NPM1 could enhance the autoacetylation of p300 thereby increasing its catalytic activity. In line with this, we also found global histone acetylation marks such as H3K9ac, H3K14ac, H2AK5ac, H3K56ac to be elevated in oral tumor tissues. We designed a water soluble inhibitor that could target p300 catalytic activity and found that it could bring about a significant reduction in the acetylation levels in oral tumors generated in nude mice consequently bringing about tumor regression. Further, acetylation of NPM1 enhances its histone chaperoning and transcriptional activation ability. We are currently trying to address the transcriptional network controlled by NPM1/AcNPM1 during oral tumorigenesis.

Our laboratory has also discovered that highly abundant human positive coactivator PC4 is a histone interactingbonafide component of chromatin involved in genome compaction and organization. Silencing PC4 expression by means of siRNA as well as lentivirus mediated stable knockdown, dramatically alters the transcription activation related epigenetic marks and thereby a huge array of genes. PC4 knockdown cells show remarkable defects in cell cycle, genome size, and also in nuclear architecture, which resembles highly progressive cancerous cells. Significantly, it was found that PC4 is down regulated in all types of Breast Cancer samples collected across the globe. The cause and functional consequences of this down regulation of PC4 is being investigated.

Epigenetic control of glioma stem cell biology in the tumor microenvironment

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Glioblastoma, with their heterogeneous tumor microenvironment, present with uniformly poor prognosis. Their hypoxic interiors are known to contribute to their aggressiveness and outcome. Often, such hypoxic microenvironment is linked with cancer stem cell (CSC) formation. CSCs are known to contribute to the chemo/radioresistance and tumor recurrence and are therefore, extremely relevant in glioma biology. Key pluripotency markers are associated with these CSCs and maintain their phenotype. Previous work has shown that aberrant site-specific methylation and genome-wide hypomethylation is associated with hypoxia-induced genomic instability in gliomas. Taking off from there, we questioned the relevance of epigenetic modifications in formation of glioma CSCs. In this work, we have elucidated the molecular mechanism responsible for the observed hypoxia-induced hypomethylation in CSCs. Our study highlights the relevance of the newly characterized demethylase, TET and its isoforms as key effectors of multipotency maintainence in gliomas.

Artemisinin induces apoptosis in HPV-39 infected human cervical cancer cells

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Introduction: Artemisinin, derived from Artemisia annua, has been suggested to have anti-cancer effects, both in vitro and in vivo. Although the primary mechanism of its anticancer activity is thought to be induction of apoptosis, detailed mechanisms are yet to be elucidated. **Objectives:** The major objectives were to investigate the anti-cancer effects of artemisinin in human cervical cancer cells, with special emphasis to inducing apoptosis and repressing cell proliferation by inhibiting the telomerase subunits, the ERα which is essential for maintenance of the cervix, and downstream components like VEGF. **Material and Methods:** Effects of artemisinin on apoptosis of ME-180 cells were measured by MTT assay, flow cytometry, DAPI and annexin V-FITC staining. Telomerase activity measured using PCR based ELISA kit. Expression of genes and proteins were quantified

by semi- quantitative RT-PCR and western blot analysis, respectively. Nanoparticles were also designed to assure better uptake at lower concentrations. **Results:** Artemisinin significantly downregulated expression of ERα and VEGF, known to induce angiogenesis. Anti-proliferative activity was also supported by decreased telomerase activity and reduced expression of hTR and hTERT subunits. Additionally, artemisinin reduced expression of the HPV-39 viral E6 and E7 components. Artemisinin-induced apoptosis was confirmed by FACS, nuclear chromatin condensation, annexin V staining. Increased expression of p53 with concomitant decrease in expression of the p53 inhibitor Mdm2, further supported that artemisinin-induced apoptosis was p53-dependent. Nanoformulations confirmed efficient uptake and activity. **Conclusions:** The results clearly indicate that artemisinin induces anti-proliferative and pro- apoptotic effects in ME-180 cells, and warrants further trial as an effective anti-cancer drug

Role of Oxygen upon protein aggregation in hypoxic tumor

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miR-214 targets HMGA1 and inhibits growth, migration & invasion in human cervical and colon cancer cells

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Introduction: High Mobility Group (HMG) proteins are non-histone chromosomal proteins with an oncogenic role in several cancers. Recent studies have demonstrated the effectiveness of microRNAs (miRNAs) in regulating the expression of oncogenes and tumor suppressor genes. **Objectives:**To study the role of miR-214 in targeting HMGA1 and its functional consequences in human cancer cells. **Materials and Methods:** qRT-PCR, western blotting, 3'UTR luciferase assays, BrdU incorporation cell proliferation assay, invasion and migration assays. **Results:** Among the miRNAs predicted to have binding sites in the 3'UTR of HMGA1, miR-214 was chosen since miR-214 and HMGA1 exhibit an inverse relationship in their expression in cervical and coloncancers in comparison with corresponding normal tissues. 3' Untranslated Region (3'UTR) luciferase assays showed that in cervical (C33A, SiHa and CaSki) and colon (SW480 and SW620) cancer cells, miR-214 reexpression significantly reduced HMGA1 wild- type 3' UTR-mediated luciferase activity but not that of its mutant. Ectopic expression of miR- 214 markedly downregulated HMGA1 both at the transcriptional as well as post- transcriptional levels in C33A, SiHa, SW480 and SW620 cells. To assess the functional consequences, either miR-214 was reintroduced or HMGA1 was knocked-down using siRNA in cervical and colon cancer cells resulting in reduced proliferation as well as their invasive and migratory potentials. **Conclusions:** These results demonstrate that HMGA1 is a novel target of miR-214 and elucidate the tumor suppressor potential of miR-214 in human colon and cervical cancer cells bydown-regulating the expression of oncogenic protein HMGA1to impair proliferation, migration and invasion. **Declaration:** The authors declare that there is no conflict of interests in presenting the above work

Role of Oxygen upon protein aggregation in hypoxic tumor

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Cell killing by blunting cell cables: Interplay between microtubule dynamics, apoptosis and drug resistance

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Perturbation of essential cell survival pathways by modulating redox homeostasis in grade IV glioblastoma multiforme

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Glioblastoma multiforme (GBM) is a grade IV brain tumor with poor prognosis and extremely high mortality rate. Therefore, development of new effective therapeutic strategies for this disease management is the need of the hour. Our lab has identified a novel pro-oxidant carbazole alkaloid (CM-5) molecule from an edible plant, which is effective in different cancers with various oncogenic mutations identified by several biophysical and biochemical analysis both in vivo and in vitro model1-6. Here we wanted to address whether CM-5 is also effective against GBM and its modes of action in this malignancy. We demonstrated that CM-5 is effective against an array of GBM cell lines (PTENmu, PTENwt EGFRwt and EGFRvIII). It inhibits mitochondrial complex-III which leads to increased threshold level of ROS that perturbs cellular homeostasis. The accumulated ROS induces DNA damage response that mediates Chk1/Chk2 upregulation and activation which are essential factors for the G0/G1 arrest in GBM cells7. We also identified that CM-5 inhibits mTORC1 and mTORC2 activity differentially based on their level of existence in U87MG and LN229 cells depending on PTEN mutation status8. Furthermore, we demonstrated that CM-5-treated G0/G1 arrested cells are less potent to form xenograft tumor in vivo. They exhibits reduced ability to migrate and form intercellular tube-like structures and become susceptible to differentiation to form astrocyte- like cells from the epithelial lineage. Taken together, we have established that complex III of ETC is one of the possible potential targets of CM-5. This nontoxic chemotherapeutic molecule enhances intracellular ROS, induces cell cycle arrest, inhibits mTORC1/mTORC2 activity and thereafter regresses GBM without effecting normal astrocytes. References Bhattacharya K.....Chitra Mandal (2010). Biochem Pharmacol;79:361-72. Samanta S..... Chitra Mandal (2013). J Med Chem;56:5709-21. Sarkar S.....Chitra Mandal (2013). Int J Cancer;132:695-706. Mandal et al. US patent. (2014); Pub No:US8637679 B2. Das R..... Chitra Mandal (2014). Apoptosis;19:149-64.

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Development and validation of a broadly distributed IHC based test for optimal treatment planning for Stage 1 and 2 IDC of breast patients: Beyond ER, PR, Her2 and Ki67

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Introduction:'Breast Cancer recurrence risk in early stage patients is currently assessed using clinical parameters and biomarker based tests including Oncotype DX and MammaPrint. Such methods are useful but insufficient as they apply only to a limited set of node negative patients and are largely prognostic with restricted chemopredictivity. There is an unmet need for a'predictive' test which will: i) Accurately estimate the 'risk of recurrence' and enable optimum treatment planning for a broader set of patients ii) Offer new 'targeted drugs'. **Objectives:**Molecularly defined tests based on signaling pathways other than proliferative/hormone dependent pathways (viz: ER/PR/Her-2-neu) would be of tremendous help in finding 'predictive biomarkers' which are indicative of not only risk of recurrence, response to chemotherapy but helpful in development of new targeted drugs. In specific, our approach is to develop test based 'predictive/targetable' biomarkers to overcome the limitations of the existing tests by being useful for assessing risk of recurrences and offer targeted therapy. (1) To develop and validate a test based on 'predictive biomarkers' for ER+/PR+/Her2-or+ breast cancer patients in Stage 1 & 2 to assess risk of recurrence and usefulness of chemotherapy. (2) License the 'predictive biomarkers technology' to a Pharma to develop new drugs. **Material and Methods:**~40 key biomarkers from multiple molecular pathways critical in pathogenesis of Breast Cancer including apoptosis, self-renewal, angiogenesis selected from literature review were analyzed by IHC on a training set comprising 400 samples as a retrospective study. Inclusion criteria: IDC, Stages I-IIIc Age <74, ER+/PR+, Her2+/-, with minimum 5-year follow up and known clinical outcome. Oncopathologists graded the slides for percentage of tumor stained and staining intensity. The IHC data was analyzed using a Statistical model developed using SVM based method, which is a robust predictor of outcome. The "OncoStem Score" that was developed stratifies patients into low or high-risk for recurrence based on a combination of 6 best bio-markers. **Results:**As per EGAPP recommendations the robustness of our assay was first confirmed in analytical validation experiments by comparing Inter-pathologist, Inter-operator, Inter- tumor block and Inter-laboratory/ site variation. While minor changes in 'OncoStem Scores' were observed, none of the variables tested had any effect on the 'outcome prediction/accuracy' of risk stratification. Importantly, when comparing Inter-pathologist variation, the Intra-class correlation (ICC) is 0.933, indicating almost perfect correlation between both Pathologists' scoring patterns. Retrospective clinical validation on additional 350 cases shows 90% accuracy in predicting risk of distant recurrence in breast cancer patients with Stage 1, 2 & 3A with ER+/PR+/Her2- or + disease. The Specificity of the test is 87%, and Sensitivity is 55%. Further, the NPV of the test is 90%. We also analyzed the 'Stage and grade' distribution of low risk patients predicted correctly. Overall 57% and 33% patients classified as 'low risk' belonged to Stage 2 and 3 respectively. Majority patients in 'low risk' had Grade 2 and 3 disease over Grade 1. We found no correlation between the OncoStem Score and Ki67 expression. Interestingly, a small head- to-head study (N=31) shows that the OncoStem assay is superior in predicting outcome compared with Oncotype Dx **Conclusions:** We have developed a robust IHC based 'prognostic and predictive' cost effective and 'broadly distributed' test- more suitable for Stage 1&2 patients in India and SE Asia. Our test will spare many node positive patients from excessive chemotherapy and will offer targeted drugs in future to high risk individuals.

Reduced DOCK4 Expression Leads to Erythroid dysplasia in -7q Myelodysplastic Syndromes

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Anemia is the predominant clinical manifestation of Myelodysplastic syndromes. Even though deletion of the 7q chromosomal region is commonly seen in MDS and leads to a worse prognosis, the pathogenic genes on this region have not been identified. DOCK4 is a GTPase exchange factor that is present on the commonly deleted 7q31 region; is found to be underexpressed in MDS bone marrow samples, and the reduced expression is associated with decreased survival in patients. We demonstrate that depletion of DOCK4 levels leads to erythroid cells with multiple morphological defects both in vivo and in vitro. Reduced expression of DOCK4 leads to disruption of the F-actin skeleton causing erythroid dysplasia that phenocopies the red cell defects seen in primary samples from -7q MDS patients. Molecularly, DOCK4 knockdown impacts Rac1 GTPase activation leading to increased phosphorylation of the actin stabilizing protein, adducin in del(7q) MDS. These data identify DOCK4 as a 7q gene whose haploinsufficiency can lead to erthyroid dysplasia.

THE INDIAN CLINICAL TRIAL ON THE QUADRIVALENT HPV VACCINE: KNOWLEDGE GAINED AND FUTURE IMPLICATIONS

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In 2009, International agency for Research on Cancer(IARC) initiated a phase 4 trial comparing the efficacy of 2 doses versusthe standard 3 doses of quadrivalent HPV vaccine (Gardasil™) in India. The trial recruited 17,729 participants- healthy unmarried girls aged 10-18 years, from different geographical regions across India, through Tata Memorial Hospital, Mumbai;NargisDutt Memorial Cancer Hospital, Barshi, Jehangir Clinical Development Centre, Pune;Christian Fellowship Community Health Centr, Ambilikai; Gujarat Cancer Research Institute, Ahmedabad, All India Institute of Medical Sciences, New Delhi; MNJ Institute of Oncology and Regional Cancer Centre, Hyderabad and Cancer Foundation of India, Kolkata. The Rajiv Gandhi Center for Biotechnology (RGCB) served as the central bio-repository and experimentalanalysis hub for the study.

After vaccination, blood samples were collected for evaluation of immune response at different time points and a speculum examination of the cervix and collection of cervical cells from these volunteers was done 18 months after their marriage or 6 months after delivery and one year intervals thereafter. Participants were followed up for their prolonged antibody response at different time points starting from one month after they receive their last dose till 36 months after vaccination and is till continuing. They are now being followed up for further confirmation of the vaccine efficacy by ruling out infection due to HPV subtypes included in the vaccine by testing their cervical specimen.

Our findings confirm that two doses of quadrivalent HPV vaccine, administered with an interval of 180 days or more, are immunologically non-inferior to the three-dose schedule and afford protection against incident and persistent HPV 16, 18, 6, and 11 infection that is similar to that afforded by three doses. We also report the first evidence to our knowledge that one dose of quadrivalent HPV vaccine induced detectable titers of HPV neutralizing antibodies and that lower vaccine-induced antibody concentrations after one dose of quadrivalent HPV vaccine provide similar protection against vaccine-targeted HPV infections compared with the higher antibody concentrations induced after two or three doses.Further long-term follow-up of vaccinated women in our study will clarify whether protection afforded after one dose of quadrivalent HPV vaccine is long lasting. Administration of three doses of HPV vaccine, or two doses as recommended by WHO, remains a challenge, and if one dose proves to be as efficacious as more doses, vaccine use will be improved and costs reduced. Data on immunogenicity, durability of antibody response, and the frequency of persistent infection after one dose of vaccine will expedite the introduction of HPV vaccination in national immunizationprograms.

Translating biology to therapy : The tale of Human papilloma virus and cervical cancer

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Introduction : Cervical cancer is one of the most common cancer in women in India accounting for 1,32,082 new cases, with mortality of 74,118 cases per year. Although HPV infection is a major risk factor, but host genetic factors / gene-environment interactions may influence cervical cancer pathogenesis. Prophylactic vaccines against HPV 16 and 18 are available commercially but no therapeutic vaccine is available. **Objectives:** We have evaluated the type specific incidence of HPV infection and HPV-16 variants. host genetic factors such as folate, Vitamin B-12, homocysteine levels, DNA repair genes and their variants vaccine strategies having both prophylactic and therapeutic potential against HPV16,18. curcumin as an adjunct to standard chemotherapy/ radiotherapy. **Methodology:** Cervical cells/ biopsies collected from cervical cancer subjects were tested for HPV using consensus/type specific primers. Variants of HPV-16 were characterized by full length sequence analysis of L1, E6 and E7. Serum folate, vitamin B12 and homocysteine analysed by ELISA using respective kits. DNA repair genes by PCR-RFLP and DNA sequencing. Chimeric VLPs were formed using DNA from HPV16 or 18 positive only cervical cancer samples, cloning of L1 and E7 was done in appropriate vector, recombinant protein expressed and purified, followed by in vitro assembly into chimeric VLPs. Immune response to CVLPs was measured by T cell proliferation assay, cytokine ELISA, cytotoxicity measured using LDH assay, and in vivo tumor induction and regression analysis done using TC-1 cells in C57BL/6J mice. The effect of curcumin was studied on cervical cancer cell lines and in cervical cancer subjects **Results:** HPV 16 showed highest incidence rate, followed by HPV-59, -52 and -18. Similar distribution of HPV-16 variants was seen from different regions of India, with the European variant E350G being the most prevalent (58%). Low levels of serum folate and vitamin B12, whereas increased levels of homocysteine were observed in cervical cancer subjects. Maximum alterations were seen in XRCC1 (codon 194 > 399 > 280) followed by ERCC4 (415 codon). Subcutaneous injection with chimeric VLPs enhanced serum IgG levels, showed lymphocyte proliferation, generated specific CTL mediated cytotoxic secretion of different cytokines. CTL generation in vitro against E7 protein essentially showed Th-1 response. Seroreactivity of young women with persistent HPV16 infection showed that CVLPs detected neutralizing antibodies against L1 capsid protein. Antibodies against L1 capsid protein were able to inhibit hemagglutination. Similar findings were obtained for HPV-18 chimeric VLPs. In- vitro curcumin treatment of cervical cancer cells led to radiosensitization. Combining curcumin with current chemotherapy and/or radiotherapy showed ability to prevent adverse events in cervical cancer patients. Conclusion: Poor folate and vitamin B12 status may contribute to cervical cancer risk through effects on one carbon metabolism and inefficient DNA repair. Supplementation with folate and vitamin B12 could be a viable non-vaccine approach for prevention of cervical cancer in India. The above study has provided a basis for rational design of protein based chimeric vaccine for controlling HPV16,18 infection and associated tumors.

Key words : Human papilloma virus, cervical cancer, chimeric VLPs

Promoter hypermethylation in GSTPi, HIC1 and CDH1 genes as a marker for early stage triple negative breast cancer

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Abstract Background.E-mail: bcdas48@hotmail.com

Triple negative (ER11/PR11/Her211) breast cancers are most frequent aggressive tumors in younger women, and are associated with early relapse and poor prognosis. Epigenetic silencing of specific tumor suppressor genes plays an important role in breast cancer initiation and progression but till date no epigenetic biomarker(s) is linked with triple negative breast cancers. In this study, five tumor suppressor genes, BRCA1, p16, GSTPi, HIC1 and CDH1 have been investigated to see if the methylation pattern could serve as a reliable indicator for early detection/progression and/or prognosis of triple negative breast cancer. **Materials and Methods:** Genomic DNA isolated from 124 primary breast tumor biopsies employed for sodium bisulfite conversion of genomic DNA was performed for analysis of promoter methylation by methylation specific polymerase chain reaction (MSP) and the results obtained correlated with the level of the expression of the genes, stage/grade of the disease and clinicopathological parameters. **Results:** Out of five specific tumor suppressor genes, GSTPi, HIC1 and CDH1 showed significantly a higher level of methylation in early stage triple negative breast cancer; GSTPi promoter was hypermethylated in 100% of cases leading to loss of expression in 50% of the TNBCs while HIC1 and CDH1 were hypermethylated in 88.88% tumors with a loss of expression in 37.5% and 25% respectively in early stage triple negative breast cancer. **Conclusion:** The results suggest that hypermethylation of these genes may serve as a potential predictive biomarker for early identification and progression of aggressive triple negative breast cancer.

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Journal of Carcinogenesis

ACOS ORAL PRESENTATIONS

12th International Conference of Asian Clinical Oncology Society, 8th-10th April 2016, New Delhi, India

Role of Axillary ultrasound, Fine needle aspiration cytology and Sentinel lymph node biopsy in clinically N0 breast cancer.

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Background: This study evaluates the combined role of axillary ultrasound, fine needle aspiration cytology and sentinel lymph node biopsy in clinically N0 axilla. **Methods:** Between January 2014 and June 2015, 150 women with early breast cancer underwent axillary ultrasound as a first investigation for nodal status. Suspicious nodes were subjected to image guided fine needle aspiration cytology. Non-suspicious and fine needle aspiration cytology negative axillary nodes proceeded to sentinel lymph node biopsy at time of primary breast surgery. All confirmed positive (cytology and frozen) cases proceeded to axillary lymph node dissection. **Results:** 52 women had positive axillary nodes at final histology. Axillary ultrasound with fine needle aspiration cytology identified 27 patients with positive axillary nodal status and had a sensitivity of 84.36 % (27/32) and specificity of 87.5% (14/16). Intra-operative frozen analysis identified a further 13 cases with sensitivity of 56.52% (13/23) and specificity of 97.56% (80/82). **Conclusion:** Overall 76.92% (40/52) patients with positive axillary metastasis were identified peri-operatively using combination of axillary ultrasound, cytology and sentinel lymph node biopsy.

Key words: Axillary Ultrasound, Fine needle aspiration cytology, Sentinel lymph node biopsy, Breast cancer.

Implication of loss of Parkin gene expression and its association with BRCA1 gene in human breast cancer

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Introduction: Breast cancer is a leading cause of cancer-related mortality that affects women worldwide.PARKIN (PARK2) is an E3 ubiquitin ligase involved in multiple signalling pathways and cellular processes. Although, dysfunction of PARK2 is associated with the progression of Parkinsonism, emerging evidences suggest that PARK2 is a tumour suppressor gene, plays important role in different types of cancer. However, till date, there is no study with respect to Parkin gene-BRCA1 association in breast cancer. **Objectives:** To investigate Parkin status in breast cancer with respect to BRCA1 gene, immunohistochemical protocol was applied on tissue sections obtained from 40 cancer patients. The expression pattern of Parkin was evaluated with the BRCA1 and other receptors like ER, PR and Her-2. Parkin expression was also correlated with clinic opathological parameters. **Material and Methods:** A total of 40 breast cancer samples and their adjacent normal tissue samples were taken from Rajiv Gandhi Cancer Institute and Research Centre according to the guidelines of the 'Institutional ethical committee'. Immunohistochemistry was done to evaluate the expression of Parkin, BRCA1 and other receptors like ER, PR and Her-2. A chi square test was done to find out any significance. **Results:** Parkin expression was found to be lost in 75% (30/40) cases. A statistically significant relationship was found between the loss of Parkin expression and age (p=0.03), BRCA1 (p=0.01) and Progesterone (p=0.01). While, no significant relation was observed between the loss of Parkin expression and tumor size, lymph node status, histological grade and other markers like ER and HER-2. **Conclusions:**These results suggest that Parkin acts as a tumor suppressor in human breast cancer which also seems to have association with BRCA1 familial cancer cases of old age. Future studies with a larger sample are still needed to confirm our findings and consider other risk factors.

Keywords: Parkin, BRCA1 and Breast Cancer.

Acknowledgment: Financial support to conduct this work by DST (Department of Science and Technology), New Delhi, is thankfully acknowledged.

Outcome with use of 12 weeks of adjuvant or neoadjuvanttrastuzumab in a resource constrained setting

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Background: Adjuvant trastuzumab has improved overall survival in women with HER2 receptor positive breast cancer. However, only a small fraction (4%) of eligible patients in resource constrained settings have access to this drug. A patient assistance program of 12 weeks of adjuvant or neoadjuvanttrastuzumab was thus started for those who did not have any access to trastuzumab due to financial constraints. We undertook a retrospective analysis of outcomes in women who were enrolled between January 2011 to December 2012 in this patient assistance program . **Methods:** Patients received four cycles of anthracycline based chemotherapy (AC/CAF/ EC/CEF) and 12 doses of weekly paclitaxel (80mg/m2) with trastuzumab (4mg/kg loading followed by 2mg/kg) in the neoadjuvant or adjuvant setting in either sequence (anthracycline followed by taxanetrastuzumab or taxanetrastuzumab followed by anthracycline).

Patients received adjuvant hormonal therapy depending on the hormone receptor status. The primary endpoint of this analysis was disease free survival (DFS). **Results:** A total of 103 patients with HER2 receptor positive breast cancer were analysed. The median age was 46 (24-65) years, 50% were premenopausal, 60.7% had stage III disease (86.8% had node positive disease) and 37% patients had ER and or PR positive disease. Forty patients (38.8%) had breast conserving surgery while the rest had modified radical mastectomy. At a median follow-up of 34 (7-46) months the 3-year DFS and overall survival was 77.2% and 82.7% respectively. Among patients who developed recurrence one had only local recurrence, 4 had both local and distant recurrence and 11 had distant metastasis alone. Of the 15 patients who developed distant metastasis 7 had brain involvement . Symptomatic cardiac dysfunction developed in four patients, two of whom died while in the other 2 ejection fraction recovered. The results are summarized in the table

Patient Characteristic and outcome with 12 weeks of adjuvant or neoadjuvantTrastuzumab

Number of Patients	Node Positive (%)	Hormone Positive (%)	DFS at 3 years	OS at 3 years	Brain Mets (%)	Grade 3/4 Cardiac Toxicity (%)
103	86.8	37	77.2	82.7	6.8	3.9

Conclusion : These results suggest that 12 weeks of neoadjuvant or adjuvant trastuzumab is an acceptable alternative in patients who lack access to full 1 year of trastuzumab.

Claudin-4 as predictors of response to neoadjuvant chemotherapy in breast cancer.

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Background: Neo-adjuvant chemotherapy (NACT) is an integral part of multi-modality approach in the management of locally advanced breast cancer and is vital to predict response in order to tailor the regime for a patient. Claudins are important transmembrane proteins in tight junction. Claudin- 3,4 & 7 are often present in breast tumour and are occasionally expressed at elevated levels. A prospective clinical study was conducted to assess whether these markers could serve as reliable predictors of response to NACT in patients with LABC. **Materials &Methods:** 30 LABC patients after complete routine and metastatic work up were subjected to trucut biopsy and the tissue evaluated, immunohistochemically for claudin-4. Three cycle NACT were given at three weekly intervals & patients assessed for clinical response after each cycle. Modified radical mastectomy was performed in all patients three weeks after the last cycle and specimen were re-evaluated for any change in the claudin-4 expression. The immunohistochemical response (change in the expression of claudin-4 marker) and the clinical response were correlated. **Results:** A statistically significant correlation was observed between clinical and immunohistochemical response to NACT. Increase in the expression of claudin-4 indicated poor response to NACT and thus a poor outcome. **Conclusions:** claudin-4 can be effectively utilized as predictors of response to NACT .

Next-generation sequencing for diagnosis of patients with hereditary breast and ovarian cancer.

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BRCA1 and *BRCA2* genes are the two most commonly mutated genes in families with Hereditary Breast and Ovarian Cancer (HBOC). However several additional breast cancer predisposition genes are now known to be associated with HBOC. Parallel sequencing of these multiple genes is possible with customized next generation sequencing panels. In the present study we evaluated twenty breast cancer patients with positive family history of breast and ovarian cancer were subjected to high throughput next generation sequencing panel testing. Genes analyzed in the panel are ATM, BARD1, BRCA1, BRCA2, BRIP1, CDH1, CHEK2, EPCAM, MLH1,MRE11A,MSH2, MSH6, MUTYH, NBN, PALB2, PMS2, PTEN, RAD50, RAD51C, STK11,and TP53. Mutations identified by NGS were validated using sanger sequencing. Software analyses by Polyphen-2, SIFT, Mutation Taster and Align-GVGD was done to predict damaging effect of novel variants. Predictive genetic testing and counselling was done for the first degree relatives. Pathogenic mutations in 7 out of 20 patients (35%) were identified. In rest of the seven patients we found several variants of unknown significance (VUS). Four patients had mutations in BRCA1 gene (c.5074+1G>A, c.4484+1G>A, c.4552C>C/T p.Q1518Ter, c.7480C>T; R2494X) and one patient had mutation in BRCA2 gene (c.9215T>A p.Val3072Glu). One of the patients had a novel nonsense mutation in MRE11 gene (c.1090C>T: p.Arg364Ter). Another patient was a double heterozygote for mutations in MSH6 and BARD1 gene. In-silico analysis, segregation study in the family and 100 normal controls were studied to confirm the pathogenicity of novel mutations. Multi-gene parallel sequencing allowed more effective and accurate diagnosis of HBOC families and supports incorporation of panel testing into clinical practice. Clinical genetic counselling for patients with novel variants and VUS in intermediate penetrance gene is complex and challenging and further studies are needed to clarify the precise management of these patients.

Biography

Dr. Pratibha Bhai is working as a Scientist at Center of Medical Genetics, Sir Ganga Ram Hospital, New Delhi, India after obtaining her doctoral degree in Medical oncology from All India Institute of Medical Sciences, New Delhi India. At her current position she is supervising cancer related molecular investigations and providing genetic counselling at Sir Ganga Ram Hospital, New Delhi India. She is doing extensive research in finding cancer predisposition mutations in families with hereditary cancer syndromes using next generation sequencing platform. Her major focus is on Breast cancer, which has now become the most common cancer among Indian women. She is also working on the identification of driver actionable mutations in tumours to identify patients who can benefit with appropriate molecular targeted therapies

Triple Negative Locally Advanced Breast Cancer: Value of interim FDG PET-CT in predicting the histopathological outcome following neoadjuvant therapy (A single centre prospective study)

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Aim: Pathological complete response (pCR) to neoadjuvant treatment correlates with improved survival of patients with triple negative locally advanced breast cancer. We prospectively investigated the ability of interim ^{18}F-FDG PET-CT to predict pathological response early. **Materials and Methods:** During 48 months, consecutive patients with locally-advanced (T4 according to AJCC 7thed) or large (T3 according to AJCC 7th ed) triple negative (absence of ER, PR & HER 2-neu expression) breast cancer patients without distant metastases (Anatomic stage IIB, IIIA, IIIB according to AJCC 7th ed) were included. All patients received neoadjuvant chemotherapy (NACT, at least 3 cycles). 18F-FDG PET-CT was performed at baseline (PET 1) and after two cycles of chemotherapy (PET 2). All patients who did not progress following completion of NACT (Stable disease / partial response / complete response according

to PERCIST criteria) were subjected to modified radical mastectomy with axillary dissection. The correlation between pathologic response (presence / absence of residual viable tumor assessed in the post-operative histopathological specimen) and standardized uptake value (SUV Max calculated per lean body weight at baseline and after two cycles) was examined. **Results:** Thirty consecutive patients were included. At baseline (PET 1), 22 patients had PET-positive (SUV Max more than blood pool activity calculated at arch of aorta) axillary lymph nodes and in nine of them FDG uptake (calculated as SUV Max per lean body weight) was higher than in the primary tumor. At surgery, 14 patients (47%) showed residual viable tumor (non-pCR) while 16 had pCR (no viable tumor in histopathology specimen). There was a strong correlation between the highest residual SUV Max at PET 2 (post 2 cycles of NACT) and pathological response (Post 3 cycles of NACT). Any site of residual FDG uptake with a SUV Max >3.0 whether in breast or axilla was predictive of non-pCR. The risk of non-pCR was 92.3% in patients with any site of residual SUV Max > 3.0 on interim PET (PET 2) vs. 11.8% in patients with SUV Max ≤ 3.0 (p = 0.0001). **Conclusions:** In cases of triple negative locally advanced breast cancer, highest residual FDG uptake after two cycles of neoadjuvant chemotherapy predicts residual disease (viable tumor tissue in post-operative histopathology specimen) at the completion of neoadjuvant treatment. Because many innovative therapeutic strategies are now available early prediction of poor response is critical.

Keywords: FDG PET/CT, breast cancer, triple negative, locally advanced

Explanations to Acronyms:

^{18}F-FDG-PET/CT:^{18}F-Florodeoxyglucose-Positron Emission Tomography/ Computed Tomography
NACT : Neo-Adjuvant Chemotherapy
PET 1 : Baseline 18F-FDG-PET/CT SCAN
PET 2 : 18F-FDG-PET/CT SCAN at the completion of 2 cycles of NACT
pCR : Pathological complete response, Pathologically no viable tumor in post-operative (post 3 cycles of NACT) histopathology specimen
non-pCR : Pathological incomplete response, Presence of viable tumor in post-operative (post 3 cycles of NACT) histopathology specimen

The role of topoisomerase [IIA] as a predictive factor for response to neoadjuvantanthracyclines based chemotherapy in locally advanced breast cancer.

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Background: Surrogate markers may be used to assess the response toneoadjuvantchemotherapy.Thepurpose of the study was to evaluate topoisomerase IIα as predictive factor for response to neoadjuvantanthracyclines based chemotherapy in locally advanced breast cancer patients. (1) tumour grade scored according to the Elston–Ellis classification, (2) hormonalreceptor (HR) status, (3) tumour cell proliferation evaluated by Ki-67 staining, (4) HER-2 and topoisomerase II alpha (TopoIIa) expression evaluated byimmunohistochemistry (IHC). **Method**:Between January 2012 andjune 2012, 50 locally advanced breast cancer patients had received 3 cycles neoadjuvant chemotherapy were studied in clinical oncology department at tanta university. Regimens including either CEF (cyclophosphamide 500mg/m^2,epirubicin100mg/m^2, 5-fluorouracil 500mg/m^2) or FAC(cyclophosphamide500mg/m^2,doxorubicin 50mg/m^2, 5 fluorouracil 500mg/^{2}). Protein expression of HER2and Topo IIα were determined by immunohistochemistry. The primary endpoint was pathological and clinicalTumour responsethat assessed clinically and bymamography, then by pathological assessment. **Results:**Of 50 primary locally advanced breast cancer patients had been assessed after 3 cycles of NACT, the clinical complete response was in 6% (3/50), clinical partial response was in 86% (43/50) and overall clinical response was 92% (46/50), 4 (8%) patients had clinical stable disease and no one developed disease progression. 1-Responders had the following biomarkers criteria: Clinical (CR): 3 patients had co-expression of topo II and HER2, hormonal receptor negative and high KI-67. Clinical(PR):43 patients majority of them had topo IIA overexpression. 2-Non responders had the following criteria: 4(8%) patients all had negative (TOPOII/HER2), low KI-67and 2 had hormonal receptor positive and another 2 had hormonal receptor negative. **Conclusion:**Our study suggests that HER2 and Topo IIα overexpression could be predictors of the response toneoadjuvantchemothrapy in both the CEF and FAC arms.

Study the role of deregulation in folate pathway in the susceptibility and severity of triple negative breast cancer and response to treatment

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Introduction: Triple-negative breast cancer (TNBC), defined as tumours lacking in oestrogen receptor (ER), progesterone receptor (PR) and overexpression of Human Epidermal Growth Factor Receptor 2 (HER-2) gene amplification, accounts for 15% of all breast carcinomas in Asian and Western populations. The incidence of TNBC is increasing at an alarming rate in North-East India and is found to be most prevalent in younger age group women who are at their reproductive age. TNBC has an unclear molecular aetiology and hence limited targeted therapies. A high homocysteine and low folate accounts for a feature of many diseases in women including cancer. **Objectives:(1)**To screen the association of genetic alterations in MTHFR and TYMS genes and the predisposition to TNBC development, severity and response to 5FU based chemotherapy. **(2)**To study the role of differential expression profile of FR-α in the pathogenesis of TNBC. **(3)** Screen the correlation of altered homocysteine levels in the development of TNBC. **Material and Methods:**This is primarily a northeast India based study of breast cancer patients who have been treated with fluorouracil (FU). Tissue sections were collected and histopathologically characterized as TNBC cases (n=), non-TNBC cases and non-neoplastic control (n=). Blood samples was collected from age-matched healthy women (n=) for comparative analysis. A structured questionnaire was formed wherein patient history, course of treatment, relapse and mortality rate was filled up and updated. MTFHR C677T mutation and 6bp deletion of 3'UTR region in TYMS gene was studied by PCR-RFLP. The protein expression pattern of Folate Receptor alpha (FR-α) and Homocysteine was performed by IHC. Statistical analysis was performed by SPSSv13 software. **Results: (1)** Mutation in MTHFR gene (C677T) is not associated with TNBC development in our cohort. **(2)***TYMS* gene 3'UTR 6bp del/ins wildtype genotype is significantly associated with the predisposition to TNBC {OR=; p=} compared to controls. **(3)** The TYMS wildtype genotype was associated with the severity {OR=; p=}, mortality {OR=; p=}, and significantly associated with the recurrence of the disease (p=). **(4)** A higher homocysteine level in tissues is one of the major factors associated with the development of TNBC. The tissue homocysteine levels were independent of the MTHFR mutation status. **(5)** The expression of Folate receptor-alpha at both protein and mRNA levels was found to be higher in the TNBC cases compared to control cases which points towards the fact that cancer cells require a high level of folate for DNA synthesis and metabolism. **(6)** The higher homocysteine levels correlated with higher FR-α levels, which is important for the localization and stabilization of FR-α in the nucleus, which is of immense importance as it is associated with activation of multiple molecular factors downstream like stem cell maintenance, cell motility and proliferation which are all hallmarks of cancer development. **Conclusions:** Alterations in the folate pathway is critically associated with the susceptibility and severity of TNBC. It is also detrimental for the response to 5FU based chemotherapy in TNBC patients; directly effecting the mortality status of the patients. Hence the pathway components also are of prognostic significance for the clinicians for better patient management, and planning of therapeutics.

Keywords: TNBC – FU –MTHFR –TYMS – Homocysteine –FR-α

Prognostic Significance of BRMS1 in Breast Cancer and it's effect on Metastasis

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Background: Breast cancer has emerged as a major health problem globally owing to it's rising incidence and mortality. The majority of metastatic breast cancers are incurable.Underlying mechanisms of metastasis in breast cancer are largely unknown. Metastatic suppressors and promoters are responsible for decelerating or accelerating the metastatic cascade, respectively. The Breast Cancer Metastasis Suppressor 1 (BRMS1) is a nuclear protein that suppresses cancer metastasis without affecting the tumorigenesis. It has been implicated in many cancers of various organs like lung, prostate, bladder and endometrium. **Aims & Objectives:** The aim of this study was to evaluate the expression of BRMS1 and establish prognostic significance with clinicopathological parameters in breast cancer. Towards this goal, we examined the gene and protein level of BRMS1 in cancer and adjacent non cancerous tissues in a cohort of North Indian breast cancer females. **Materials& Methods:** Quantitative real time Polymerase Chain Reaction (Q-PCR)and immunohistochemistry (IHC) were employed to decipher the mRNA and protein levels in 85 breast cancer and adjacent non cancerous tissues. Out of 85 breast cancer tissues, 54 were non metastatic and 31 were metastatic. **Results:** mRNAexpression of BRMS1 was significantly down regulated in non cancerous tissues as compared to cancer tissues (9.73 ± 3.77; $p < 0.05$). Similarly, metastatic tissues had a lower level of BRMS1 when compared with non metastatic tissue (4.23 ± 1.68; $p < 0.05$). Out of all the clinicopathological parameters evaluated, BRMS1 levels were strongly associated with advanced stage (3.16 ± 1.53; $p < 0.01$) and grade (3.32 ± 1.78; $p < 0.01$). Many of differentially expressed genes are not promising candidate biomarkersdue to discrepancy in mRNA and protein level. Thus IHC experiments with anti-BRMS1monoclonal antibody were carried out which demonstrated that translational level analysis also corroborated same results. We discarded 13.8 % (10 of 85) of samples since they were undetectable for the transcript levels of BRMS1 and proceeded with 86.2% (75 of 85) tissues. BRMS1 nuclear expression was 1 positive in 17.3%(13/75) breast cancer cases, 2 positive in 8% (06/75) breast cases, 3 positive in 30.6%(23/75) cases and negative in 30.6% (33/75) breast cases.Reduced BRMS1 protein levels were strongly associated with advanced stage (12.63 ± 4.17; $p < 0.01$) and grade (13.32 ± 3.92; $p < 0.01$). **Conclusion:**Reduced BRMS1 expression is a strong prognostic biomarker in breast cancer patients for advanced stage and grade and predictor of metastasis in breast cancer. BRMS1 expression may be helpful to clinician to identify an aggressive subset of breast cancer patients and those with propensity for metastatic manifestation which may require alternate therapeutic strategy.

Keywords: BRMS1, breast cancer, metastasis

Computer-aided detection of diagnostically relevant tubule region in H&E stained breast cancer histopathology images.

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Background: Breast cancer (BC) is the second most common cancer (after lung cancer) in women both in the developed and less developed countries. As per the Nottingham grading system, tubule formation score is one of the most important parameters for grading BC histopathology images. In this paper, we propose an automated and efficient detection technique for tubule region segmentation and scoring to assist pathologists in BC diagnosis. **Material and Methods:** A total of 140 hematoxylin and eosin (H&E) stained breast histopathology samples from 70 patients at the Tata Medical Center (TMC) Kolkata were obtained and scanned at 40x optical magnification (1pixel =1.6μm). The size of the each image was 2048 x 1536 pixels (width x height). The proposed methodology comprises of two parts; the first part detects tumor nuclei and the second part identifieslumina. The tubules are formed by grouping closely located tumor nuclei and lumina. The images were first pre-processed using color normalization and mean-shift smoothing. After pre-processing, simple iterative clustering (SLIC) superpixels algorithm was used to group the similar and uniform pixels with similar spectrum and those adjacent in space. In this study, superpixels region size was set to 10 and spatial regularizer to 0.003. In order to identify tumor nuclei and lumina in the image, we extracted 16 features including morphological, textural and fractal features. Finally, a Random forest classifier, combined with 150 binary decision trees, was trained to identify and select those superpixels containing tumor nuclei and lumina. Graph partitioning algorithm was subsequently used to partition pixel-wise undirected graph into tumor nuclei and lumina. The node of the graph denotes individual pixels inside the superpixels of nucleus. Pixels outside the superpixels of the nucleus were assigned as lumina. **Results:** The extensive experiments show that the proposed algorithm can segment tumor nuclei and lumina, thereby identifying the tubules. For quantitative evaluation of the proposed segmentation method, the ground-truth image database of 140 breast histology images was created with the help of two expert pathologists of TMC, Kolkata. The quantitative evaluation of proposed result shows 98.67% segmentation accuracy; the error rate is 0.045.

Table 1: Comparison of the proposed method with existing one

Authors	Accuracy
Existing method	.91(0.03)
Our proposed method	.9867(0.01)

Conclusion: In conclusion, we have presented an accurate technique for computer aided automated segmentation of tubule in images of H&E stained breast cancer biopsies which was further validated with expert pathologists ground truth images. It may be suggested that an automatic tubuleregion detection in BC slides can be developed to assist the pathologists with the help of these promising preliminary results.

Mastectomy skin flap necrosis with premammary fascial skin flaps: Double blind RCT

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Background: In the modern era of breast oncology, the optimum flap thickness supported by robust scientific evidence is yet to be defined. Our study attempts to establish that raising mastectomy flaps at the level of premammary fascia(thick flaps) with cold steel scalpel decreases the incidence of post operative Mastectomy skin necrosis(MSN). **Material and methods:** We conducted a 2x2 factorial, randomised, double blind trial.160 ladies with carcinoma breast planned for simple or modified radical mastectomy(without immediate reconstruction) were randomised into four groups with 40 patients each(Table). Flap raising at premammary fascia(thick flap) was compared against the conventional technique of raising flaps between the large and small fat globules(thin flap).Two tools of flap dissection were compared - cold scalpel with electrodiathermy. Patients with previous history of breast surgery/infection/trauma or burn were excluded from the study. Patients were followed for 30 days after surgery

for assessment of postoperative outcomes. Our primary outcome measure was the development of MSN.

Group(group number)	No. of patients	Necrosis (%)	Relative risk(95% C.I.) p=0.002
Thick flap & Scalpel(1)	40	1(2.5)	1.0
Thin flap & electrodiathermy(2)	40	4(10)	4(0.5-34.2)
Thick flap & Scalpel(3)	40	3(7.5)	3(0.3-27.6)
Thin flap & electrodiathermy(4)	40	12(30)	12(1.6-87.9)

Results: The baseline characteristics i.e.patient profile(age, BMI, breast volume), disease profile(tumour size, location, stage of cancer), treatment received(neoadjuvant chemotherapy, type of mastectomy) were distributed non significantly across the 4 study groups.Overall incidence of MSN was12%. MSN was observed in 12 patients in the group with thin flap & electrodiathermy as opposed to 1 seen in the group with thick flap & scalpel(RR of MSN,12;95% confidence interval,1.6 to 87.9; P=0.002) (Fisher's exact test).14 out of 20 patients with MSN subsequently required surgical intervention. Single factor analysis showed that there is an increased risk of development of MSN with thin flap when compared with thick flap(RR for development of MSN, 4; 95%confidence interval, 1.4-11.4;P= 0.007)(Fisher's exact test). The secondary outcome measures analysed were Seroma, Surgical site infection, blood loss, time taken, total drain output, number of days with drain. **Conclusion:** There is an increased risk of development of MSN when raising skin flaps using conventional technique i.e.between the large and small fat globules(thin flaps). Long term patient follow up is need to observe the loco regional cancer control after raising flaps at premammary fascia(thick flaps).

Adjunct Role of Shear Wave Elastography to B-mode Ultrasound in Characterizing Breast Masses

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Introduction: The Breast Imaging Reporting and Data System (BI-RADS) withB-mode ultrasound (US) providesstandardized terminology to describe features of breast masses and recommendations for management. BI-RADS category 3 (probably benign) and 4a (low suspicion of malignancy) have a less than 2% and 10% risk respectively for malignancy and BIRADS 4a lesions are recommended biopsy. Improved characterization of these masses may allow follow up monitoring and circumvent biopsy. **Objectives:**To determine the adjunct role of shear wave elastography (SWE) to USin characterizing difficult to diagnose breast masses. **Material and Methods:** A prospective study (Jan 2012 to December 2014) was performed on patients with breast mass. An US was done and BI-RADS category assigned. BIRADS 3 /4 masses were included. SWE and biopsy of mass was undertaken. Qualitative (colour, shape, homogeneity) and quantitative SWE [maximum (Emax), minimum (Emin) , mean (Emean) and lesion-to fat elasticity ratio (Erat)] parameters were estimated. Independent blinded analysis of US/SWE images were done. SWE features of benign (BM) and malignant mass (MM) were identified and best quantitative SWE cut-offs estimated. Modified BI-RADS' was obtained by adding individual SWE parameters to US BI-RADS 3 and 4a category masses by up/downgrading the BIRADS category accordingly. The diagnostic accuracy of modified BI-RADS' and US BI-RADS alone were compared. **Results:** Patients (N=119) , mean age 43±13.6 years, with mean mass size of 2.7±1.4 cm were studied.BI-RADS 3 masses were 42, BI-RADS 4, 77[4a (10) ,4b(24) and 4c(43)]. US sensitivity and specificity in detecting malignancy was 96.8% and 70.2% respectively. Qualitative SWE BM parameters were oval/round shape, homogenous/reasonably homogenous and of blue(dark/light) or green color. MM were irregular, inhomogenous and red/orange in color. SWE quantitative cut offs for characterizing masses were- Emin46kPa, Emean102 kPa, Emax 140kPaand Erat8.Modified BI-RADS'using SWEparameters yielded best results with - Ecolor(improved specificity from 70.2% to 78.9%), Emean and Emax(enhancing specificity from 70.2% to 75.4%) **Conclusion**: SWE combined with US significantly improves specificity of breast masses that are difficult to characterize.

Keywords- Shear wave elastography, B-mode Ultrasound, Breast masses

Sentinel lymph node biopsy for breast carcinoma as a day care procedure: Experience from a tertiary care centre in India.

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Background: Intraoperative frozen section analysis for sentinel lymph node biopsy (SLNB) is routinely performed at many centres. However, lack of frozen section facilities in developing countries may warrant a second procedure under general anaesthesia (GA)for those with positive nodes. Thus, performing SLNB under local anaesthesia (LA) may circumvent this problem. **Methods:** Between December 2013 and September 2015, 109 patients with either EBC or LABC after neo adjuvant chemotherapy (NACT) and clinically negative axillae, underwent SLNB as day care procedure using various combinations of radioisotope, blue dye and a fluorescent dye (fluorescein sodium). All specimens were examined using paraffin embedded sections. Those with positive nodes subsequently underwent ALND under general anaesthesia with either mastectomy or BCS. **Results:** Sentinel node identification rate was 90% in EBC (45/50) and 78% in LABC (46/59). Fluorescent nodes were identified in 57% (49/86) patients. Median no. of nodes dissected in both EBC and LABC patients were 2 (range:0-4). Overall positivity rate was 26.3% (24/91) and these patients were spared two procedures under GA. Of the 24 patients with positive sentinel nodes, 5 patients had positive non sentinel nodes on ALND. There were no untoward effects of anaesthetic or tracer dyes. **Conclusion:** Performing SLNB as a day care procedure can be safely and effectively used in settings without facilities for frozen section analysis, thus avoiding the necessity of a second exposure to general anaesthesia.

Keywords: SLNB, day care, frozen section

CD99L2 Isoforms Regulate Transendothelial Migration of Leukocyte in the inflammatoryresponse

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Introduction:CD99L2 is a glycoprotein found on the surfaces of leukocytes and concentrated at the borders of endothelial cells. There are only two proteins related to CD99L2 in the human and mouse genomes. One of these, XGA, is a red blood cell surface antigen and other one is CD99. A similar protein in mouse functions as an adhesion molecule during leukocyte extravasation. Alternate splicing results in nine transcript variants in human. It is widely expressed in most of human organs such as brain, kidney, heart, lung, liver, spleen, and small intestine. Expression of CD99L2 increased in cancer cells. CD99L2 amino acid sequences revealed homology to those of CD99 with 32% amino acid identity. It is encoded by a gene on the X chromosome like CD99. Unlike CD99, the gene encoding CD99L2 is not located in the pseudoautosomal region The recruitment of

specific leukocyte subtypes to the site of tissue injury is the cornerstone of inflammation and disease progression.CD99L2 Plays a role in a late step of leukocyte extravasation helping cells to overcome the endothelial basement membrane. The role of CD99L2 isoforms in leukocytes transendothelial migration (TEM) /diapedasis has remained to be elucidated. Here we studied the role of alternative isoforms in the TEM of leukocytes at the time of inflammation. **Objectives:** To investigates the role of CD99L2 isofroms in the transendothelial migration of leukocytes **Material and Methods:**Cells used in this study are WEHI-274.1, bEnd.3, MCF-7, U937and HUVEC. Production of DNA constructs were done from Human CD99L2 cDNA clone BC030536, clone BCO25729. Semi quantitative RT-PCR and quantitative RT-PCR used for expression. Wild type and dominant negative form of CD99L2 isoform, tagged with GFPwere generated and constructed in the pcDNA3.1-hg plasmid vector. Each construct was transfected in WHEI 274.1 and stable cell line were made. Stable cell lines were used for functional assay like cell adhesion, transendothelial migration. Site directed mutagenesis was done to make mutant of isoforms. Transient transfections were done in MCF-7 cells to perform Proximity ligation assay to confirm co expression. **Results:**we investigated the role of CD99L2 isoform II, III, IV, V, VI and VII in the transendotheial migration of leucocytes. Sequence analysis predicts that CD99L2 II, III, IV and V might be transmembrane proteins, whereas CD99L2 VI and VII mightbe secretory proteins. Our rt PCR and real-time PCR results showed that C99L2 II, III, IV and V are expressed both in monocytes (U937 cells) and endothelial cells (HUVEC). The interactions between each isoform were evaluated by proximity ligation assay (PLA), for which we tagged each isoform with Myc and HA and transfected them into MCF-7 cells. CD99L2 II, III, IV and V play important roles in fine-tuning of transendothelial migration of monocytes by making a complex. Our functional assays (cell binding assay and transmigration assay) and PLA revealed the roles of the conserved domains present in CD99L2 isoforms in diapedasis. CD99L2 isoforms regulate transendothelial migration by controlling affinity of β1 integrin. The treatment of U937 with LPS and HUVECs with TNF-α and IL-β leads to changes in the expression of CD99L2 isoforms. **Conclusions:**This study suggests that CD99L2 regulate leukocytes transendothelial migration by generating alternative splicing forms. CD99L2 may be an excellent target for the design of therapeutic interventions.Therapeutic treatment involving inhibition of CD99L2 would be a significant promise in remediation of inflammatory conditions and disease progression.

Key words:CD99L2, Transendoethelial migration, inflammation, Leukocyte

Comparison of Three Palliative Radiotherapy Schedules in Metastatic Brain Tumors : A Prospective Study

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Background: Palliative radiotherapy with less duration remain the standard radiotherapy schedule in metastatic brain tumors. We did a phase III randomized trial to compare three radiotherapy schedules in patients with metastatic brain tumors. **Methods:** This study was conducted in a tertiary cancer centre in North India from December 2011 to October 2013. Forty six patients with metastatic brain tumors were randomized in 3 Arms : Arm I had 15 patients receiving radiation in dose of 30 Gray in 10 fractions, Arm II had16 patients receiving dose of 20 Gray in 5 fractions and Arm III having 15 patients receiving dose of 12 Gray in 2 fractions. The endpoints were response rate, acute toxicity, quality of life and median survival. Acute toxicity was evaluated weekly during treatment using common toxicity criteria (CTC v 3.0). **Results:** Radiological response 40%, 56% 33%, Acute toxicity were 20%, 19% & 47%, Quality of life 60%, 75% & 53, and median survival are 6 month, 7.5 month and 5 month respectively in Arm I, II, III . **Conclusion:** Statistically there were no significant differences betweenradiological responses, acute toxicity, quality of life, but median survival was better with Arm II, hence best radiotherapy schedulein patients with metastatic brain tumors in our study was Arm II (20 Gray in 5 fractions).

Antineoplasmic role of *Helicteresisora*Bark Ethanolic extract(HIBE) on the cancer progression targeting neovascularization and apoptosis.

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Introduction: The new challenge in conventions of anticancer therapy is to recognize the multi compartment nature of the tumour microenvironment which reflexes in the radically different approaches toward the discovery of new treatments. Resistance to apoptosis and progressing angiogenesis are such important parameters which are required for tumour growth, invasion and metastatic dissemination targeted during anticancer therapeutics. The search now seeks a herbal based phytomedicine specifically targeting these two parameter and there by inhibiting the tumour growth. **Objectives:**To develop phytomedicine with dual specific action targeting angiogenesis and apoptosis. **Material and methods:** *Helicteresisora* Bark was collected, processed and ethanolic extract was prepared(HIBE). Antiproliferative activity against DLA, A549 and MCF-7 to determine IC_{50} value. *In-vivo* antitumour activity of HIBE in murine asciteslymphoma (DLA) to measure tumour parameters and peritoneal angiogenesis.Immunohistochemistry (IHC) studies to measure CD31 counts, angiogenesis assessment by CAM, Rat Corneal vascularization assay. Apoptotic assays to measure DNA fragmentation, endonuclease activity and Giemsa stain. Altered gene expression profile by RT-PCR, Immunoblots, IHC. **Results:** Antiproliferative index against three different cell lines resulted in minimal IC_{50} concentration 20μg/ml. In-vivo treatment of HIBE at 100mg/Kg body weight (i.p) resulted in regressed tumour growth with ascites secretion and increasing survivality of animals. Tumour induced peritoneal neovessel formation was abrogated as per CD31 counts, cell morphology studies indicated the formation of apoptotic bodies,altered cellular events like fragmentation of nucleus induced by caspase activated DNAse and changes in cell morphology like membrane belebbing, cell shrinkage and apoptotic bodies. The mechanism behind these events is due to altered expression of HIF-1, VEGF-A, Flt-1, MMp-2 and 9. **Conclusions:** A herbal based phytomedicine HIBE could activate dual signalling by inhibit angiogenesis and promoting apoptosis which could be further investigated by isolation bioactive principle and validation of the drug in future.

FAT1 modulates the expression of molecular regulators of hypoxia and stemness in glioma

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Introduction: Glioblastoma (GBM), arising from supporting glial cells, are the most common and most aggressive form of brain tumors with patient survival of 12–15 months after diagnosis. FAT1 gene, encoding a transmembrane protein, is an ortholog of the Drosophila tumor suppressor gene *'fat'*. FAT1 is reported to have dual role, it may function as oncogene or tumor suppressor in different human cancers. Our lab previously identified the oncogenic role of FAT1 in human glioma where knockdown of *FAT1* was found to inhibit migration/invasion of glioma cells and downregulate the expression of pro-inflammatory molecules. Hypoxia is one of the most pervasive micro-environmental stresses in GBM. **Objectives:** Here, we analyzed the functional role of *FAT1* gene in regulating the expression of hypoxia and stemness markers in GBM under hypoxia. **Material and Methods:** *FAT1* and the markers of hypoxia and stemness were analyzed at mRNA level in 31 GBM tissue samples. Correlation and cluster analysis were done using SPSS 11.5 and Cluster

3.0 softwares. U87MG and A172 glioma cell lines were used for in-vitro analysis. Cells were transfected with FAT1 specific siRNA or control siRNA, maintained under normoxic (20% O_2) and severe hypoxic (0.2% O_2) conditions and expression of hypoxia and stemness markers was analyzed 72hrs post-siRNA transfection.

Results: In GBM tissue samples, a positive correlation of FAT1 expression with hypoxia (*HIF1α, VEGF, PGK1* and *CA9*) and the stemness marker (*SOX2*) was observed. These correlations were also validated using heat map analysis Cluster 3.0. Kaplan-Meier analysis showed an inverse relationship of GBM patient's survival with *FAT1* and *SOX2* expression. In U87MG & A172 cell lines, increasedFAT1 expression along with the expression of hypoxia and stemness markers was observed on treatment with severe hypoxia (0.2% O_2) as compared to their normoxic (20% O_2) controls. Upon transfection with FAT1 siRNA, we observed decreased mRNA expression of hypoxia markers (*HIF1α, VEGF, PGK1* and *CA9*) and stemness markers (*SOX2, OCT4, Nestin* and *REST*) in cells maintained under severe hypoxia. **Conclusions:**Therapeutic targeting of pathways operative in GBM has had limited success so far and thus new targets are needed to be identified for therapeutic intervention. Our results suggest *FAT1* to be a novel molecule regulating the expression of hypoxia and stemness markers in GBM and FAT1 may emerge as a target for therapeutic intervention.

Function and diagnostic value of Anosmin-1 in gastric cancer progression

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Introduction: Gastric cancer (GC) is a major global health problem that urgently requires novel molecular biomarkers for patient stratification as well as therapeutic targets. Anosmin-1 (ANOS1) gene encodes a cell adhesion molecule that plays diverse roles in multiple malignancies. **Objectives:**To evaluate the expression and functions of ANOS1 in GC. **Material and Methods:**We performed global expression profiling of GC cell lines and siRNA experiments to determine the effect of ANOS1 expression on phenotype. We evaluated the association of ANOS1 mRNA and protein levels in patients' tissue and sera with clinicopathological factors of GC subtypes. **Results:**Differential expression of ANOS1 mRNA by GC cell lines correlated positively to levels of ITGAV, FOXC2 and NODAL mRNAs and inversely with those of TFPI2. Inhibiting ANOS1 expression decreased the proliferation, invasion and migration of GC cells. The mean level of ANOS1 mRNA was significantly higher in 237 GC tissues compared with the corresponding noncancerous adjacent tissues. Elevated ANOS1 levels associated significantly with the phenotypes of GC, shorter disease-free and overall survival. ANOS1 expression was a more significant prognostic marker for diffuse and distal nondiffuse GC. ANOS1 concentrations in sera increased sequentially in sera of healthy subjects, localized GC and disseminated GCs. Prognosis was worse for patients with preoperative serum ANOS1 ≥600 pg/m compared with those with <600 pg/ml. **Conclusions:**ANOS1 may represent a biomarker for GC phenotypes and as a target for therapy.

Functional role of MAGEA3 in pancreatic cancer

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Introduction: Cancer-testis antigens (CTAs) are group of proteinsnormally expressed only in germ cells; however, also expressed in different cancer cell types. Out of the known CTAs, MAGEA3 (Melanoma antigen family A, 3) has been reported to be expressed in many malignanciesincluding pancreatic cancer (PCa). In PCa patients the expression of MAGEA3 significantly correlates with poor prognosis. Biochemical evidence has shown that MAGEA3 interacts with TRIM28 (a RING E3 ubiquitin ligase) and enhances its ubiquitin ligase activity. In other cancers, MAGEA3 knockdown results in increased accumulation of p53 target genes in response to DNA damage. Moreover, recently MAGEA3 is proposed to be an oncogene. Though studies in other cancers have indicated MAGEA3 involvement in cancer promotion by regulating cell cycle and apoptosis, but its role in PCa pathogenesis is yet to be elucidated.Based on the aforementioned background and rationale, we have hypothesized that MAGEA3 has a functional role in pancreatic cancer initiation and/or progression. **Objectives:**Toinvestigate the functional role of MAGEA3 in pancreatic cancer cells growth and metastasis. **Material and Methods:** MultiplePCa cell lines were screened for MAGEA3 expression through quantitative PCR (qPCR) and immunoblot analysis. MAGEA3 was ectopically expressed in cell lines, and the functional role of MAGEA3 in these cells was evaluated through growth kinetic assay. Effect of MAGEA3 overexpression on cell cycle progression was also checked through FACS analysis. Parental and empty vector transfected cells were used as controls. MAGEA3 overexpressing cells and corresponding control cells were subjected to qPCR analysis and expression level of genes involved in cell cycle regulation andcell survivalwas determined. Co-immunoprecipitation (IP)wasdone to check the interaction between MAGEA3 and TRIM28 in MAGEA3-overexpressing cell lines. **Results:** Screening of cell lines with qPCR showed differential levelof MAGEA3 expression in PCa cell lines. The growth kinetic assay showed increased proliferation rate and decreased doubling time upon ectopic expression of MAGEA3. Gene expression analysis showed alteration in the level of genes involved in cell cycle progression and/or cell survival. Moreover, the Co-IP experimentconfirmed the interaction between MAGEA3 and TRIM28 in the ectopically MAGEA3 expressing cells. **Conclusions:** The present study indicates the functional involvement of MAGEA3 in PCacells' aggressiveness and encourages for further investigation through conditional knockdown of this gene in pancreatic cancer cells. The interaction of MAGEA3, with a well-known transcriptional regulator TRIM28/KAP1 emphasises on the existence of possible molecular regulatory mechanisms by which MAGEA3 alters the expression level of cell cycle/survival related genes in pancreatic cancer cells.

Title –Redefining indications for Radical resection inGallbladder cancer – A high volume centre's experience from North India.

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Background: Gallbladder carcinoma (GBC) is characterized bydismal 5-year overallsurvival (5–10%). Early detection and R0 resection offers the only chance for cure, butunfortunately, is possible in only small proportion. This study was undertaken to assess the clinical profile and outcome of GBC patients amenable to definitive surgical resection and to evaluate the predictors of long term survival in these patients. **Material &Methods:** A large, single center, retrospective study was conducted over five year period (2010-2014) to identify case subjects withGBCthat underwent radical/ extended radical surgeries with a curative intent (n=140). Their clinicopathological, surgical data and clinical outcome were recorded andanalyzed. **Results:** Of the total 140 patients, 80% of patients (n=112) underwent curative radical cholecystectomy while 20% patients (n=28) were found inoperable due to metastatic disease.Mean age at diagnosis was 51.2 years (Range - 25-78 years). Incidental Gall bladder carcinoma was detected in 17% patients (N=24).75% patients(n=105) underwent radical cholecystectomy,22 patientsout of theseunderwentadditional adjacent organ resection (with acceptable morbidity) while 5% patients underwent simple cholecystectomy.Node positive disease was seen in 33 patients (29%) with mean node yield of 5.7(range is 3-27). Majority of the tumor were diagnosed in T3 stage (34.3%, n=48). Extended resections improved survival in patients with T3/T4N+ disease. About 40% of patients (n=45) with curative resection (n=112) received adjuvant chemotherapyon the basis of final pathologic staging (node positive/T3 and above). Median follow-up duration was 26 months (Range=8-48 months). Overall Median Disease Free Survival (D.F.S.) was 8.8 months (Range = 3 - 30 months). Median Disease Specific Survival (D.S.S.) was 24.7 months

(Range=4-50 months).Locoregional recurrence was observed in 8 patients with mean time to recurrence being 10 months. T (p=.04) and N stage (p=.01) significantly determined the clinical outcome. T3N+ve disease had better survival after extended resectionalprocedures. **Conclusion:** R0 resection offers the only chance of curein GBC. T3N+ve disease had better survival after extended procedures. In addition to the R0 surgical resection, factorssuch as tumor (T) stage,adjacentorgan infiltration, lymph node status, presence of lymphovascular invasion (LVI) and stage influencedthe survival.Role of the adjuvant combination chemotherapyin adjuvant setting may offer survival benefit though it remains to be validated in prospective randomized studies.

"Epidemiological study of Gallbladder cancer patients from North Indian Gangetic planes"

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Background: Gall bladder carcinoma (GBC) is characterized by dismal prognosis owing to paucity of early signs and symptoms. North Indian Gangetic planes report one of the highest incidences of GBC in the world.Understanding the epidemiology of gallbladder cancer has and will continue to provide valuable insights into determining risk factors for GBC. **Material and methods:** Prospective study of all GBC patients reporting in our hospital over last 3 years to evaluate the epidemiological profile of GBC patients from our region. **Results:** The peak incidence of GBC was in 31-50 years age group [58%]. Male to female ratio was 1:4.83, with mean age for females [Mean – 49.1 years] significantly lower than male counterpart [Mean - 54.9 years] (p value =0.000423). 84% of them consumed mustard oil (home made/loose packed) as predominant medium of cooking. 38% of patients consumed tobacco, 20% were smokers [all male patients] while 5% consmed alcohol. Majority of the patients of GBC in our study, were from low socioeconomic strata (68%) [Kuppuswamy class IV, V (lower class)]. GBC was more commonly observed in females with age of menarche < 14 years [83%], age of 1st child birth < 20 years [56%]. Females with > 2 children had higher incidence [57%]. Gall stones were present in 390 out of 490 patients [80%]. Incidental GBC was detected in 158 out of 490 patients [32%] and most had undergone open cholecystectomy. Pain abdomen was the most common presenting complaint found in almost all patients of GBC [98%]. Significant proportion of the patients presented with distant metastasis (stage IVB) (52%). Most common histological subtype of GBC was adenocarcinoma (78%). **Conclusion:** This data emphasizes high prevalence of GBC in northern India. Current data suggest that the epidemiology of GBC is constantly evolving, with much of this change caused by lifestyle, cultural, mixing of different ethnicities and dietary factors. Balanced diet, prevention of malnutrirtion/adulteration, tobacco prevention, early intervention for cholelithiasis – may help in decreasing the incidence of this dreaded disease. More structured studies need to be carried out to ascertain risk factors for GBC in our population subgroup.

Association between early tumour shrinkage and outcomes in *RAS*-wild type patients with metastatic colorectal cancer receiving first-line FOLFOX or FOLFIRI + cetuximab once every 2 weeks in the APEC study.

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Background: Early tumour shrinkage (ETS) has been correlated with improved long-term outcomes in patients with *KRAS/RAS*-wild type (WT) metastatic colorectal cancer (mCRC) treated with weekly cetuximab (Erbitux ®) in the CRYSTAL and OPUS (at 8 weeks) and FIRE-3 (at 6 weeks) studies. The present analysis was conducted to evaluate the association between ETS at 8 weeks and progression-free survival (PFS) and overall survival (OS) in the *RAS*-WT population from the Asia-Pacific, multicentre, nonrandomized, phase 2 APEC study that enrolled 289 patients with *KRAS*-WT tumours.

Materials and methods: Eligible patients received cetuximab once every 2 weeks + FOLFOX or FOLFIRI (as per investigator's choice). Study treatment was continued until disease progression, dose-limiting toxicity or consent withdrawal. *RAS* status was assessed retrospectively by ion torrent NGS on evaluable samples. ETS and no ETS was categorized as ≥20% or <20% decrease respectively in the sum of longest diameters of target lesions between baseline and 8 weeks after start of treatment.

Results: Median PFS and OS in the total *RAS*-WT population (n=167) was 13.0 and 28.4 months, respectively. ETS was observed in 81.8% (130/159) of evaluable patients and was associated with longer PFS and OS (Table); there were no major differences between patients receiving FOLFOX vs FOLFIRI. There were no unexpected safety findings.

***RAS*-WT, ETS-Evaluable Patients (n=159)**		**ETS ≥20%**	**ETS <20%**	**Total RAS evaluable**
OS	n	130	29	159
	# of events (%)	81 (62.3%)	20 (69.0%)	101 (63.5%)
	HR (95% CI)	0.584 (0.357-0.954)		-
	Median, mo (95% CI)	30.3 (26.3-33.2)	16.4 (10.3-31.2)	28.5 (24.5-32.3)
PFS	n	130	29	159
	# of events (%)	90 (69.2%)	19 (65.5%)	109 (68.6%)
	HR (95% CI)	0.721 (0.438-1.186)		-
	Median, mo (95% CI)	14.0 (11.2-14.9)	7.5 (3.6-16.6)	13.3 (11.1-14.8)

Conclusions: ETS at 8 weeks appears to be associated with longer PFS and OS in *RAS*-WT patients receiving FOLFOX or FOLFIRI + cetuximab (Erbitux ®) once every 2 weeks in the phase 2 APEC study. These findings are in line with subgroup analyses of former studies involving weekly cetuximab.

RADICAL TREATMENT OF RECTAL CANCER IN ELDERLY IS FEASIBLE THAN FEARED: RESULTS FROM A TERTIARY CANCER CENTRE

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Regional Cancer Centre

Introduction: The thought of subjecting an elderly patient diagnosed with rectal cancer to protocol based NeoadjuvantChemoradiation (NACTRT), surgery and adjuvant chemotherapy is sought with fear due to multiple comorbidities and impaired functional status associated with ageing. Hence, many a times the treatment is compromised and it is a fact that they are underrepresented in most of clinical studies. This study is aimed at analyzing the perioperative and oncologic outcomes after protocol based curative intent treatment of rectal cancer in the elderly, defined as those with age more than 70 years. **Patients & Methods:** Analysis of Medical records of elderly patients≥70 years of age who were treated for rectal cancer at Regional Cancer Centre (RCC), Thiruvanathapuram from 2008 to 2012 was done**. Results:** In five years period, a total of 339 rectal cancer patients were treated with curative intent, of which 75 patients were ≥ 70 years of age. Half of the them (54%) had one or more comorbidities. Sixty cases (80%) werelocally advanced at presentation and 47 (63%) completed NACTRT

without dose modification (50.4 Gy). Anterior resection was performed in 48 (64%) ; with covering stoma in four; of which three remained permanent. Rest of patients underwent Abdominoperineal resection.Three patients (4%) died within 30 days due to leak, sepsis and cardiopulmonary causes. Two colostomies were performed for delayed leaks. Two thirds (65%) received adjuvant chemotherapy, one third (37%) could complete full course. The median survival was 28 months. The 3 year Disease Free Survival (DFS) and Overall (OS) were 83.9% & 80.3% respectively. There were 11 distant recurrences including one locoregional recurrence. **Conclusion:** Curative Surgical Resection after chemoradiation ismuch feasible than feared in elderly patients despite multiple comorbidities.

Epigenetic silencing of *miR-200* family is associated with regulation of *ZEB1/ZEB2* in gastric cancer metastasis

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Introduction: Epigenetic silencing of miRNAs with tumor suppressor activity by CpG island methylation plays an important role in the development and progression of gastric cancer. **Objectives:** To determine the asociationwithregulation of *ZEB1/ZEB2* in gastric cancer metastasisdetecting tumor-associated aberrant methylation in the serum/plasma of patients with gastric cancer. **Material and Methods:** The extent of promoter methylation of the *miR200-ba429, miR200-c141* was assessed qualitatively using methylation-specific PCR (MSP)in 122 gastric cancers staged from I to IV. The immunohistochemical assessment of ZEB1, ZEB2,E-cadherin, and MUC-1 gene expression was done in gastric cancer tissues. **Results:**The methylation frequency for the *miR200-ba429, miR200-c141, and E-cadherin*gene according to MSP techniques was significantly higher in AGCs than in EGCs (88% and 68%, 83% and 52%, 64% and 52%, $P<0.05$). Significant positive correlation of *miR200-ba429, miR200-c141* hypermethylation with ZEB1/ZEB2 and MUC1expression was identified in gastric cancer. Methylation status of miRNA 200 family as well as expression of ZEB1/2, E-cadherin, and MUC1 was significantly correlated with tumor differentiation and clinical stages ($P<0.05$). **Conclusions:**The ZEB1/2-miRNA 200 family feedback loop might be a promising molecular target for gastric carcinogenesis and metastasis.

Key words: miR-200, epigenetics, ZEB1/2

ROLE OF PROTEIN EXPRESSION OF MLH1, MSH2 AND MGMT GENES IN THE DEVELOPMENT OF COLORECTAL CANCER IN INDIAN POPULATION

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Background: Genetic/ epigenetic changes possibly causing the development of colorectal cancer (CRC) in various genes may be also be reflected at the protein level. The present study evaluated the role of genetic/ epigenetic disruption in certain genes (MLH1, MSH2 and MGMT), particularly at the level of protein expression in CRC. **Materials & Methods:** A total of 240 consecutive surgically resected fresh tissue specimens comprising of equal number of tumor tissues and adjacent non tumorous regions of primary sporadic CRC undergoing upfront surgery were collected. Immunochemical detection for the identification of tumor and control tissues was performed by hematoxylin and eosin staining. **Results:** Absence of protein expression of MLH1, MSH2 and MGMT genes was observed in 50%, 67.5% and 72.5% cases, respectively. Immunochemical detection for the identification of tumor and control tissues was performed by hematoxylin and eosin staining. Overall, tumor stage 3 and 4 showed an absence of expression in 37.5%, 27.5% and 22.5% cases, respectively. Among the cases with presence of lymphatic invasion, loss of expression was observed in MLH1, MSH2 and MGMT genes in 35%, 25% and 20% cases, respectively. Significant associations were observed for protein expression with tumor stage (p-value <0.034) and lymphatic invasion (p-value <0.031). **Conclusion:** The conjunctional occurrence of loss of protein expression in more than one gene may act synergistically in affecting the aggressiveness of this disease and initiating tumor formation at these sites and may work in unison in deciding the overall fate of the disease.

Clinical profile & therapy of hepatocellular carcinoma in a tertiary care hospital in Andhrapradesh from South India.(A study of 182 cases)

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Background: Hepatocellular carcinoma (HCC) is an aggressive & fatal disease globally. Purpose of the study is to analyse the detailed clinical profile including clinical presentation,etiology (Hepatitis virus B,C) & biochemical,radiological profile along with therapy of HCC patients presented to our centre from year 2000-2015. **Material&Methods:** Retrospective chart review of 182 patients with HCC was done.HCC was diagnosed according to EASL criteria-USG/CT/MRI of the abdomen and/or serum alpha-fetoprotein and/or histology (where indicated).Detailed clinical and laboratory parameters were noted.Barcelona Clinic Liver Cancer (BCLC) staging was done. **Results:** Data analysis of 182 patients (male 162, female 20) with HCC showed the median age at presentation was 56 years (range 50-60 yrs) with a male predilection and a small peak observed in early 30s (17%,31/182 cases).Hepatitis virus as an etiological agent was observed in (38.5%,70/182 cases) with hepatitis B accounting for (35.7%,65/182 cases) and hepatitis C (2.75%,5/182 cases).AFP level was elevated in (77.5%,76/98 cases) & more than 500 units observed in (44%,43/98 cases) which is practically diagnostic of HCC and significantly high level (>5000 –1,00,000 units) observed in (30%,30/98 cases) & normal range seen in (22%,22/98 cases).Most of the patients presented with advanced disease (80.5%).The most common symptoms were pain abdomen,loss of appetite and weight in 90% of cases.Radiological profile showed classical features of HCC on triple phase CT abdomen in 80% of cases with an average tumor size of 7-9cm and portal vein invasion seen in 40%of cases.80% of cases showed an elevated ALP levels,50% of cases have high normal total leucocyte count,60% showed low normal platelet count and 30% of cases with low Hb.20% of patients (36/182 cases) underwent surgery, 50% (91/182 cases) recieved oral/iv chemotherapy,30% (55/182 cases) of patients recieved best supportive care.20% (36/182 cases) of them received sorafenib and showed promising results despite few drug interruptions/dose reductions related to toxicity & is the current standard practice for advanced disease even at our centre.**Conclusions:** Hepatitis B infection is the predominant cause for HCC.Serum alpha-fetoprotein was diagnostic in more than 75% of study patients & its level correlates with disease burden,outcome.Most of the patients present with advanced disease & poor PS,precluding the curative therapies.Treated patients had better outcome than untreated ones.Universal immunization with hepatitis B vaccination will reduce the HBV infection rates & in part HCC burden in near future.

Key words:HCC (Hepatocellular carcinoma), AFP (Alpha fetoprotein), HBV (Hepatitis B virus)

Survival outcome of geriatric patients with resectable gastric cancer

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Background: Radical surgical resection is the only curative modality for patients with gastric cancer. However, surgery may compromise outcome and even lead to death in medically unfit or frail patients. With the global increase in ageing populations of patients with resectable gastric cancer, there is an urgent clinical need to address the impact of surgical resection in elderly patients with gastric cancer. The aim of this study was to evaluate the prognostic factor on survival outcome in elderly patients with resectable gastric cancer. **Material And Methods:** A total of 488 patients of 70 years and older diagnosed with gastric cancer, confirmed by pathological examination between January 2007 and December 2012 at Chang Gung Memorial Hospital (CGMH) Linkou branch, were included in this study. All patients received either radical surgical resection or medical treatment alone. Patients underwent palliative surgery or with other active concurrent cancer(s) were excluded. Totally, 445 patients (91.2%) and 43 patients (8.8%) received operation (OP) and medical treatment (non-OP), respectively. All patients were categorized into OP group or non-OP group for survival analysis. **Results:** The distribution is similar between OP and non-OP groups in tumor stage, histological tumor grade and percentage of receiving chemotherapy. Compared to OP group, non-OP patients had significantly older age, poorer performance scale, higher numbers of comorbidities, higher CGMH risk score, and more admission from emergency department. The median survival time is 43 months in overall cohort. OP patients had significantly better survival outcome than non-OP patients (median survival, 50.3 vs 16.2 months, $p<0.001$). In univariate analysis of prognostic factors for survival outcome, older age, existence of previous cancer history, poor histological tumor grade, advanced tumor stage, higher Charlson comorbidity index (CCI), poor performance scale, admission from emergency department and non-OP group were significant prognostic factors. However, only older age, existence of previous cancer history, advanced tumor stage, poor performance scale, and admission from emergency department were independent prognostic factors in the multivariate model. Overall, the hazard ratio for survival outcome was 0.36 (95%CI, 0.25-0.53, $p<0.001$), favoring OP group. In subgroup analysis, patient with 80 years and older, AJCC stage I or III, CCI > 2 and CGMH risk score > 20 had no significant difference in survival outcome between OP and non-OP groups. **Conclusions:** Our study showed that surgical resection was an important prognostic variable in geriatric patients with resectable gastric cancer. However, surgical resection did not prolong survival outcome among those with 80 years or older, high numbers of comorbidities, AJCC stage I or III and high CGMH risk score. These results might provide valuable information to clinicians and geriatric patients for the decision-making process of gastric cancer surgery.

To assess the outcome and tolerance of adjuvant chemoradiotherapy in patients with non metastatic resectable gastric cancer.

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Background: Management of gastric adenocarcinoma continue to evolve and the primary curative treatment is surgical resection. However in view of high incidence of loco regional and distant failure with surgery alone, it is recommended that patients with resected gastric cancer should receive adjuvant treatment. The overall survival and disease free survivalis significantly better in patients who were treated with adjuvant chemoradiation as compared to surgery alone. However, chemoradiotherapyis associated with significantly increased toxicity (grade 3 and 4), particularly hematologic and gastrointestinal. **Material&Methods:** A total of 30 patients underwent adjuvantchemoradiotherapy (between April 2013 and October 2014)in non metastaticcompletely resected gastric adenocarcinoma. The adjuvant treatment consisted of 5FU 425 mg/m^{2}plusleucovorin 20 mg/m^2 for five days, followed by radiotherapy using 3DCRT technique with a dose of 45Gy (1.8Gy per fraction) to stomach bed, gastric remnant and regional draining lymph nodes, with modified doses of 5FU and leucovorin on the first four and the last three days of radiotherapy. One month after radiotherapy, two cycles of 5FU 425 mg/m^2 plus leucovorin 20 mg/m^{2}for five days were given one month apart. The primary endpoint was 1 yearoverall survival and disease free survival. **Results:** The mean age was 54.5 years and male:female ratio was 4:1. The AJCC stage distribution included 3 patients (10%) with stage I and 18 patients with Stage II (60%) and 30% with Stage III disease. Most common site was antrum and pylorus (15 patients – 50%). Nearly 77%(23) patients were lymph node positive in postoperative specimen .The median follow up was 12 months. The overall survival at 1 year was 70% and disease free survival at the end of 1 year was 63.33%. Grade 3 hematologicaland gastrointestinal toxicities were seen in 10% and 16.6% cases respectively. **Conclusion:**Chemoradiotherapy as adjuvant therapy for resected gastric cancer is a safe and well tolerated regimen. Adding Adjuvant Chemoradiotherapy improves overall survival and disease free survival compared with surgery alone or with adjuvant chemotherapy. Post op chemoradiotherapy, hence should be the standard of care in resectable gastric cancer patients.

Short course ofQuercetin Eradicate Helicobacter pylori bacterium :Reducedrisk to gastric cancer

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Background: Recent studies show that Helicobacter pyloribacterium is themajor cause of gastric ulcer which leads to gastric cancer.People with H.pylori infection are more likely to develop gastric cancer than those who are not infected with theH.pylori.Quercetin (QU, Flavonoid secondary metabolite ubiquitously present in*Argyreiaspeciosa* (Linn. f.) has promisingeffects on ulcer and multiple type of cancer. Present study was to be investigatedweather a short course of QU eradicatedH. pyloribacterium caused gastric ulcer which is major risk factor for gastric cancer. **Material Method:** Chronic H.pyloriinduced gastric ulcer was created by Werawatganon. D,2014 rat model.Those having H.pylori induced gastric ulcer were assigned to the HpGU, some of H.pylori induced gastric ulcerrats were treated with a one week course of QU were assigned to the HpGU-QU both of groups are compared with healthy rat as positive control assigned to the Pc group. Apparent association between H .pylori induced gastric ulcer andgastric cancer was explained by changes in ascorbic acid(AA) concentrations and level of reactive oxygen species in gut caused by H.pylori infection. Eradicating Effect of QU on H. pylori induced gastric ulcer examined by macromolecular leakage, leukocyte adherence, leukocyte rolling, and platelet activity. **Result:** In vivo, we found that there is higher concentration of AA and reactive oxygen in H.pyloriinfected rats as compared with positive control ($p<0.01$). Querectin decrease leukocyte adhesion as compared withHpGU group ($p<0.001$). There is decrease in average macromoleculeleakage inHpGU-QU group as compared with HpGU.**Conclusion:** Data provide direct supportive evidence for gastric cancer caused byH.pylori bacterium and QU increased eradication of H.pylori, a potential source for reducing the risk of gastric cancer

Key words: Helicobacter pylori bacterium, Macromolecular leakage,Ascorbic acid,Leukocyte rolling,Gastric cancer

SIRT1 inhibition in pancreatic cancer: contrasting effect *in vitro* and *in vivo*

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Introduction: Gemcitabine remains the cornerstone for pancreatic cancer treatment, although most patients become resilient to the therapy. Up-regulated in pancreatic cancer, Sirtuin 1(SIRT1) is involved in tumorigenesis and drug resistance through deacetylation of downstream targets. However the mechanism through which SIRT1 regulates drug sensitivity in cancer cells is largely unknown. **Objectives:** This study aims to investigate the role of SIRT1 in mediating chemosensitivity in pancreatic cancer models *in vitro* and *in vivo*. **Material and Methods:** PANC-1 cell proliferation was assessed using cyQuant assay (Life Technologies) post treatment with gemcitabine and/or EX527 SIRT1 inhibitor.Apoptotic cell death and cell cycle were assayed through annexin V/ propidum iodide staining by flow cytometry. Cell senescence was carried out using β-Galactosidase Staining Kit (CST). QPCR, western blot and immunofluorescence were employed to study the downstream gene and protein expressions following treatments. *In vivo* study was performed in PANC-1 subcutaneous xenograft tumour model. **Results:** We demonstrate that gemcitabine or SIRT1 inhibitor (EX527) mono treatment reduces PANC-1 cell proliferation *in vitro*. EX527 enhances sensitivity of PANC-1 cells to gemcitabine treatment through increased apoptosis. However, EX527 displayed no beneficial effect either as a monotreatment or in combination with gemcitabine in the modulation of cell cycle progression. Combination treatment did not reverse the two phenomena known to affect drug sensitivity, namely EMT and senescence, which are both induced by gemcitabine. Unexpectedly, EX527 promoted PANC-1 xenograft tumour growth in SCID mice compared to control group. Dual treatment with EX527 and gemcitabine displayed no synergistic effect compared to gemcitabine alone. **Conclusions:** The study reveals that SIRT1 is involved in chemoresistance and that inhibiting SIRT1 activity with EX527 sensitised PANC-1 cells to gemcitabine treatment *in vitro*. Sensitisation of cells is shown to be mainly through induction of micronuclei formation as a result of DNA damage and apoptosis *in vitro*. However, the absence of positive combinatorial effects *in vivo*, indicate possible effects on cells of the tumor microenvironment and suggests caution regarding the clinical relevance of tissue culture findings with EX527.

Keywords: Sirtuin, cancer, gemcitabine, EX527

Quantification of signaling protein, p38beta in pancreatic cancer and design of peptide inhibitors against the same

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In**troduction:** Pancreatic cancer is the fourth leading cause of cancer death. The majority of cases are diagnosed in the advanced stages, making curative therapy impossible and leading to poor prognosis and incidence equalling mortality. Molecular marker and imaging have not proven to be accurate modalities for screening of pancreatic cancer. It has been demonstrated that p38 MAPK selectively functions as a sensor of oxidative stress during the initiation of tumorigenesis as its apoptotic and antiproliferative effects are suppressed by uncoupling of the production of ROS (Reactive Oxygen Species) from p38 MAPK activation. This study aims to develop p38b as a protein marker for pancreatic cancer and to design peptide inhibitor against the same. **Objectives:** (1)To develop p38b as a protein marker for pancreatic cancer (2)To design peptide inhibitor against the same **Material and Methods:** This study was performed on 35 pancreatic cancer patients and 10 healthy groups and 10 chronic pancreatitis patient as control groups. Blood samples were collected and serum was separated. Serum levels of p38b expression were evaluated by Surface plasmon resonance (SPR) technology and ELISA, where samples were allowed to flow over anti-p38b antibody immobilized sensor chip. The peptide inhibitors were designed to inhibit the activity of p38[2] and the kinetic assay was done by SPR and ELISA. **Results:** The pancreatic cancer patients (n=35) in the study showed two fold higher level of p38β serum concentration (4.67 ng/μl, 95% CI 4.13-5.21) than controls (n=10) group (2.93 ng/μl, 95% CI 2.58-3.28) ($P < 0.0009$). Among them, 15 patients continued the treatment and showed significant ($P < 0.0002$) decline in p38β after treatment (2.92 ng/μl, 95% CI 2.58-3.28). The patients with tumor growth (T1+T2) and stage (I+II) after therapy had reduced concentration of p38β. This study was followed by the design of specific peptide inhibitors based on the structure of active site of p38b. The kinetic assay had shown the dissociation constant, (KD) to be 3.16 X 10-8 M and IC50, 25nM by SPR and ELISA, respectively. The peptide inhibitor also significantly reduced viability and induced cytotoxicity in PANC-1 cells. The expression levels of p38b increases according to the stage and can evolve as a potential marker in pancreatic cancer. **Conclusions:**

- p38β protein overexpressed in pancreatic cancer patients than normal individual or chronic pancreatitis patients.
- The level of p38β decreased in pancreatic cancer patients having chemotherapy or surgery

in early stage.

- SPR technology, which has been used here for quantification of serum p38β levels, can be set as a platform for widespread use and better manifestation for correlating the p38β levels in different stages of anti-cancer therapy.
- p38β can be used as a molecular marker for pancreatic cancer.
- p38β can be a specific therapeutic target molecule for pancreatic cancer.
- VWCS peptide, showed good binding and inhibition results with p38β protein
- VWCS also showed significant cytotoxic effect with PANC-1 cell line, which validates its effectiveness.

Predictors of response to locoregional therapy in hepatocellular carcinoma patients

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Introduction: Hepatocellular carcinoma (HCC) is the most common primary liver malignancy worldwide. HCC is biologically very heterogeneous and may have different outcomes depending upon the treatment given. C-Reactive Protein (CRP) is an inflammatory cytokine which is produced by hepatocytes. The association of CRP with disease prognosis have been reported among different gastrointestinal tumors including esophageal, gastric, colorectal, pancreatic cancers and HCC. For HCC, locoregional therapy consisting of ablation, transarterial chemoembolization / chemotherapy is the commonly used non-surgical treatment. Prior studies have reported an association of elevated CRP with poor outcome in HCC patients. Hence, CRP may have a possible role of in assessment of treatment response in patients of HCC **Objectives:**To assess predictors of response to locoregional therapy in patients with hepatocellular carcinoma **Material and Methods:**Between Nov 2014-Dec 2015, consecutive diagnosed patients of HCC reporting to our Liver clinic were evaluated. They were subjected to laboratory investigations including liver and renal function tests, complete hemogram serum alphafetoprotein estimation and a multiphasic magnetic resonance imaging (MRI) .Those found suitable for locoregional therapy as per the Barcelona Clinic Staging (BCLC) were included. Serum CRP level was measured at baseline and one month post therapy using high sensitivity CRP (hs-CRP) immunoassay. Multiphasic magnetic resonance imaging (MRI) was performed at one month post treatment to assess tumor response based on the modified RECIST criteria The results were correlated with the hs-CRP **Results:**Total of 172 consecutive HCC patients were recruited during study duration. Of these 103 were excluded (58 lost to follow up, 22 had BCLC D stage, 19 had BCLC C stage and 4 underwent surgery) and 69 patients were included in this study. Treatment response was analyzed with reference to age, gender, etiology, size and number of tumours and CTP score. The mean value of hs-CRP in patients with CR (complete response), PR(partial response), SD (stable disease) and PD (progressive disease) at baseline were 7.07 ± 7.4,8.05 ± 7.4, 4.37 ± 3.2and 10.48 ± 9.0 mg/L respectively. Comparison of hs-CRP of CR at base line with PR, SD and PD was not found significant. Correlation of complete response with baseline size of tumour (4.2 ± 3.5 cms)and 1 month

post therapy hs-CRP level (5.97 ± 6.2mg/L) was statistically ($p<0.001$ and $p=0.003$ respectively) significant. Reduction of hs-CRP level from base line was observed at one month post therapy in patients showing complete response on MRI whereas rise of level was observed in patients showing PR, SD or PD. **Conclusions:**The hs-CRP estimation at one month post treatment will be useful in predicting treatment response. Higher hs- CRP level (15.18 ± 12 mg/L) is associated with poor response.

Epithelial-to-mesenchymal transition in urinary bladder cancer: its clinicopathological correlation and prognostic significance.

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Introduction: Epithelial-to-mesenchymal transition (EMT) is a key feature in cancer progression where epithelial cells losecell-cell adhesion structures, change theirpolarity, modulate the organization of their cytoskeletal systems,show increased motility and resistance to anoikis/ apoptosis and become invasive mesenchymal cells. Salient features of EMT program in cancer cells include fibroblastic phenotypc, downregulation of the epithelial markers, increased expression of mesenchymal proteins and induction of Twist and Snail-family transcription factors. EMT has been identified as the key feature in the pathogenesis of urinary bladder cancer. Bladder cancer has a highly variable prognosis which depends on the pathological stage and grade of the tumor. Molecular biomarkers may help to elucidate biologic features to identify patients at high risk for recurrence, metastasis and progression and therefore, possess prognostic significance. **Objective:** The objective of this study is to investigate the expression and role of EMT-molecular markers in the pathogenesis of urinary bladder cancer and suggest possible clinical applications for diagnosis and prognosis. **Material and Methods:**The present work has been undertaken to examine the quantitative expression of EMT markers including E-cadherin, N-cadherin, vimentin, Snail, Twist, Zeb-1 and Slug by real time-quantitative PCR (RT-qPCR) and immunohistochemistry (IHC) in tumor tissues of non muscle invasive bladder cancer (NMIBC) and muscle invasive bladder cancer (MIBC) patients who were enrolled in Urology OPD at Sanjay Gandhi Post Graduate Institute of Medical Sciences (SGPGIMS), Lucknow. The tumor samples were obtained via urethral resection or radical cystectomy and immediately stored in either liquid nitrogen or fixed in formalin and then embedded in paraffin. The bladder tissues from the patients undergoing transurethral resection of prostate (TURP) for benign prostatic hyperplasia (BPH) with no obvious malignancy and had cold cup bladder biopsy were treated as normal. The correlation between the quantitative expression results, EMT-marker proteins' immunoreactivity, histological grade, and pathological stage of the tumor was analyzed. **Results:** The expression of EMT-markers was characterized in thirty human urinary bladder cancer samples using RT-qPCR and IHC. Based on the results of RT-qPCR, muscle invasive tumors exhibited inverse correlation between epithelial marker, E-cadherin and mesenchymal markers, N-cadherin and vimentin. Abnormal activation of EMT transcription factors have been shown to be negatively correlated with E-cadherin but positively associated with mesenchymal proteins in muscle invasive tumors. Immunohistochemical results revealed that the staining intensity and therefore, IHC score of epithelial marker proteins correlated negatively while mesenchymal marker proteins and transcription factors correlated positively with the histological grade and pathological stage of the urinary bladder cancer. **Conclusions:** Results of the current study show that EMT pathway may play a role in the pathogenesis of urinary bladder cancer. Molecular validation of EMT marker proteins in bladder cancer as evident by correlation of expression and IHC results with clinical features may prove to be a sensitive and effective diagnostic and prognostic tool. It mighthelp in improving early detection of recurrence in low grade NMIBC nevertheless further studies are required in more number of clinical samples.

A novel testis specific heat-shock protein 70-2 (HSP70-2): potential therapeutic target for renal cell cancer.

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Background : Renal cell carcinoma (RCC) represents one of the most resistant tumors to radiotherapy and chemotherapy. Current treatment options for RCC patients are limited because of the lack of therapeutic targets. Testis specific heat-shock protein 70-2 (HSP70-2), a member of HSP70 chaperone family, has been shown to be involved in various cancers. In the present study, we investigated the association of HSP70-2 with various malignant features of cancer cells, in order to develop a novel target for RCC.**Materials and Methods:** Reverse transcription-polymerase chain reaction (RT-PCR) and by Western blotting technique was used for gene and protein expression detection. Indirect immunofluorescence (IIF) and flow cytometry was emplyoyed for cytoplasmic localization, colocalization in various subcellular compartments and surface localization respectively. The gene silencing approach using plasmid driven shRNA targets was used to silence HSP70-2 mRNA.MTT assay, colony formation assay, scratch assay, and chemo-taxis driven migration/ invasion assays were performed. **Results** : HSP70-2 mRNA and protein expression was investigated in A704, ACHN and Caki-1 cells derived from RCC patients by RT-PCR and by Immunoblotting. Validation of HSP70-2 protein expression was carried out by indirect immunofluorescence (IIF) and flow cytometry for cytoplasmic localization, colocalization in various subcellular compartments and surface localization respectively. The gene silencing approach employing plasmid driven shRNA targets was used to examine the involvement of HSP70-2 in cancer cell viability, cell growth, colony formation, migration, invasion and wound healing in high grade invasive A704 and Caki-1 cells. Our RT-PCR and Western blotting data showed HSP70-2 expression in all RCC cells. Our results showed that HSP70-2 was predominantly expressed in cytoplasm and colocalized with endoplasmic reticulum, mitochondria, Golgi body and plasma membrane but not with the nuclear envelope. Knockdown of HSP70-2 expression in RCC cells with specific shRNA demonstrated significant reduction in cellular proliferation, colony formation, migration, invasion and wound healing properties. **Conclusion** : Our findings demonstrate that HSP70-2 is expressed in various RCC cell line models. For the first time, we have put forth an evidence of potential role of HSP70-2 in various malignant properties of RCC cells indicating that HSP70-2 could serve as a novel potential therapeutic target for the RCC.

Ga-PSMA PET/CT in evaluation of primary prostate cancer: Experience from a tertiary care centre in India

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Introduction: Adenocarcinoma of prostate is the second most common cause of cancer death among men. Prostate-specific membrane antigen (PSMA) represents a cell surface target suitable for imaging metastatic lesions as it is expressed by nearly all prostate cancer cells with enhanced expression levels in poorly differentiated, metastatic, and hormone-refractory carcinomas.[7,8] Recently labelling procedures have been developed to label PSMA ligands with ^{68}Gallium (^{68}Ga) which makes them suitable for PET imaging. **Objectives:** To evaluate the role of Ga-68 PSMA PET/CT in evaluation of primary prostate cancer. **Materials & Methods:** Total 344 patients underwent Ga-68 PSMA PET/CT study in our department for various indicationsbetween March 2014 and August 2015. Out of

them eighty eight patients (n =88) mean age 70.27+/- 5.56 ranging from 44 to 84 years, with suspected primary prostate cancer, who underwent Ga-68 PSMA PET/CT scan as part of staging work upwere evaluated retrospectively. All the patients underwent prostate biopsy within two weeks of the scan. Size and SUVmax of the evident prostatic lesion on Ga-68 PSMA PET/CT scans were measured and SUVmax> 3 was considered as criteria for PET positivity. Histopathological analysis of biopsy specimen was considered as reference standard for the diagnosis of the prostate cancer. Scan parameters were correlated with histopathological report and various parameters like sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy of Ga-68 PSMA PET/CT were calculated. **Results:** The sensitivity, specificity, PPV, NPV and accuracy of Ga-68 PSMA PET CT for the detection of primary prostate cancer were 96%, 50%, 88%, 75% & 87% respectively.The median SUVmax of primary lesionin biopsy proven subjects was 6.5,which was significantly higher than the mean SUVmaxobtained in biopsy negative subjects was 2.8. However, the study failed to find any significant correlation between SUVmax of the primary lesion and Gleason's score (r=0.007)& PSA levels(r=0.17). Ga-68 PSMA scan identified additional bony and visceral (lung & liver) metastasis in 19 cases. **Conclusion:** Our preliminary experience suggests that Ga-68 PSMA PET/CT scan is a good modality for evaluation of primary prostate cancer, correlating well with histopathological analysisand finding additional sites of metastasis, thereby guiding their overall clinical management.

Prognostic value of Lymph node density in carcinoma of urinary bladder in patients under going radical cystectomy

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Background: Radical cystectomy (RC) and pelvic lymph node dissection (PLND) is standard treatment for muscle-invasive bladder cancer. Multiple nodal factors including number and extent of involved nodes, perinodal extension (PNE) and lymph node density (LNd) can predict survival. This study attempts to analyse the prognostic importance of LNd and to evaluate its cutoff value that co relate with survival in patients who underwent RC and PLND. **Material and Methods:** Between 2005 and 2011, 246 patients underwent radical cystectomy with pelvic node dissection.Of these 78 patients had positive nodes and complete clinical data for analysis and hence were chosen for the study. Age,extent of PLND, lymph node removed, presence of PNE and LNd were identified as interrelated variables . We divided patients into two categories of lymph node density LNd < 15 and LNd> 15. Factors affecting survival were analyzed using Kaplan-Meier plots and log rank test to test for significance. **Results**: On cox regression analysis patients with higher tumor stage, perinodal extension and higher LNd were found to have significantly poorer survival both in univariate and multivariate analysis. Patients with LNd less than 15 had better survival than those with LNd more than 15. Analysis between groups based on LNd shows statistically significant difference in mortality observed across these groups with 23.5% and 92.5% deaths in LNd less then 15 and more than 15 respectively. **Conclusion**: LNd is the one of strongest predictor of cancer-specific survival. Proposed LNd threshold have shown to be independent predictors of cancer-specific survival. It can be used as predictor of disease recurrence and may helps in selecting the patients who need adjuvant treatment.

Role of Ras Association Domain Family1A (RASSF1A) gene inpathogenesis in Urothelial Carcinoma of Bladder

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Background: Bladder cancer is 9th most common cancer and 13th most common cause of cancer death worldwide. Silencing of tumor suppressor genes by epigenetic modification is an important mechanism involved in the pathogenesis of cancer.One of these putative tumor suppressors is the RAS associationdomain family gene, RASSF1. The gene encodes 2 major isoforms,RASSF1A and RASSF1C, which are derived from alternative splicingand promoter usage. RASSF1A is predicted to encode a39-kDa protein consisting of a diacylglycerol (DAG)-binding domainand a Ras-association domain whereas RASSF1C encodes a32-kDa protein lacking the DAG-binding domain. Both alternative transcripts are expressed in various types of normal tissues.Interestingly, expression of RASSF1A transcripts is found to be absent or downregulatedin a number of epithelial cancers. Multiple studies have suggested a variety of roles forRASSF1A in suppressing carcinogenesis. RASSF1A restrictsunscheduled proliferation, survival, and migration. Aberrant RASSF1A promoter methylation can be a potential biomarker in the diagnosis/ prognosis of Urothelial Carcinoma of Bladder (UBC). **Methods**: 45 patients with urothelial carcinoma of bladder were enrolled. Tissue samples (Tumor and Adjacent non tumor) were collected from UBC patients to determine expression of RASSF1A and RASSF1C at mRNA level by Q-PCR. Methylation status of RASSF1A promoter was evaluated by Methylation Specific PCR(MS-PCR). Protein expression of RASSF1A was checked by Western blot and IHC. Further status of RASSF1A and RASSF1C was checked in bladder cancer cells (HT1376, T24). Cells were treated with demethylating drug Decitabine to see its effect on RASSF1A and RASSF1C expression. After treatment expression of RASSF1A and RASSF1C were assessed at mRNA level by Q-PCR and expression of RASSF1A at protein level by western blot. Methylation status of RASSF1Apromoter was evaluated by MS-PCR. **Results:** No significant difference was observed in RASSF1C expression in tumor tissue compared to adjacent normal tissue sampleswhile Expression of RASSF1A gene was significantly ($p<0.05$) lowerat mRNA level in tumor tissue of patients as compared to adjacent normal tissue samples. Decreased expression of RASSF1A was also observed at protein level by Western blot and IHC. Hypermethylation of RASSF1A was observed which was significantly correlated with decreased expression of RASSF1A gene. In bladder cancer cells (HT1376 & T24) RASSF1C transcript was detectable while negligible expression of RASSF1A was found at mRNA and protein level. After treatment with Decitabine methylation of RASSF1A promoter was less which was correlated with increased expression of RASSF1A at mRNA and protein level. **Conclusion:**Our data demonstrate that RASSF1Aexpression is down-regulated in primary tumors by aberrant promoter hypermethylation, suggesting that epigenetic inactivation of RASSF1A may play a critical role in bladder carcinogenesis. Our data suggest that RASSF1A can be exploited in future as a novel biomarker for Bladder cancer and may aid in the early detection and prognosis of the disease.

LASERS IN CARCINOMA PENIS-AN ERA OF ORGAN PRESERVATION

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Introduction: Carcinoma penis isa common genitourinary malignancy in developing countries like India. The treatment ofcarcinoma penishas been surgery (partial/total penectomy)oremasculation procedures .All of which are associated with devastating anatomical,functional,and psychological outcome .We studied whether laser could be used in thetreatment of this condition andsubsequently improvethequality of life **Material And Methods:** This isa prospective interventional study of patients with carcinoma penis between January 2014 to December 2015. Patients with clinical stage1 disease were decided in MDCtobe treated with laser excision .The clinical stage,pathologicalfactorsand follow up were studied and tabulated **Results:** 11 patientswere part of the study. All of them haddisease confined to the glans penis .All patientswere subjected to a prepped stove biopsy and subsequently underwent laser excision. Mean age was 52yearspre operativebiopsies were squamous cell carcinoma grade 1(7),grade2(3)and grade3(1). CO2laser wasused for excision. All patients underwent wide local excision with theraw arealeft to heal by secondary intension. Final histopathology report

wassquamous cell carcinoma grade1(6),grade2(4),grade3(1),marginswereneg ative among all SCC 1,But were close in SCC 2, positive inSCC 3.At a mean follow up of 3 monthswe had 2 local recurrences .One wassalvaged with arepeat laser excision and the other with a partial penectomy. At 6 months of follow up all patients were disease free. **Conclusion:** Laser excision of penile carcinomaisan option in small superficial lesion of penis. It does provide good outcomes comparable to the surgical excision but associated with better psychological benefits.

STUDY OF MICROVESSEL DENSITY BY IMMUNOHISTOCHEMICAL MARKER CD105 IN URINARY BLADDER NEOPLASMS: ARE ANTI-ANGIOGENIC DRUGS USEFUL?

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Introduction: Transitional cell carcinomas of urinary bladder have a somewhat unpredictable biological behaviour and to assess the tumor progression and clinical behaviour more objective prognosticators have to be used. Angiogenesis is a crucial pathogenic mechanism for this type of urothelial carcinoma and can be a potential therapeutic target. **Material And Methods:** Forty cases of urinary bladder neoplasms graded according to WHO/ ISUP classification 2004 and twenty cases of non neoplastic lesions were analysed for microvessel density using a highly specific endothelial marker CD 105. **Results:** Increase in MVD with increase in the grade of tumorwas found to be statistically significant (p value<0.05). The mean MVD in high grade and low grade neoplasms was 229.2±9.49 (no. / mm^2) and 158.87±8.90 (no. / mm^2) respectively. PUNLMP cases had a mean MVD of 109.12±7.43, lower as compared to both low and high grade neoplasms. Vasculature in high grade neoplasm were mostly of aberrant morphology, tortuous and without clear lumens. The difference in microvessel density between non neoplastic and neoplastic lesions was also statistically significant. (p value < 0.05). **Conclusion:** Association between microvessel density and grade, assessment of tumor vascularization by calculating themicrovessel density might be useful in both predicting patient outcome and selecting those who would benefit more with anti- angiogenic drugs on individual basis.

Clinical determinants of Self Sample careHPV testing in the Detection of High Grade Cervical Intraepithelial Neoplasia

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Background: Evaluation of determinants of screening tests helps to improve detection rates of the disease. Aim was to study some clinical determinants of self collected vaginal sample for careHPV testing in the detection of high grade Cervical Intraepithelial Neoplasia (CIN). **Methods:** A cross sectional study was conducted in a rural community on 5032 for cervical screening on women on 30 to 59 years. Self collected vaginal sample for careHPV (VHPV), visual inspection of cervix with acetic acid (VIA) and Papanicolaou (Pap) tests were the screening methods. Any screening test positive was referred for colposcopy and directed biopsy. Ratio of viral load expressed in relative light units (RLU) and positive controls set at a cut-off (CO) of 1 pg/ml and above was used as positive for careHPV. The association of VHV was studied with age, clinical sign, menstrual history of women, VIA and Pap for CINII+ or CINIII+ detection. **Results:** The positivity of VHPV was 2.9% as compared to 2.8% for Pap and 5.5% for VIA. VHPV Sensitivity for CINII+ and CINIII+ was 40.6% and 53.8% in all ages versus 47.6% and 62.5% in younger age respectively. Average viral load of VPHV was significantly high in CINIII+ as compared to the rest of the grades. VIA positivity was not associated with VHPV in the detection of CINII+. Younger age and Pap positivity were associated with VHPV. **Conclusion:** Study demonstrated the feasibility of using careHPV in vaginal samples among younger age increases detection rates of high grade CIN and also population coverage due self sampling approach.

Key words: careHPV, self sampling, Cervical Intraepithelial Neoplasia

Role of HE4 in prediction of optimal cytoreduction in ovarian cancer patients receiving neoadjuvant chemotherapy.

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Background: Level of cytoreduction is the most important prognostic factor in the management of advance stage carcinoma ovary. Neoadjuvant chemotherapy approach is reasonable to achieve optimal cytoreduction with minimum morbidity. Currently, there are lack of factors which can predict chances of optimal cytoreduction after neoadjuvant treatment. We investigated the role of new biomarker Human Epididymis protein 4 (HE4) in predicting optimal cytoreduction after neoadjuvant chemotherapy approach. **Materials & Methods:** This prospective study was undertaken in department of surgical oncology, King George Medical University, Lucknow. Ethical clearance for the study was taken from research branch of university. Informed consent was taken from all enrolled patients. Study includes total 44 patients, including 28 (63.6%) stage IIIC and 16 (36.4%) stage IV patients, undergoing treatment from October 2013- January 2015. Standard neoadjuvant chemotherapy (three to four cycles of Paclitexal and Carboplatin) was given after confirming the diagnosis with FNAC or biopsy. Serum HE4 levels along with imaging was done before starting of neoadjuvant chemotherapy and before surgery. Level of cytoreduction was recorded as optimal if maximum diameter of residual disease was 1 cm or less. Out of 44 patients, 29 (66%) patients underwent optimal cytoreduction. Histology includes, 38 serous adenocarcinoma and 6 mucinous adenocarcinoma. SPSS version 21 was used for the statistical analysis. **Results:** Mean change in values of HE4 before and after neoadjuvant chemotherapy was 1125.02+/-384.72 (p=0.0001). There is significant association between normalization of HE4 levels after neoadjuvant chemotherapy and achievement of optimal cytoreduction (p=0.0001). Sensitivity and specificity of the HE4 was 96.5% and 100% respectively. Positive and negative predictive value of HE4 was 100% and 93.8% respectively. Overall accuracy of HE4 to predict optimal cytoreduction was found to be 97.7%. The area under the receiver operating characteristic curve was 98% (p=0.0001). **Conclusion:** The result of this study shows that HE4 is a useful biomarker that can be used with good clinical value to predict optimal cytoreduction in advanced stage ovarian carcinoma patients receiving neoadjuvant chemotherapy.

Awareness of cervical cancer risk factors and symptoms -A pilot survey in a small village of Bihar.

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Introduction: Lack of awareness of risk factors and symptoms for cancer may lead to late diagnosis and poor prognosis. **Objective:** Toassess the community awareness about cervical cancer risk factors and symptoms and perceptions about prevention and cure of cervical cancer in order to contribute data to inform interventions to improve cervical cancer survival. **Design:** A Pilot survey. **Setting and participants:** We conducted this study in Golma a village in Saharsa Distict .The sample included 350 persons aged 18 years and above. **Data collection methods and analysis:** We collected data using a structured questionnaire in Hindi. Logistic regressions were used to determine the associations between socio-demographic and outcome variables. **Results:** Most participants (344/350) had heard about cervical cancer. Known risk

factors including multiple sexual partners, human papillomavirus infection, and early onset of sexual activity, were recognized by 66%, 42%, and 54% of respondents respectively. 63% of participants also believed that prolonged use of family planning pills and injections caused cervical cancer. The majority of participants recognized symptoms of cervical cancer including intermenstrual bleeding (85%), post-menopausal bleeding (76%), and offensive vaginal discharge (74%). 70% of participants believed that cervical cancer is preventable and 70% believed that it could be cured if diagnosed at an

A pilot study of sentinel lymph node biopsy in oral cancer using blue dye

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Back ground Sentinel Lymph Node (SLN) biopsy using a combination of radioisotopes and blue dyes have a good accuracy rate in predicting subclinical neck nodal metastases in head and neck cancers. However, the limited availability of lymphoscintigraphy facilities in India requires exploration of alternative methods of SLN detection. We evaluated the feasibility of using methylene blue dye alone in detecting SLN in Oral cancer patients who underwent standard Neck dissection. **Material and Methods**: 20 patients with oral squamous cell cancers(N0, N+ and Post irradiated) underwent SLN biopsy using peri tumoural methylene blue dye injection. After accurately assessing the stage and grade of the cancer, the patient was posted for surgery under general anesthesia. Just before giving incision in the neck for elective neck dissection, 5ml of 1% Methylene blue dye was injected in to the mucosa around either the tumour mass or around the biopsy cavity if a previous excision has been performed. The time duration between injecting the dye and raising the neck flap was within 20 min. Blue stained lymph node were appreciated , dissected out and sent for histopathological examination. Then the planned neck dissection was performed. **Results:** The mean age of patients was 43 years (range: 25–60 years). The most common sub sites were tongue (60 %) .Sixty percent (n=12) of the patients were tobacco/ betel users and 40% (n=8) were alcoholics.SLN was identified in 8/9 in N0 neck and 7/9 in N+ neck cases. No SLN was identified in Irradiated neck. SLN identification rate was 88.8% in N0 and 77.7% in N+ Neck. In 11 patients (55 %) more than one SLN was identified. Mean SLN yield was 2 (median=2) with the highest yield in Tongue cancers (mean =2.25).SLN was positive for metastasis on Standard Histopathological Examination in 1/8 in N0 neck and 3/7 in N+ neck cases. **Conclusion:** Methylene blue dye alone can be successfully used for SLN identification in early oral cancers with a good accuracy. This method will be of use especially in resource limited countries and centres where nuclear medicine facilities are not widely available. However, it has to be validated by larger randomised multi institutional trials for wider applicability.

Role of MMP13 gene expression in evaluation of Radiation response in Oral Squamous cell Carcinoma.

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Introduction: Oral squamous cell carcinoma is one of the most common cancer occurring worldwide and due adverse effect of tobacco (both chewing and smoking) and alcohol consumption. MMP13 (Matrix Metalloproteinase 13) is crucial gene for tumor invasion and metastatic spread of cancer. The expression of MMP13 mRNA alters several signaling pathways involved in the development and prognosis of OSCC. Their expression may help in predicting radiotherapy treatment response in OSCC patients. **Objectives:** This study was conducted to analyze the mRNA expression of MMP13 gene and its relation to clinicopathological characteristics (age, abusing habits, clinical T-stages) and treatment responses of OSCC patients undergoing Radiotherapy. **Material and Methods:** The study included tissue specimens obtained via biopsy of 160 patients with OSCC who were recommended for radiotherapy treatment and 80 healthy control tissues. Ethical approval was taken from the Institutional Ethics Committee of K.G. Medical University Lucknow before the start of the study. Informed written consent was taken from all the participants before their inclusion into this study. **Results:** The qRT-PCR studies demonstrated significant increase in the mRNA expression of MMP13 gene in OSCC when compared with matched control tissues. Our results revealing significant increase ($p<0.001$) in the mRNA expression (30.21 folds) of MMP13 in OSCC patients above 45 years was found to act in-tandem in the progression of OSCC. Significant increase ($p<0.001$) in mRNA expression of MMP13 was found more in OSCC patients, which are prone to consumption of tobacco, smoke and alcohol synergistically for both treated responder and non-responders when compared with controls. Our results revealed that this gene was significant ($p<0.001$) in early (10.33 folds) as well as advanced stage (47.88 folds) of OSCC patients which were non-responder after radiotherapy treatment. Our data provides a correlation of this gene with age, substance abuse and clinical T-stages. **Conclusions:** This study found that elevated expression of MMP13 in non-responder OSCC patients after radiotherapy may be aligned with radio-resistance in OSCC. Since the overexpression of MMP13mRNA levels alter many signaling pathways found to be involved in the development and prognosis of OSCC, which may lead to the consideration that altered level of this gene may be helpful in predicting radiotherapy treatment response in OSCC patients. These results advance our knowledge involving this gene in the resistance to the response of radiation therapy and could be used as potential marker for the radio-therapy treatment.

Keywords: Radiotherapy, Treatment Response, MMP13,

Development of Nanofabricated Mucoadhesive Buccal Patch Containing 5-Fluorouracil for Treatment of Oral Squamous Cell Carcinoma

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Introduction: Oral squamous cell carcinoma represents 90% of all oral malignancy affecting tongue and floor of the mouth.[1]The current therapy with 5-fluorouracil suffers from many drawbacks including hepatic degradation and poor specificity.[2]Entrapment of 5-fluorouracil in solid lipid nanoparticles and their fabrication in buccal patch will help in efficient site specific delivery of the drug. **Objectives:**Preparation of solid lipid nanoparticles entrapping 5-fluorouracil and their fabrication in mucoadhesive buccal patch. **Material and Methods:** Solid lipid nanoparticles were prepared by high speed homogenization and ultrasonication technique. They were evaluated for size, zeta potential, %entrapment, drug loading, percent yield, surface morphology, drug release and compatibility. Mucoadhesive buccal patch were prepared by solvent casting method and were further evaluated for content uniformity, folding endurance, radial swelling, residence time, bioadhesion force and drug release. **Results:** Nanoparticles of size 112±30nm and zeta potential 34.0±0.8mV were obtained with 64.9±2.3% entrapmentand 32.6±1.4% drug loading along with 66.86±2.7% of yield. SEM and TEM micrograph revealed spherical surface morphologyand were in accordance to particle size. Nanoparticles showed 71.31±1.10%drug release with biphasic nature and were found to be compatible. Buccal patch showed uniform drug content with greater folding endurance moreover, they showed 85-90% of swelling index and residence time of

4-6.5h. The bioadhesion force of the patch were found to be 66.50±3.43 X 10^2 kg $m^{-1}s^{-2}$ with 61.31±1.10% of drug release in 8h.**Conclusions:** Nanofabricated mucoadhesive buccal patch of 5-fluorouracil may be used for effective treatment of Oral squamous cell carcinoma and needs further*in-vivo* evaluation.

Key Words: Oral squamous cell carcinoma, 5-fluorouracil, buccal patch.

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Aspiration Pneumonia in Irradiated Head and Neck Cancer Patients From The Perspective of a Developing Country

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Background: Head and Neck cancers are one of the most common cancers in our country. It's often complicated with aspiration pneumonia, especially in irradiated patients. The Incidence of aspiration alone is as high as 68% and that of aspiration pneumonia is 14.54% with a mortality rate of 10%. There is paucity of data on risk factors for developing aspiration pneumonia from the developing world. To the best of our knowledge there is no study that does risk stratification of irradiated head and neck cancer patients who are likely to develop aspiration pneumonia. Hence the need for our study. **Materials and Methods:** In this retrospective study, all consecutive patients treated with primary or post-operative RT(radiotherapy) with curative intent for head and neck cancer in a tertiaryhealthcare centre in South India, from July 2014 to December 2015, were included. All patients treated with palliative intent, patients who abandoned treatment and those whose data was not available,were excluded. Patients were identified from the departmental database and manual extraction of data was done from the case files. Data was assessed from the time of diagnosis to the response assessment. **Results:** Results were analysed using chi square and Fischer's test to identify risk factors associated with aspiration pneumonia. Dysphagia (grade III-IV) Mucositis (grade III-IV), presence of feeding tube, Diabetes mellitus, Tuberculosis(TB) and treatment interruptions with grade 3 or more toxicities) were proven statistically significant. On Univariate analysis out of the 6 risk factors only TB, Mucositis(grade III-IV) and presence feeding tube were proven to be statistically significant and were taken up for multivariate logistic regression. After applying Multivariate Logistic regression, an equation that predicts the development of aspiration pneumonia was created.

Variables analysis	No Aspiration pneumonia	Percent	Aspiration pneumonia	Percent	P value
Site					
Oral cavity	78	84.8%	14	15.2%	
Oropharynx	34	85.0%	6	15.0%	
Hypopharynx	21	75.0%	7	25.0%	
Larynx	21	91.3%	2	8.7%	
Nasopharynx	5	83.3%	1	16.7%	0.5
Tube feeding					
Yes	75	77.3%	22	22.7%	
No	94	91.3%	9	8.7%	0.006
Treatment interruption due to grade 3 toxicity or more					
Yes	94	79.0%	25	21.0%	0.009
No	75	92.6%	6	7.4%	
TB					
Yes	6	42.9%	8	57.1%	<.0001
No	163	87.6%	23	12.4%	
Diabetes					
Yes	13	68.4%	6	31.6%	0.042
No	156	86.2%	25	13.8%	
dysphagia					
I-II	89	91.8%	8	8.2%	
III-IV	80	77.7%	23	22.3%	0.006
Mucositis 3+					
I-II	74	93.7%	5	6.3%	
III-IV	95	78.5%	26	21.5%	0.004

Conclusion: Development of aspiration pneumonia is associated with presence of feeding tube, dysphagia(III-IV), mucositis(III-IV), treatment interruption with grade III or more toxicity, TB and diabetes. The proposed equation for predicting aspiration pneumonia needs to be validated by further studies so that risk stratification can be done.

Polymorphisms of DNA Base-excision Repair genesXRCC1 and hOGG1 and Nasopharyngeal Carcinoma in Naga population

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Introduction: Nasopharyngeal Carcinoma (NPC) is arare tumour in most parts of the world;however,its incidence rateis high insome geographical regions and certain ethnic groups, particularly in SouthernChina and Southeast Asia.X-Ray repair cross-complementing protein 1(XRCC1) and human 8-oxo-guanine glycosylase-1 (hOGG1) genes are the key enzymes in the Base Excision Repair (BER) pathway. **Objective:** This study sought to determine whetherthe non- synonymous single nucleotide polymorphism(SNP) of XRCC1 includingrs25487(Arg399Gln),rs25489(Arg280His), rs1799782 (Arg194Trp), and hOGG1rs1052133 (Ser326Cys) were associated with the risk of NPC among the Naga Population. **Materials and Method:** Histologically confirmed NPC patients were enrolled from Pathology OPD, Naga Hospital Authority Kohima, Nagaland andcancer free controlsmatched by age,sex and tribe. DNA was isolated from whole blood with QIAamp DNA Mini Kit (Qiagen, USA).The genetic variants of the four SNPs was determined by using PCR-RFLP method. **Result:** 54 NPC cases (M:F ratio 2:1,mean age: 49±11.8 yrs) were included in the study. In case of Arg399Gln, both Arg/Gln genotype (OR=1.48,Chi sq.=1.76,p=0.18,) and Gln/Gln genotype (OR=0.58,chi sq.=0.74,p=0.39) and allelic frequency (OR=1.1, Chi sq.=0.1,p=0.75) showed nonsignificant correlation with NPC. Similarly, in Arg280His**,** Arg/His genotype(OR=0.59, Chi sq=2.07,p=0.15) and His/His genotype(OR=0.91, Chisq.=0.00,p=0.94) and allelic frequency (OR=0.61,Chi sq.=0.97,p=0.32) and in hOGG1Ser326Cys, Ser/Cys genotype (OR=1.57,Chi sq.=1.35,p=0.24) and Cys/Cys genotype (OR=1.57,Chi sq.=1.23,p=0.26) and allelic frequency (OR=1.23,Chi sq.=0.51,p=0.47)showed no association with NPC. Incase ofArg194Trp,Arg/Trp genotype (OR=0.96,Chi sq.=0.02,p=0.88) and allelic frequency (OR=0.74,Chi sq.=0.89,p=0.34) showed nocorrelation with NPC. However,Trp/Trp genotype showed a positive correlation with NPC(OR=0.00,Chi sq.=8.1, p=0.00). In case of life style factors,both alcohol consumption (OR=2.45,Chi sq.=9.6,p=0.00) and tobacco chewing(OR=3.79, Chi sq=20.4,p=0.00) showed highly significant correlation with NPC risk whereas smoking(OR=1.48, Chi sq.=1.7,p=0.18) didn't show any correlation with NPC. **Conclusion:**The present studyprovides an estimate of allele and genotype distributions of XRCC1 Arg399Gln, Arg280His, Arg194Trp and hOGG1 Ser326Cys polymorphisms, where only XRCC1Trp280Trpgenotype,alcohol consumption and tobacco chewing are found to be associated with increased risk of NPC in Naga population.

Keywords: Nasopharyngeal carcinoma(NPC),X-Ray repair cross-complementing protein 1 (XRCC1) ,human 8-oxo-guanine glycosylase 1 (hOGG1)

Prospective study on assessment of radiation induced volume changes in parotid and submandibular glands in patients with head and neck cancer receiving Intensity Modulated radiotherapy with or without concurrent chemotherapy

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Background: Radiation therapy (RT) has played an important role in the treatment of patients with head and neck cancers. One of the most frequent and debilitating long term side effects of RT for these patients is xerostomia. Dry mouth affects patient's quality of life, including speech, taste, sleep, mastication, and deglutition. The submandibular glands are important for producing saliva, and the parotid glands assume a major role in stimulating salivary flow. Intensity-modulated radiotherapy (IMRT) for head and neck cancers can spare the parotid glands, leading to significant reductions in the incidence and severity of xerostomia, especially with mean doses to the glands of less than 26 Gy. IMRT can also spare the submandibular glands and prevent xerostomia when the mean dose to the submandibular glands is approximately 25.9 Gy (range, 21–34.9 Gy). Volumetric and geometric changes in target volumes and Parotids during IMRT need to be quantified, as local control and post radiotherapy salivary production are well predicted by dose-volume effects. **Aim and Objectives:** To evaluate radiation induced volume changes in the parotid glands and submandibular glands in patients with head and neck cancer receiving IMRT, correlation with the mean doses received by the glands and assessment of timings of the volume changes during fractionated RT. **Materials and Methods:** Fourty five patients of Head and Neck Cancers, satisfying the inclusion criteria were included from May 2015 to Dec 2015 and were treated with radical or post-operative Radiotherapy using IMRT with or without Chemotherapy. Radiotherapy planning CT scans were done at pre RT, after 40 Gy and on completion of treatment for each patient. Parotid and submandibular gland volumes were re contoured on each study scan and rechecked with same observer. The volumes (V0- Volume on initial CT scan) and mean doses to the parotid and submandibular glands were calculated from the Dose-volume histograms (DVHs) of the IMRT plan, done on pre RT scan. The re contoured volumes of parotid and submandibular glands on the CT after 40 Gy (V1) and on completion (V2) were noted. Volume changes of the glands were assessed and statistical analysis was done to see any correlation between the mean dose and volume changes of the glands and also with the weight loss. **Results:** The total mean dose to the parotid glands in IMRT patients was 24.47 Gy (for the ipsilateral and contra lateral parotid glands they were 41.61 Gy and 26.13 Gy, respectively). For IMRT patients, the total mean doses to spared and irradiated submandibular glands were 7.39 Gy and 58.04 Gy, respectively. The average volume loss after 4 weeks of RT, upon completing RT versus before RT were 22.12%, 31.12%, and between 4th week to completion of RT 11.56% for the parotid glands and 25.26%, 32.93% and between 4th week to completion of RT 10.28% for the submandibular glands, respectively. The average mean volumes of both parotid glands and submandibular glands after 4 weeks of RT and upon completing RT were significantly smaller than before RT ($P < .001$).We observed volume loss during RT in the parotid and the submandibular glands. The average rates of volume loss during the first 4 weeks of RT (22.12% and 25.26% respectively) were larger than in the last 2/3 weeks of RT (11.56% and 10.28% respectively). Volume loss at higher doses (>30 Gy) to the glands was significantly larger than at low doses (<30 Gy; $P < .001$). **Conclusions:** The parotid and submandibular glands shrunk during RT. These gland volume reductions correlated significantly with the mean dose to the irradiated glands; the spared glands showed few changes.

Key Words: Head and neck cancer, Intensity-modulated radiotherapy, Parotid gland

Upregulation of survivin isoforms and coorelation of survivin 2B with p53 protein in human oral cancers

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Introduction: Survivin, a member of IAP family is a promising candidate for targeted cancer therapy as its high expression in tumors is known to be associated with poor clinical outcome, more aggressive

clinicopathologic features, resistance to radiation and chemotherapy as compared to no or low expression in normal tissues .Earlier studies from our lab have shown that 46% of oral squamous carcinomas exhibit inactivation of p53.Interestingly survivin is a p53 target gene. p53 family member proteins p63 and p73 have been identified to be important for p53 dependent apoptosis.b **Objectives:**Our study aims to determine the expression of survivin isoforms in oral cancers and to identify the isoform associated with oral tumorigenesis and the correlation of the expression of p53 family member proteins if any with the expression of survivin. **Material and Methods:**The expression of 5 survivin isoforms in 12 normal tissues from healthy individuals and 45 adjacent normal and tumor tissues was analyzed by real-time PCR and was correlated with clinicopathological features of the patients. The expression of wild type survivin and p53 family members in adjacent normals and tumor tissues was assessed by immunohistochemistry. **Results:**Survivin wild type shows a 27 fold upregulation and survivin isoforms ΔEx3 and 2B show a 11 fold upregulation in tumor tissues compared to normal. No significant association was observed between specific survivin isoforms and tumor stage, differentiation and nodal status. p53 protein exhibited a significant ($p<0.05$) correlation with the expression of pro-apoptotic survivin isoform 2B. **Conclusions:**Upregulation of wild type survivin and anti-apoptotic isoform ΔEx3 may imply role for them in oral tumorigenesis. Also upregulation and significant correlation of the pro-apoptotic isoforms 2B with p53 expression may suggest that it may be positively regulated by p53. The expression of survivin splice variants and p53 family members will be assessed in a larger cohort to delineate their associations.

Response to induction chemotherapy as a predictor for definitive treatment in stage IV head neck squamous cell carcinoma

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Purpose: Induction chemotherapy is not considered as a standard treatment in locally advanced head and neck cancer. The aim of this study is to predict the response of induction chemotherapy in patients with bulky locally advanced head and neck squamous cell carcinoma, who are not feasible for any upfront radical treatment. **Materials And Methods:**31 patients (stage IVA and IVB, T4, N3) LAHN$CC were treated with induction ICfrom April 2013 to September 2015. ECOG Performance status was ≤ 2 and they underwent 2 cycles of 3 weekly IC (Taxane and Cisplatin). Patient who responded (CR + PR), underwent Radical treatment (CTRT or Sx →CTRT) and nonresponders were treated with palliative treatment. The response rates, toxicity (accordance with RTOG), completion rate of radical treatment post NACT and overall survival are reported. **Results:** Median follow up and age of patients was 7 months (2-28 months) and 54 (30-74) yearsrespectively. Ratio of M: Fwas 29:2. Out of a total of 31 patients, site wise distribution was as follows: oral cavity-13(41.9%),or opharyngeal-7(22.6%), laryngopharynx-8(25.8%) and unknown primary with neck secondaryUNP-3(9.7%) respectively. After 2 cycles of IC, 19 patients(61.29%) responded, following which they underwent radical treatment and remaining 12 (38.71%)were treated with palliative treatment. On site wise subgroup analysis of radically treated patients (>50% response), 6 patients were of oral cavity, 6 patients oforopharyngeal ,6of laryngopharynx and 1 patients of UNP, of which only 2 patients of Oral Cavity underwent surgery followed by CTRT and remaining patientswere treated with CTRT. At the end of treatment maximum 15 patients had grade 2 mucositis, 4 patients had grade 3 mucositis and 2 patients developed grade 2 hematological toxicities in radical treatment group. No toxicity related mortality was seen. The completionrate of radical treatment post IC was 93.5%. The median OS was 15 month ((95% CI 6-23). 15 Patients are alive in which 4 patients are alive with disease.Total 9 patients died and 7 patients were lost to follow up. **Conclusion:** The protocol introduces a novel algorithm for management of patients with bulky locally advanced head and neck squamous cell carcinoma, who are not feasible for upfront radical treatment. It is designed to triage patients who are sensitive to chemotherapy to radical treatment whereas those who are not sensitive are treated with palliative treatment. Use of IC is safe & effective in selected cohort of patients with LAHNSCC.

The Impact of Triple Positive Pathological findings in the Prognosis of Oral cavity malignancy

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Introduction: Perineural invasion (PNI), Lymphovascular invasion (LVI), and Extracapsular spread (ECS) of lymph nodes are adverse histopahtological factors associated with the risk of local and regional recurrences among patients with oral squamous cell carcinoma. **Objectives:**The aim of this study was to evaluate the prognostic impact of PNI, LVI and ECS individually and combination of PNI, LVI and ECS in patients with squamous cell carcinoma of the oral cavity. **Material and Methods:** Retrospective analysis of the patients with oral cancer treated in a tertiary care centre with minimum of 5 year follow up. In total, 134 patients registered in our hospital and diagnosed with oral cavity squamous cell carcinoma who underwent treatment from 2006 to 2010 were consider for the study. Local / regional recurrence and 5-year survival rates were analyzed. **Results:** Patients with PNI, LVI, or ECS presented pathologically had 5-year overall survival rates of 55%, 48.1%, and 35.6%, respectively. Patients with both ECS and PNI or both ECS and LVI presented had 5-year overall survival rates of 33.1% and 23.6%, respectively. Patients with triple-positive status (PNI, LVI, and ECS) had a 5-year overall survival rate of 21%. The 5-year local/regional control rate for patients with both ECS and PNI or both ECS and LVI was 28% and 42.2% respectively; for all three factors, it was 26.7%. **Conclusions:** Triple-positive pathological status (PNI, LVI, ECS) in oral cavity carcinoma are related to dismal prognosis. ECS and PNI, or ECS and LVI experienced very low 5-year local/regional control rates, 5-year overall. Further studies and more aggressive treatment are necessary to improve these clinical outcomes.

Long-term outcomes and toxicity with re-irradiation for recurrent/second primary head and neck cancer

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Background: Re-irradiation (re-RT)to recurrent/second primary (SP) head and neck cancers (HNC) was unheard of till recent. Butwith better availability of radiotherapy techniques (especially IMRT), renewed confidence in physician for delivering a second course of radiation for radical intent and physician's improving ability to identify patients suitable for re-RT have replaced chemotherapy and best supportive care as treatment of choice for unresectablelocally recurrent HNC. Past decade has witnessed growing evidence favoring role of re-irradiation.This study is an another attempt to explore the long-term feasibility and efficacywith re-irradiation deliveredto locally recurrent HNC. **Materials & Methods:** It is a retrospective analysis of 48 patients with loco-regional recurrent or SP of oral, oropharyngeal, laryngeal or hypopharyngeal sites with histology squamous cell carcinoma treated with IMRT- re-RT between 2000 – 2013. End points were loco-regional control (LRC), overall survival (OS) and late toxicity assessment. Kaplan-Meier curve and Log-rank test was used for comparison between groups. Multivariate analysis were computed through a Cox proportional hazard model. **Results :**Of 48 patients included in this study 36 (75%) underwent re-RT with curative intent and 12 (25 %) underwent adjuvant re-RT with or without concurrent chemotherapy. The median follow up of patients was 14.98 months. Median LRC was 49.57 months and 2 years LRC rate was 41%. Univariate analysis done to explore prognostic factors affecting median LRC showed statistically significant better results with two factors: initial surgical resection followed by adjuvant RT ± CCT, and complete response (CR) achieved at 3 months of completion. Multivariate analysis confirmed these two factors to be significantly associated with better

median LRC. Median OS was 28.22 months and 2 years OS was 55.9 %. Univariate analysis showed 3 factors significantly affecting median OS: Initial surgical resection followed by adjuvant RT ± CCT, CR achieved at 3 months and interval between two RT of atleast 2 years.Multivariate analysis using cox proportional hazard model revealedonly first two factors to be significantly with better median OS.There was no patient with grade IV acute toxicity. Late toxicity with re-RT were tolerable. There were no patients with myelopathy or catastrophic events such as osteoradionecrosis and carotid blow out. 3 patients needed tracheostomy, 1 each developed brachial plexopathy, esophageal stricture and trismus. **Conclusion:**re-RT is feasible, effective with tolerable toxicity, however should be offered with selective patients subgroup.

IMPACT OF RITUXIMAB ADDITION TO CHOP IN DLBCL ON IHC PROGNOSTIC MARKERS

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Background: Addition of rituximab to CHOP chemotherapy in patients with diffuse large B cell lymphoma (DLBCL) has been shown to have a survival benefit. Further analysis of treatment outcome differences with addition of rituximab, based on expression of immune-histochemical parameters like DLBCL subtype (Germinal/Non-Germinal center), Ki67, and bcl-2 have been stated rarely in literature with no data from India. Therefore, we have undertaken this study. **Materials And Methods:** It is a retrospective study undertaken at Kidwai Memorial Institute of Oncology, a tertiary care center in south India. A total of 109 patients were included in the study. 66 patients received CHOP and 43 received RCHOP as treatment. Subtype analysis into GCB (Germinal centre B-cell type) and non-GCB was done in all the patients. Ki 67 cutoff of 70% or more was used to classify into high and low. Ki 67 analysis was available for 73 patients and BCL-2 analysis for 97 patients. The x^2 test was used to examine relationships between variables. Survival curves were estimated by the Kaplan-Meier analysis, using the log-rank test. **Results:** Of the total patients, 66 received CHOP and 43 received RCHOP, with a significant survival advantage with the latter (24 m vs 38 m; P<0.05). Further analysis of these two subgroups was done based on subtype (GCB/NGCB), Ki 67, and bcl-2. In the CHOP group, GCB had a survival advantage over NGCB (32 m vs 14 m; P<0.05), whereas, in the RCHOP group, no significant difference was seen (44 m 34.5 m; P=0.76). In RCHOP group, low Ki67 had a survival advantage over high ki67 (43.5 m vs 30 m; P<0.05), whereas, no significant difference was seen in CHOP group (26.5 m vs 24.5 m; P=0.6). Bcl-2 negativity had a survival advantage in CHOP (31 m vs 20.5 m; P<0.05) as well as RCHOP group (39 m vs 26.5 m; P<0.05). **Conclusion:** Addition of rituximab to CHOP nullified the negative prognostic impact of non-GCB subtype and brought it similar to that of GCB subtype. Whereas, it aggravated the negative prognostic impact of high Ki67 and had no significant effect on that of bcl-2 positivity.

TABLE 1. Summarising the impact of various IHC markers in CHOP and RCHOP group.

	N	MEDIAN OS	P VALUE
CHOP	66	24	<0.05
RCHOP	43	38	
CHOP GROUP			
GCB	40	32	<0.05
NGCB	25	14	
HIGH Ki67	24	24.5	0.6
LOW Ki67	18	26.5	
BCL-2 NEG	28	31.0	<0.05
BCL-2 POS	30	20.5	
RCHOP GROUP			
GCB	20	44	0.76
NGCB	22	34.5	
HIGH Ki67	18	30	<0.05
LOW Ki67	13	43.5	
BCL-2 NEG	23	39	<0.05
BCL-2 POS	16	26.5	

Reporting quality of life among patients of chronic myeloid leukemia on long-term Imatinib Therapy

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Background: Imatinib therapy brought major advancement in the treatment of chronic myeloid leukemia (CML) with regard to survival. However, life-long therapy alters patients' quality of life and this issue is under reported in India. The present study aims to report quality of life among patients of CML on long term Imatinib treatment. **Methods:** Patients of CML (N=221) who had received at least 6 months of Imatinib were assessed usingEORTC QLQ C30 and EORTC QLQ CML 24 scales. Student's t test and one-way ANOVA were used forcarrying out the analysis. **Results:** Among 221 patientsof CML 133 were males and 88 were females[median age 39 years]. On EORTC QLQ C30 analysis, none of the socio-demographic variables were associated with overall quality of life. Of dimensions of quality of life, physical functioning differs significantly with gender (t=2.70, p<0.05), age (t=2.53, p<0.05) and socio-economic status (F=4.92, p<0.05).Also gender differs significantly withemotional functioning (t=4.04, p<0.05). With regard to symptoms, pain (t=2.32,p<0.05) differs significantly with gender; and fatigue with socio-economic status (F=3.90,p<0.05). On EORTC QLQ CML24 analysis, gender was found to differ significantly withdimensions of symptom burden (t=2.93, p<0.05), impact on worry/mood (t=3.22, p<0.05) and impact on daily life (t=2.07, p<0.05). Also, socio-economic status differs significantly with satisfaction with social life scale (F=3.27,p<0.05) and impact on daily life scale (F=4.45,p<0.05). **Conclusion:** Gender, age and socio-economic status were parameters that were significantly associated with quality of life dimensions. Females reported high on symptoms like fatigue, pain, overall symptom burden and impact on worry/mood. Whereas males reported high on functioning scales.

Anti-viral therapy versus regular monitoring for the prevention of chemotherapy-induced HBV reactivation in patients with lymphomaand resolved HBV infection: cost-effectiveness study

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Background: Optimal preventive strategies are unknown for chemotherapy-induced hepatitis B virus (HBV) reactivation in patients with lymphoma and resolved HBV infection who received rituximab- cyclophosphamide, doxorubicin, vincristine, and prednisolone (CHOP) as first-line chemotherapy. **Materials and Methods:** We compared the relative cost-effectiveness of prophylactic antiviral therapy from the start of chemotherapy

to 6 months after completion of chemotherapy (Option A) and monthly HBV DNA monitoring and antiviral therapy upon HBV reactivation for 48 weeks (Option B) through decision tree analysis. Probabilities of HBV-related events and survival were estimated from published studies, and the cost was calculated according to the perspective of Taiwan's National Health Insurance Program. Sensitivity analysis was performed to examine the impact of the efficacy (defined asprevention of HBV-related death or liver decompensation) and the cost of different interventions. **Results:** The long-term follow-up of our prospective study on patients with lymphoma indicated that the estimated 3-year overall survival ratewas 52.3% (95% confidence interval [CI] 50.2 – 54.4) for patients with HBV reactivation after rituximab-CHOP chemotherapy and 78.2% (95% CI 72.3-84.1)for those without (P=0.033). The probability sensitivity analysis indicated that Option A had significantly lower incremental cost-effectiveness ratio (ICER) (median US$63 154 and US$101 010for Options A and B, respectively, P<0.001) and especially for high-risk (negative for anti-HBs antibody at baseline) subgroup (median USD$59 304 for Option A and USD$170 971for Option B, P<0.001). **Conclusions:** Prophylactic antiviral therapy is more cost-effective than regular HBV DNA monitoring in most settings. Identification of high-risk subgroups most vulnerable to HBV-related complications may further improve the cost effectiveness of prophylactic antiviral therapy in HBV endemic areas.

Background: Mutations in the Bcr-Abl kinase domain may cause, or contribute to, resistance to tyrosine kinase inhibitors (TKIs) in chronic myeloid leukemia patients. *BCR-ABL1* kinase domain point mutations are detectable in ~50% of patients with treatment failure and progression. More than 80 amino acid substitutions have been reported in association with resistance to Imatinib. **Materials And Methods:** This was a retrospective observational study. We analyzed patients from 2003 to 2015 who were tested for Imatinib resistance mutation analysis (IRMA) in view of suboptimal responses while on Imatinib or Imatinib failure. Failures were distinguished as either primary (failure to achieve a given response at a given time) or secondary (loss of response) according to European LeukemiaNet recommendations for the management of chronic myeloid leukemia. Direct sequencing of the BCR-ABL transcript by the Sanger method was used for IRMA testing. **Results:** Bcr-Abl kinase domain mutations were seen in 18

IRMA indication	**Number (285)**
Primary Failure	114
Secondary Failure	171
Mutations detected	**94 (32.9 %)**
ATP binding region	28
Other P-LOOP	26
SUBSTRATE binding region	16
SH2 Contact	7
A-LOOP	3
C-Helix	1
Others	13
No mutation detected	**191 (67.1%)**

patients (15.78%) of primary failureand in 76 patients(44.44%) of secondary failure. 96 patients (84.21%) of primary failure and 95 patients (55.55%) of secondary failure showed no mutations. The responseassessedto second line TKI and dose hike of Imatinibin the form ofCCyR/ <1% Bcr-Ablat 12months was 53.87% for Nilotinib, 53.84% for Dasatinib and 56.09% for Imatinib dose hike group. The adverse effects, both haematological and non haematological were higher in patients on higher doses of Imatinib than Nilotinib and Dasatinib. Neutropenia was the most common hematological adverse effect observed. In non haematological adverse effects musculoskeletal pains was common with high dose Imatinib and Dasatinib, and skin rash in those on Nilotinib. **Conclusion:** *BCR-ABL1* kinase domain point mutations were detected in 32.9% of patients with treatment failure and progression. T315I (ATP binding region) is the most common mutation observed followed by G250E. 26 types of amino acid substitutions were found. Higher percentage of mutations were found in those with secondary failure. More than 50% of patients had optimal response to second line TKI and dose hike of Imatinib.

Study of expression-pattern of CD25 in de novo acute myeloid leukemia and its association with fms-like tyrosine kinase-3 –internal tandem duplication (FLT3-ITD) mutation.

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Background: CD25 (IL-2 receptor-α) expression has shown to be an independent poor prognostic marker in young (age < 60 years) de novo AML patients. Recently, positive expression of CD25 in combination with CD34/CD123/CD99 is shown to be associated with FLT3-ITD mutated AML which is a high risk AML group. We evaluated the expression pattern of CD25 in AML blasts and its association with FLT3-ITD mutation. **Methods:**We studied CD25 expression and FLT3 mutations in 125 AML patients. Flow cytometric immunophenotyping (FCI) was performed using 8-color comprehensive antibody panel on Navios Cytometer and data was analyzed using Kaluza-v1.3 software. Positive expression of CD25 was defined with cut off >20% positive blasts. For FLT3-ITD mutations, genomic DNA was subjected to multiplexed PCR with fluorescently labeled primers. PCR was followed by capillary electrophoresis. **Results:** We studied CD25 expression in 125 AML cases (age- 1-68 years & M:F-73:52). Of them, CD25 was found to be positive (cases > 20% blasts) in 33 (26.4%) cases. CD25 expression was commonly seen in AML with <60 years-of-age (28%) as compared to AML with ≥ 60 years-of-age (9%). Molecular studies were available in 50 AML cases. Of these 50 AML, CD25 was positive in 12 (24%) cases and FLT3-ITD mutations was also found in 12 (24%) cases. Sensitivity and specificity of CD25 positive expression in identifying AML with FLT-ITD mutation was 58.3% and 86.8% respectively. On Fisher Exact Test analysis this association was found to be statistically significant with p=0.004. **Conclusion:** CD25 shows variable expression in AML cases and commonly seen in AML <60 years-of-age. CD25 is highly specific flow cytometric marker in the determination of AML with FLT3 mutations. It may be considered as a surrogated marker for FLT3-ITD mutation in AML.

Comparison of four neuropathy assessment scales in evaluation of treatment emergent neuropathy in newly diagnosed patients of multiple myeloma treated with bortezomib based regimen.

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Background: Treatment emergent peripheral neuropathy (TEPN) is a distressing and potentially dose limiting side-effect of bortezomib containing regimen for multiple myeloma (MM). The reporting of extent and severity of TEPN is variable due to use of different neuropathy scales. Presently, most investigators use National Cancer Institute Common Toxicity Criteria for Adverse Events (NCI CTCAE) for reporting of TEPN. **Patients and methods:** We prospectively evaluated the incidence of TEPN in treatment naïve patients of MM receiving cyclophosphamide,

bortezomib and dexamethasone (CyBorD) on days 1, 8, 15 and 22 of each 28-day cycle, by clinical evaluation, nerve conduction study (NCS) and four different neuropathy scores- NCI CTC v4.0, Total neuropathy score reduced (TNSr) and clinical (TNSc) and Numerical Response Scale (NRS) for neuropathic pain. TNSr includes results of nerve conduction study in addition to the clinical parameters used in TNSc. Post-treatment increment by one grade for NCI-CTC, by score of ≥2 for TNSr and TNSc, and by score of ≥1 for NRS defined TEPN. **Results:** A total of twenty six patients received CyBorD regimen. Twenty patients completed follow-up. After a median of 7 (range: 3.5-11) months, the rates of occurrence of TEPN differed when the four scales were used; viz. NCI CTC=45% (n=9), TNSr=55% (n=11), TNSc=40% (n=8) and NRS=40% (n=8). All four scales showed worsening following treatment with CyBorD ($p<0.01$ for all scales). TNSr could pick up higher number of cases with TEPN in comparison to any other score, most notably in comparison to NCI CTC. Among 12 patients who did not have TEPN by NCI CTC scale, 41.7% (n=5), 16.7% (n=2) and 8.3% (n=1) patients satisfied the criteria for TEPN by TNSr, TNSc and, NRS, respectively. The higher detection rate of neuropathy by TNSr is probably due to incorporation of electrophysiological parameters which increases its sensitivity. TNSc showed correlation with TNSr (r=0.533). **Conclusions**: NCI-CTC may be suboptimal in comparison to TNSr in assessment of TEPN in patients of MM on bortezomib based therapy. Use of TNSr which incorporates electrophysiological studies, can help in better evaluation and understanding of bortezomib induced neuropathy. However, TNSr requires nerve conduction studies which are not universally available. TNSc is a simple and objective bedside tool which correlates with TNSr. NRS can be used as a subjective measure in assessment of neuropathic pain in patients receiving bortezomib.

Docetaxel-based doublet versus pemetrexed-baseddoublet as second-line therapy intyrosine kinase inhibitorstreated advanced non–small-cell lung cancer patients with EGFR mutations: A multicenter retrospective study

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Background: The purpose of thisstudy was to evaluate the efficacy and safety of docetaxel-based or pemetrexed-based doublet therapies as second-line therapy after failure of first-line EGFR TKI therapy in NSCLC patients with EGFR mutations. **Materials and Methods:** Between January 2008 and December 2014, One hundred and ninety-eight EGFR mutation positive patients with metastatic NSCLC (stage IV) were treated with TKIs as first-line palliative chemotherapy. Our analysisincluded 69 patients who failed EGFR TKI therapy and received second-line cytotoxicchemotherapy. **Results:** Among the 198 NSCLC patients, 69 patients with EGFR mutations who failed first-line TKI were enrolled and evaluable. Thirty-eight patients treated with a docetaxel-based doublet and 31patients were treatedusing pemetrexed-based doublet. Median progression-free survival was 3.5 months in the docetaxel-based doublet group and 5.1 months in the pemetrexed-based group (HR 1.457; 95%CI: 0.8904 to 2.7204; p=0.0295). The median overall survival was 7.9 months for the docetaxel-based doublet group and 9.8 months for pemetrexed-based doublet group (HR0.6101; 95% CI: 0.3375 to 1.103; p=0.1019). **Conclusion:** Pemetrexed-based doubletshows an improvement in PFS compared with docetaxel-baseddoublet inNSCLC patients with EGFR mutations who failed first-line EGFR TKI treatment.

Prognostic factors to predict long-term survival in patients with stage IV adenocarcinoma of lung: a retrospective analysis from a medical center

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Introduction: Outcome of patients with advanced lung cancer treated with platinum-based doublet chemotherapy are usually poor, with overall survival range from 8~13 months. However, the overall survival is improved to 21~28 months in the era of EGFR tyrosine kinase inhibitor. Long-term survival is also reported in substantial group. **Objectives:** This study aimed to explore the prognostic factors to predict long-term survival in the era of EGFR tyrosine kinase inhibitor. **Material and Methods:** Between Jan 2005 and Dec 2009, a total of 1030 patients diagnosed with stage IV adenocarcinoma of lung at the Linkou Chang Gung Memorial Hospital were enrolled. Patients were divided into long-term survivor cohort (patients who survive more than five years) and comparison cohort (patients who survive less than five years). Clinical feature and pathologic information are collected retrospectively to analyze prognostic factors. **Results:** A total 52 patients in long-term survivorship cohort and 978 patients in comparison cohort were enrolled for analysis. Median survival time was 71.3 months in long-term survivor cohort and 8.7 months in comparison cohort. Patients in long-term survivor cohort significantly differed from comparison group in median age (57 vs. 64, p=0.006), performance status (ECOG 0-1 96% vs. 67.9%, p<0.001), extrathoracic spread (42.3% vs. 79.6%, p<0.001) and involved organ number (three or more than three organs 1.9% vs. 32.9%, p<0.001). EGFR mutation status was not significantly different between two group (exon 19 deletion and/or exon 20 L858R 19.2% vs. 6.4%, p=0.270). Significant odds ratio (OR) of factors predicting long-term survival are age<60 years (OR 2.34 to age>60 years, 95% CI 1.32-4.15; p=0.003), performance status ECOG 0-1 (OR 11.75 to ECOG 2-4, 95% CI 2.84-48.59; p<0.001), absence of extrathoracic spread (OR 5.31 to presence of extrathoracic spread, 95% CI 3.00-9.40; p<0.001), and longest EGFR TKI duration>1 year (N=518, OR 22.97 to longest EGFR TKI duration<1 year, 95% CI 9.55-55.2; p<0.001). **Conclusions:** In this retrospective study, prognostic factors to predict long-term survival in patients with stage IV adenocarcinoma of lung are age, performance status, absence of extrathoracic spread and longest EGFR TKI duration more than one year.

Multiplexed Diagnostic Assay for Detection of Targetable Mutations in Lung Adenocarcinoma Using SNaPShot PCR Technique

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Introduction & Objectives: Conventional therapeutic solutions in NSCLC are not effective to treat the disease. Despite of all developments in understanding of the disease, mortality of lung cancer patients remains high. Recent developments of personalized therapy has given promising results in terms of improved survival of NSCLC patients. Thus, we were interested to develop a cost effective and sensitive diagnostic assay for targetable mutation detection. Here, we present a multiplexed diagnostic assay using SNaPShot PCR technique from FFPE samples. **Methodology:** Multiplex PCR was optimized to amplify hotspot regions from 9 targetable genes followed by single base extension reaction using SNaPShot PCR and fragment analysis on ABI 3500 sequencer. **Results:** The successfully

developed mutation profiling assay was divided into 3 multiplexed reactions, covering 23 actionable genotypes of *EGFR, KRAS, BRAF, PIK3CA, Her2, AKT1, NRAS, MEK1* and *PTEN* genes. The assay was standardized and validated on blood samples, cell lines and FFPE samples expressing good sensitivity and specificity for wild type and mutant genotypes. We have performed the assay on 81 lung adenocarcinoma samples. We found 25% of EGFR mutation which is concordant with frequency we reported earlier. Besides, we also found one patient with co-occurrence of *EGFR* L858R and *KRAS* G12C and one more patient with co-occurrence of *EGFR* L858R, *PIK3CA* E542K and *EGFR* T790M. **Conclusion:** Multiplexed diagnostic assay using SNaPShot PCR is very economical, specific and sensitive to detect mutations in FFPE samples. The assay has been implemented in routine diagnostic at our Centre.

FNAC Cell Blocks for the detection of Epidermal growth factor receptor (EGFR) mutations in the non-small-cell lung cancer.

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Introduction: The presence or absence of Epidermal growth factor receptor (EGFR) mutations play an essential role in deciding initial treatment of the patients with the advanced non-small-cell lung cancer (NSCLC). Tissue for the histology and mutation testing is usually obtained by a bronchoscopic biopsy or by a CT-guided Tru-cut biopsy from the lung mass. Because a thick-bore needle is required for a Tru-cut biopsy, complications are more frequent. Fine needle aspiration cytology (FNAC) using 22/24 SWG needle is a sensitive, economic, and rapid method for diagnosing lung cancer. FNAC is minimally invasive with less complications and less pain that a Tru-cut biopsy. However, whether adequate amount of tissue for molecular testing, in addition to histology/cytology, can be obtained via the FNAC procedure is debatable. We retrospectively evaluated FNAC cell blocks prepared from CT-guided fine needle aspirated for adequacy of tissue for estimation of EGFR mutation studies by RT-PCR and report the result in this paper. We also report the EGFR mutation status in the initial 110 blocks.

Objective: To estimate the incidence of EGFR mutation in non-small cell lung cancer patients using FNAC cell blocks. **Material and Methods:** DNA was isolated from the tissue derived from FNAC cell blocks using Qiagen FFPE-DNA Isolation Kit. Following DNA isolation, Taqman based Real-Time PCR was carried out to detect somatic mutations in Exons 18, 19 and 21. **Results:** Out of total 115 FNAC blocks, 110 (95.65%) blocks had adequate amount of tumor tissue from which DNA was isolated. Mutations were found only in 39/110 (35.45%) samples. Out of all types of mutations, 25 patients had mutations in exon 18, 9 patients had mutations in exon 19 and 5 patients had mutations in exon 21. **Conclusions:** As evident from our results, the incidence of EGFR mutation in patients of Rajasthan is approximately 34%. Majority of the patients had mutations in exon 18 followed by exon 19 and exon 21. Hence, adequate amount of tissue was available in 95.65% of FNAC blocks from which DNA was isolated and used for the molecular analysis.

TaqMan PCR Assay Results

Total No of Samples: 110

Exons	Mutation	No of Samples
18	G719C/S	25
19	Deletions	9
21	L858R	5
Total Mutations		39/110

ORAL PAPER PRESENTATION FOR AWARDS

8th APRIL 2016 IACR MID-LEVEL SCIENTIST AWARDS DR. VIRENDRA BALKRISHNA KAMAT AWARD and RAMNATH HIRALAL JAJU AWARD

Abstract No.	Title	Name	Affiliation
OR 01	Metformin induces modulation of differentiation markers in colorectal cancer in vitro	Amar Preet Kaur	AIIMS, New Delhi
OR 02	Effect of Biophytum Sensitivum and its isolated compound amentoflavone on the inhibition of experimental metastasis and the possible mechanism of action	Guruvayoorappan.C	Regional Cancer Centre, Thiruvananthapuram
OR 03	Derivation of a multi-gene signature of hypoxia and Notch signalling pathways and its prognostic value in glioblastoma patients	Khushboo Irshad	AIIMS, New Delhi
OR 04	Clinical and functional implications of miRNAs and their targets in esophageal cancer	Rinu Sharma	Guru GobindIndraprastha University, New Delhi
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OR 07	Targeting Cancer Stem Cells using Chemokine Receptor CXCR4	Shiba Ansari	AIIMS, New Delhi
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OR 01: Metformin induces modulation of differentiation markers in colorectal cancer in vitro

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Background: Metformin is an anti-diabetic drug that has anti-carcinogenic activity. Its anticancer activity may be attributable to its ability to induce differentiation in cancer stem cells (CSCs). CSCs are resistant to conventional chemotherapy. We wanted to investigate if inducing differentiation can help target CSCs. **Materials and methods:** HCT116, a colon cancer cell line was cultured *in vitro*. MTT assay helped establish maximum tolerable non-toxic dose for Metformin. The cells were treated with selected doses of Metformin for 2-3 weeks. Metformin-induced apoptosis was evaluated using flow cytometry (Annexin V, PI). Cell cycle analysis was performed using PI. Induction of differentiation was analyzed by evaluating expression of CDX1 (transcription factor) by RT-PCR and appearance of Cytokeratin 20 (CK20), a positive marker of differentiation by flow cytometry. Percentage of CSCs were analysed using CSC markers - CD44 (alexa fluor 647) and CD166 (PE) by flow cytometry. **Results:** On the basis of MTT results, three doses of metformin were selected – 0.5,1 and 2.5 mM. After metformin treatment for two weeks apoptosis assay revealed no significant apoptosis in cells. Cell cycle analysis revealed that with 2.5mM metformin, maximum no of cells were in G2M phase. Expression of CK20 and CDX1 was also found to be altered by flow cytometry and RT-PCR respectively. **Conclusion:** Our findings indicate that metformin may induce differentiation in the undifferentiated CSC present in colorectal cancer cell line HCT116, thereby indicating its potential therapeutic role in targeting resistant CSCs.

Key words: Cancer stem cells (CSCs), Metformin, differentiation.

OR 02: Effect of *Biophytum Sensitivum* and its isolated compound amentoflavone on the inhibition of experimental metastasis and the possible mechanism of action

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Introduction: The major clinical challenge for cancer therapy remains the eradication (or prevention) of metastasis. Many plants and natural products have been screened, in past, against cancer cell lines or in animal tumor models and have provided significant results which nudges us to look for more natural products from the traditional system of medicine. **Hypothesis:** *Biophytum sensitivum* and Amentoflavone possess antimetastatic efficacy **Materials and Methods:** Metastasis was induced in C57BL/6 mice using B16F-10 melanoma cells and monitored for their life span and the lung tumour nodule formation in the presence and absence of *Biophytum sensitivum* or amentoflavone treatment. Lung collagen hydroxyl proline content as well as the expression of prolyl hydroxylase and lysyl oxidase were carried out. Lung hexosamine, uronic acid as well as serum sialic acid and γGT levels were also analyzed. MMP-2, MMP-9, TIMP-1 and TIMP-2 expression in metastatic lungs were assessed. Further the effect of *Biophytum sensitivum* or amentoflavone on the activation and nuclear translocation of transcription factors were also analyzed **Results and Discussion:** *Biophytum sensitivum* or Amentoflavone treatment significantly showed increased lifespan accompanied with significantly less ($p<0.001$) tumor nodules. Lung collagen hydroxyproline, hexosamine, uronic acid as well as serum sialic acid and γGT showed marked reduction after *Biophytum sensitivum* or amentoflavone treatment. Significant inhibition in prolyl hydroxylase, lysyl oxidase, MMP-2 and MMP-9 expression were also observed after *Biophytum sensitivum* or amentoflavone treatment. Expression of TIMP-1 and TIMP-2 were increased. *Biophytum sensitivum* or Amentoflavone treatment also inhibited the invasion of B16F-10 melanoma cells. The activation of transcription factors such as p65, p50, c-Rel, c-fos, CREB and ATF-2 were inhibited in B16F-10 cells by *Biophytum sensitivum* or amentoflavone treatment **Conclusion:** Inhibition of tumor cell proliferation and invasion by *Biophytum sensitivum* or amentoflavone contribute to its antimetastatic/ therapeutic efficacy.

OR 03: Derivation of a multi-gene signature of hypoxia and Notch signalling pathways and its prognostic value in glioblastoma patients

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Introduction: Notch signaling pathway has been implicated in glioma progression. Hypoxia is known to cooperate with Notch signaling and exacerbate many cancers. Since glioblastoma (GBM) typically exhibits intratumoral hypoxia, we analyzed the association between the two pathways in human GBM specimens. An *in-vitro* validation was also carried out in a glioma cell line enriched in stem cells under low oxygenation. **Objectives:** The present study was undertaken to identify a gene expression signature that characterizes Notch pathway response in hypoxic GBM tumors and gliomaspheres and could assist in prognostication. **Material and Methods:** The transcript levels of Notch receptors, Delta-like/Jagged ligands and Hes/Hey target genes of Notch pathway; and hypoxia markers were evaluated in 35 GBM tumors by q-PCR. Spearman's correlation, gene clustering and other statistical analyses were applied to analyze the relationship between hypoxia level and Notch pathway up regulation. The expression of individual as well as collective genes was correlated with patient survival. Expression analysis was also carried out in U87MG cultured in stem cell culture conditions under hypoxia using q-PCR/ Western blot. **Results:** HIF-1α expression (followed by PGK1, OPN and VEGF) correlates with the expression of maximum Notch pathway genes. Well-differentiated tumor clusters of high HIF-1α/PGK1-expressors are produced based on the differential expression of Notch pathway genes. Logistic regression results in a five hypoxia marker combination (HIF1α/ PGK1/VEGF/CA9/OPN) as the best determinant of Notch signalling augmentation. A similar Notch-axis (Notch1/Dll1/Hes1/Hes6/Hey1/ Hey2) is activated in U87MG gliomaspheres under hypoxia. An inverse correlation exists between patient survival and unregulated components of the hypoxia-Notch gene signature. **Conclusions:** Our results delineate the Notch-axis maximally associated with hypoxia in human GBM, which might be prognostically important. Its upregulation in hypoxiaexposed gliomaspheres, and not monolayer cultures, demonstrates gliomaspheres as the better *in-vitro* model of hypoxia-Notch interactions.

Keywords: Glioblastoma, Hypoxia-Notch axis, prognosis

OR 04: Clinical and functional implications of miRNAs and their targets in esophageal cancer

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Introduction: Esophageal cancer (EC) is the third most common cancer of the digestive tract with overall 5-year survival rate being less than 20%. Understanding of the molecular mechanism underlying the disease and identification of reliable diagnostic markers may dramatically increase the survival of patients by improving the chances of timely detection and intervention. Growing evidence suggests importance of aberrant microRNA expression in development and progression of cancer. **Objectives:** To decipher the clinical and functional significance of miRNAs and their targets in esophageal cancer. **Material and Methods:** We evaluated the expression of a panel of miRNA-mRNA in EC patients using qRTPCR and risk score analysis was performed. Linear regression models were fitted using the cancer status and each of the risk score followed by ROC curve analysis to estimate the sensitivity and specificity of the panel. Pathways targeted by the aberrantly expressed miRNAs were identified by pathway enrichment analysis. Further, the role of one of the significantly altered miRNA (miR107) was elucidated by overexpressing it in KYSE-410 cells followed by MTT assay, cell cycle analysis and scratch assay. miRNA targets predicted by in-silico approach were validated by western blot and luciferase reporter assay. **Results:** The analysis revealed significant dysregulation of miRNA-mRNA panel comprising of miR107, miR-144, SPRED1 and PUR alpha in EC tissues. The miRNAmRNA panel showed enhanced sensitivity and specificity in terms of discriminating EC tissues from distant non malignant tissues. Moreover, relative levels of circulating miRNAs in serum significantly distinguished EC patients from normal controls with a high sensitivity. Functional validation of miR-107 revealed it to have tumor suppressor role in esophageal cancer by downregulating its newly identified target and its overexpression led to decreased proliferation and migration of esophageal cancer cells. **Conclusions:** miRNA-mRNA signature panel analyzed herein might have potential diagnostic implications in esophageal cancer. Our findings also provide insight into the functional role of miR107.

OR 05: The adaptive role of Unfolded Protein Response (UPR) in tumour drug resistance.

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Introduction: Drug resistance in cancer cells limits efficacy of both traditional and targeted chemotherapeutic agents. Understanding cellular and molecular mechanisms of drug resistance is important to sensitize drug resistant cells to chemotherapeutics and also for effective interventions against relapsed tumors. **Objectives:**To develop drug resistant cells and tumourigenicity study in SCID mice model; (2) to compare differences in the biology of tumor growth, if any and (3) to study the signaling mechanisms involved in the progression of the tumor by studying drug resistant form of tumors **Material and Methods:**Cancer cell lines, DLD 1 and A549 were used to make drug resistant cells by treating with lethal dose of chemotherapeutics. The drug selected cells and the parental cells were used for tumourigenicity study in a SCID mice model. The differences in biology of tumour growth and underlying signalling mechanism were studied using bioimaging, gross & histopathology, proteomics, immunoblotting and immunohistochemistry. Results were confirmed in primary human tumor tissue as well **Results:**Drug resistant cells induced a much more Invasive and metastatic tumour. Unfolded Protein Response pathway was more active in drug resistant cells, which was found to be a prolonged response associated with invasiveness and metastasis. The results of the *in vitro* and *in vivo* animal studies were confirmed in primary human tumor tissue. **Conclusions:**Unresolved UPR in drug resistant, metastatic and relapsed tumours may be contributing to typical hall marks of cancer and hence have potential to be targeted for their effective chemo- sensitisation.

OR 06: Radiation induced Multinucleated Giant Cells formed by homotypic cell fusion undergo NHEJ repair to survive and generate recurrent Glioblastoma cells

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Introduction: Treatment in Glioblastoma is challenging due to lack of understanding of molecular pathways leading to survival of residual resistant (RR) GBM cells. **Objectives:** To elucidate molecular mechanisms responsible for survival and relapse of RR cells for therapeutic interventions. **Material and Methods:** *in vitro* cellular and *in vivo* orthotopic mouse model of radiation resistance from fresh naïve primary GBM patient samples and cell lines were used in this study. **Results:** We show a small percentage of inherently radiation resistant (RR) GBM cells that survive lethal dose of radiation become non-apoptotic, non-proliferative and undergo homotypic cell fusions forming multinucleated and giant cells (MNGCs). Interestingly, cell fusion leads to senescence which reverses and give rise to mononuclated relapse population. Inhibiting MNGC formation abrogate relapse. Furthermore, RR cells activate ATM-Chk2 or ATR-Chk1- RPA2 and upregulate SETMAR, which leads to dimethylation of H3K36. H3K36me2 recruit Ku80 and Mre11 to enhance DSB repair by Non homologous End Joining (NHEJ) pathway. Accordingly we demonstrate that mutating H3.3 at lysine 36 abolished NHEJ repair response by decreasing association of early NHEJ repair components at DSBs and alleviate the survival of resistant cells. Importantly we show orthotopic injections of glioma cells with mutant H3.3K36A in mouse brain as seen with wild type H3K36 confirming the importance of H3k36me2 in the survival of RR cells. **Conclusions:** We identified radiation induced homotypic cell fusions of resistant Glioma cells and H3k36me2 mediated NHEJ repair of DNA in RR cells as mechanisms that targets residual resistant cells and preventing relapse in GBM.

OR 07: Targeting Cancer Stem Cells using Chemokine Receptor CXCR4

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Introduction: Recent advances in the field of cancer biology have revealed the critical role of CXCR4 receptor and its ligand CXCL12 in the metastasis of various types of cancer. CXCL12-CXCR4 axis mediates tumor progression by controlling cancer cell survival, proliferation and migration. CXCR4 is overexpressed in cancer stem cells and therefore, development of targeted therapeutics using CXCR4 ligands offers a promising approach for cancer treatment. Studies have reported DV1 peptide ligand (derived from vMIP II) to possess high affinity and antagonistic activity for chemokine receptor CXCR4.**Objective:** To target CXCR4 receptors using Avidin-PLGA nanoparticles tagged with biotinylated DV1 peptide ligand in glioblastoma cell lines **Material and Methods:** Avidin-PLGA nanoparticles were prepared by double emulsion solvent evaporation technique and characterized for size (by TEM) and surface functionality for avidin groups (by confocal microscopy). For specific targeting of CXCR4 receptors, Targeted nanoparticles (Peptide-Avidin PLGA NP) were prepared by tagging biotinylated DV1 peptide onto the surface of Avidin PLGA nanoparticles. Untagged nanoparticles were used as Control nanoparticles (Avidin PLGA NP). U87MG (CXCR4 +ve) and Neuro-2a (CXCR4 –ve) cell lines were taken as test and control cells respectively. Analysis was done by confocal microscope. **Results:** Experimental results revealed significantly enhanced uptake of Targeted nanoparticles in U87MG cells as compared to Neuro-2a cells thereby confirming specificity of Targeted nanoparticles for CXCR4 receptors. **Conclusions:** Our results suggest that PLGA NP tagged with DV1 peptide can be used for targeted therapy to CXCR4 expressing cells which can have clinical application in treatment of cancer and other diseases.

OR 08: CXCL12 is a key regulator in tumor microenvironment of cervical cancer: An in vitro study

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Introduction: CXCL12 is a small pro-inflammatory cytokine, signals through chemokine receptor CXCR4. The importance of CXCL12/CXCR4 axis is coming to the fore in several divergent signaling pathway-initiating signals related to cell survival and/or proliferation and cancer metastasis. **Objectives:** Defining the role of CXCL12 in tumor microenvironment of cervical cancer. **Material and Methods:** In this study 28 Normal, 62 primary tumor and 7 cell lines were used. To address the above objective we use qPCR, methylation specific PCR (MSP), bisulphite sequencing, ELISA, Cell Migration and invasion Assay, Colony formation and Apoptosis Assay. **Results:** Results: Our expression profiling showed that CXCL12 is downregulated and upregulated in 39% and 10% of tumor biopsies respectively while 51% of the tumor biopsies showed no significant change. Cervical cancer cell lines showed either little or undetectable expression of CXCL12. Promoter methylation analysis showed that CXCL12 promoter is frequently hypermethylated in cervical cancer biopsies and cell lines. Inhibition of DNA methyltransferase (DNMTs) restores the expression of CXCL12 in cervical cancer cell line SiHa. Our functional assay using cell lines showed that presence of recombinant CXCL12, inhibits cell migration, invasion, anchorage independent growth and induces anoikis in Cervical cancer cells. It also inhibits the expression of CXCL12 in normal cervical cells. **Conclusions:** Our study suggests the tumor suppressor functions of CXCL12 in cervical cancer indicating that (a) silencing of CXCL12 in cervical cancer cells make it more prone to being attracted to CXCL12 expressed at secondary sites of metastases; and (b) CXCL12

OR 09: Promoter hypermethylation in GSTPi, HIC1 and CDH1 genes as a marker for early stage triple negative breast cancer

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Background: Triple negative (ER-/PR-/Her2-) breast cancers are most frequent aggressive tumors in younger women, and are associated with early relapse and poor prognosis. Epigenetic silencing of specific tumor suppressor genes plays an important role in breast cancer initiation and progression but till date no epigenetic biomarker(s) is linked with triple negative breast cancers. In this study, five tumor suppressor genes, BRCA1, p16, GSTPi, HIC1 and CDH1 have been investigated to see if the methylation pattern could serve as a reliable indicator for early detection/progression and/or prognosis of triple negative breast cancer. **Material and Methods:** Genomic DNA isolated from 124 primary breast tumor biopsies employed for sodium bisulfite conversion of genomic DNA was performed for analysis of promoter methylation by methylation specific polymerase chain reaction (MSP) and the results obtained correlated with the level of the expression of the genes, stage/grade of the disease and clinicopathological parameters. **Results:** Out of five specific tumor suppressor genes, GSTPi, HIC1 and CDH1 showed significantly a higher level of methylation in early stage triple negative breast cancer; GSTPi promoter was hypermethylated in 100% of cases leading to loss of expression in 50% of the TNBCs while HIC1 and CDH1 were hypermethylated in 88.88% tumors with a loss of expression in 37.5% and 25% respectively in early stage triple negative breast cancer. **Conclusions:** The results suggest that hypermethylation of these genes may serve as a potential predictive biomarker for early identification and progression of aggressive triple negative breast cancer.

OR 10: Molecular mechanism of TRAIL induced antiangiogenesis involves down-regulation of VEGF gene expression and dephosphorylation of VEGF –R1 and R2.

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Introduction: Tumor progression involves surplus angiogenesis mediated by Vascular Endothelial Growth Factor (VEGF). During these processes tumor cells down regulate expression of death receptors (DR's) which lead to inhibition of apoptosis, thereby supports cell survival. **Objectives:** Investigate the effects of tumor necrosis factor-related apoptosisinducing ligand (TRAIL) on VEGF-induced angiogenesis. **Material and Methods:** Cells lines like HUVEC, HeLa, Kelly and MCF-7 were used. Methods followed are Cell Viability Assay, In-Vivo Peritoneal Assay, In-vitro Tube formation, Rat Cornea Micropocket assay, Wound Healing assay, Promoter-Reporter analysis, Immunoprecipitation and Immunoblotting and Real time PCR. **Results:** Tumor cells differentially express DR's, we studied the sensitivity of cancer cells lines towards TRAIL by testing three cell lines, of which Hela was resistant to TRAIL. TRAIL in suboptimal concentration enhances antiangiogenesis in mouse model. It also decreases the secretion of VEGF into the ascites. TRAIL inhibits formation of blood vessel like tubes in HUVEC in-vitro and also suppresses VEGF induced blood vessel formation in corneal micropocket assay. Our studies also show that protein TRAIL inhibits VEGF promoted cell migration during wound closure. TRAIL regulates VEGF gene and VEGF receptor expression at gene and mRNA level. **Conclusions:** Therefore, TRAIL can be used as an effective approach to induce anti-angiogenesis.

9th APRIL 2016 IACR YOUNG SCIENTIST AWARDS SITARAM JOGLEKAR AWARD and MANGALA BAMNE AWARD

Abstract No.	Title	Name	Affiliation
OR 11	p63 regulates Activin A - mediated migration in human oral cancer cells	Dhanashree Mundhe	TMC, ACTREC Mumbai
OR 12	Differential proteomic analysis reveals role of a novel serine threonine kinase DCLK3 and 14-3-3 zeta in residual radiation resistant and relapse cells	Jacinth Rajendra	TMC , ACTREC Mumbai of Glioblastoma
OR 13	INPP4A thinks out of the cell: Novel localization to exosomes mediates epithelial-fibroblast crosstalk and regulates cell proliferation	Kritika Khanna	CSIR-IGIB,Delhi
OR 14	Role of an anti-viral host micro-RNA in HPV-16 induced Head and Neck Cancer	Malay Kumar, Sannigrahi	PGIMER,Chandigarh
OR 15	Status and clinical relevance of epithelial-mesenchymal transition associated miRNA-200c and miRNA-141 in eyelid sebaceous gland carcinoma	Mansi Bhardwaj	All India Institute of Medical Sciences,Delhi
OR 16	Deciphering the Diversity of Somatic Alterations and Salmonella Infection in Gallbladder Cancer by Whole Exome Sequencing	Prajish Sundaram	ACTREC,Mumbai
OR 17	Modulation of tobacco carcinogen induced early molecular markers by various doses of Polymeric black tea polyphenols (PBPs) in lung and liver of A/J mice	Rasika R Hudlikar	Cancer Research Institute, ACTREC, Mumbai
OR 18	INPP4A goes nuclear: nucleo-cytoplasmic shuttling and Integrative Biology, of INPP4A regulates cell proliferation and apoptosis	Rituparna Chaudhuri	Institute of Genomics Delhi
OR 19	Testis specific heat-shock protein 70-2 (HSP70-2); a novel potential therapeutic target for renal cell carcinoma	Swarnendra Singh	National Institute of Immunology, New Delhi
OR 20	Regulation of p73 and Its Role in Suppressing Metastasis	Dr. B. R. Ambedkar, Yatendra Kumar Satija	Center for Biomedical Research (ACBR), University of Delh

OR 11: p63 regulates Activin A - mediated migration in human oral cancer cells

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Introduction: Activin A, a member of TGFβ superfamily, was recently shown to be overexpressed in OSCC & associated with poor prognosis. Our lab has recently demonstrated overexpression of ΔNp63 isoform in OSCC tissues & cell lines. Further microarray analysis of p63 knockdown clones revealed significant downregulation of Activin A mRNA in oral cancer cells. **Objectives:** The present study aims to assess the possible regulation of Activin A by p63 and its effects on cellular migration**. Material and Methods:** qRT-PCR was used to analyse the expression of Activin A in oral cancer cells. The binding of p63 to the Activin A promoter was assessed by ChIP assay. The role of p63-activin A signaling axis in migration of oral cancer cells was examined in p63 stable knockdown clones of oral cancer cells, AW8507 & SCC040 using transwell assay. **Results:** Our studies revealed significant upregulation of Activin A in majority of oral cell lines as compared to that in normal oral cells. We further demonstrate the binding of p63 to Activin βA promoter in AW8507 & SCC040 cells. The downregulation of Activin A in ΔNp63 knockdown oral cancer clones was associated with reduced migratory capacity which was rescued post treatment with recombinant Activin A, and which was also associated with increased SMAD 2 phosphorylation. **Conclusions:** Our studies suggest that overexpression of p63 in OSCC may lead to the transcriptional activation of Activin A. The upregulated Activin A possibly promotes migration of the OSCC cells at least partly via the canonical Activin A-SMAD signaling axis. This is the first study to demonstrate the regulation of Activin A signaling by p63 in OSCC.

OR 12: Differential proteomic analysis reveals role of a novel serine threonine kinase DCLK3 and 14-3-3 zeta in residual radiation resistant and relapse cells of Glioblastoma

Jacinth Rajendr, Keshava Datta, Raja Reddy, Nilesh Gardi, Ekjot Kaur, Ketaki Patkar, Aliasgar, Kakoli Bose , Amit Dutt, Harsha Gowda, Shilpee Dutt

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Introduction: Glioblastoma (GBM) recurs due to our inability to target residual radiation resistant (RR) cells after multimodal GBM treatment. **Objectives:** This study aims to decipher the targetable differential proteins governing the survival of the residual resistant population. **Material and Methods:** An in vitro radiation resistant model was developed from patient samples and cell lines. The RR cells - < 10% of the parent population were subjected to iTRAQ based quantitative proteomic analysis. **Results:** We have identified and validated a novel serine threonine kinase DCLK3 to be most upregulated in the residual RR cells of Glioblastoma. Analysis of different tumour samples (242) from COSMIC database shows overexpression of DCLK3 in 232 tumours. Furthermore, out of 8 missense deleterious mutations found in this gene, 6 are in the kinase domain suggesting the importance of DLCK3 kinase activity in tumour progression. Additionally, A GENE STRING analysis of the differential proteins from our data reveals putative interaction of DCLK3 with 14-3-3 zeta. The apoptotic regulating function of 14-3-3 zeta is dependent on phosphorylation at specific Serine and Threonine residues. We hypothesis DCLK3 mediated interaction and phosphorylation of 14-3-3 zeta facilitates RR cell survival. Indeed *in silico* docking of DCLK3 with 14-3-3 zeta confirms interaction of the DCLK3 kinase domain with 14-3-3 zeta. *In vitro* and *in vivo* are ongoing to confirm the importance of these proteins and their interaction in GBM recurrence. **Conclusion:**We have identified a novel serine-threonine kinase DCLK3 in RR cells of GBM as a potential therapeutic target.

OR 13: INPP4A thinks out of the cell: Novel localization to exosomes mediates epithelial-fibroblast crosstalk and regulates cell proliferation

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Introduction: Phosphoinositide 3- kinase (PI3K) signaling pathway regulates essential cellular processes like cell proliferation, apoptosis, angiogenesis and migration. Deregulation of this pathway has been associated with cellular transformation, highlighting its key role in oncogenesis. Exosomes and microvesicles (MVs) are nano-sized extracellular vesicles which are important players in inter-cellular communication and thereby influence the tumor microenvironment. Inositol polyphosphate 4-phosphatase (INPP4A)**,** a critical negative regulator of the PI3K pathway present in the cytoplasm and at the cell membrane, is important for maintaining lung homeostasis. In the present study, we report for the first time that exosomes carrying INPP4A can regulate proliferation of the recipient cells. **Objective:** The current study aims to investigate the role of this novel extracellular INPP4A in the cellular microenvironment. **Material and Methods:** INPP4A levels were checked in the sera and bronchoalveolar lavage fluid of human subjects using ELISA. *In vitro*, INPP4A was probed in exosomes and MVs which were isolated using differential centrifugation of the conditioned media of various cell lines. Transferring exosomes from stable INPP4A-GFP epithelial cells onto normal fibroblasts and consequently probing GFP in the recipients ascertained the uptake of exosomal INPP4A. To explore the epithelial-fibroblast crosstalk mediated by the internalised INPP4A, cell proliferation of the recipient cells was assessed using flow cytometry. **Results:** We report novel localization of INPP4A in exosomes of cultured cells and in body fluids like sera and BALF. We demonstrate that enzymatically active INPP4A can be transferred between cells via the extracellular vesicles and is critical for cell-cell communication. INPP4A transferred from epithelial cell derived exosomes to lung fibroblasts reduces proliferation of the recipient cells, highlighting the role of exosomal INPP4A in maintaining a check on fibroblast growth. This suggests that downregulation of INPP4, as in cancers, may relinquish this control and lead to fibroblast hyper-proliferation, thereby altering tissue homeostasis. **Conclusion:** Since INPP4 is known to be downregulated in a variety of cancers, this study is particularly interesting as it suggests that loss of INPP4A can not only regulate the cell's growth abilities, but impede vital intercellular communication leading to development of a hyperproliferative niche. Our future plans include comparing the levels of secretory INPP4A in various cell lines from cancerous and normal origin, as well as in tissues from cancer patients. A deeper understanding of the role of exosomal INPP4A could also make it an attractive candidate as a potential circulating biomarker.

Key Words: Cell proliferation, Exosomes, PI3K pathway

OR 14: Role of an anti-viral host micro-RNA in HPV-16 induced Head and Neck Cancer

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Introduction: Human papillomaviruses (HPV) are small DNA tumor viruses that are present in 20% of Head and Neck Cancer (HNC). Recent studies have shown the interesting perspective that viral gene expression is regulated by host microRNAs (miRNAs). **Material and Methods:**In-silico approach was used to identify host miRNAs with HPV16 mRNAs as putative target. Differential expression of identified miRNAs was determined by qRT-PCR in HPV16 positive (UPCI:SCC090, CaSki, SiHa),

HPV negative (UPCI:SCC116, HaCat) cell lines, and, HPV-16 positive/ HPV negative tissue samples. Putative targets of identified miRNAs were identified by bioinformatic approach and their RNA levels were determined by qRT-PCR in HPV positive and negative cell lines, and tissue samples. Overexpression/inhibition studies with miRNA mimic/inhibitor were done to identify affected viral and host oncogenic pathways. DNA Methylation and Histone acetylation studies were performed to identify epigenetic regulation of the identified miRNA. **Results:**We identified 10 miRNAs with HPV-16 as putative target. Hsa-miR-139-3p was found to be the best anti-viral miRNA candidate as it was significantly down-regulated in HPV-16positive tissuesamples and cell lines.Hsa-miR-139-3p targets HPV-16 mRNA, and, its anti-proliferative effect was found to be due to suppression of HPV-16 oncogenic components (high risk E6 and E7 proteins) and the resulting rescue of major tumor suppressor proteins (p53, p21 and p16). Over-expression of this miRNA leads to inhibition of cellular proliferation, accumulation of cells in G2/M phase and cell death. Further, in HPV-16 positive cases, Hsa-miR-139-3p was down-regulated by promoter methylation. **Conclusions:**Our results suggest hsa-miR-139-3p may be involved in pathophysiology of HPV-16 positive HNSCC.

OR 15: Status and clinical relevance of epithelial-mesenchymal transition associated miRNA-200c and miRNA-141 in eyelid sebaceous gland carcinoma

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Introduction: Eyelid sebaceous gland carcinoma (SGC) is the most common eyelid malignancy. miRNA-200c and miRNA-141 are tumour suppressors which regulate epithelial-mesenchymal transition (EMT), leading to tumour progression in various malignancies. However, their status in eyelid SGC remains unexplored. **Objectives:** The present study was designed to determine status and prognostic significance of miRNA-200c and miRNA-141 in eyelid SGC. Their association with Ecadherin, ZEB1 and ZEB2 was also studied. **Materials and Methods:** Prospective analysis of 42 eyelid SGC patients was undertaken. Staging was done (AJCC guidelines, 2009) and patients were followed up for 7-44 months. Expression levels of miRNA-200c, miRNA-141 were determined by quantitative real time PCR. Results were correlated with clinicopathological features, survival and other EMT regulators. **Results:** Mean age of eyelid SGC patients was 58.7 ±13.9 years. Low expression levels of miRNA-200c and miRNA-141 were seen in 86% and 67% cases respectively. miRNA200c correlated significantly with advanced tumour stage, large tumour size and poor histopathological differentiation. miRNA-141 correlated with large tumour size and lymph node metastasis. Patients with low miRNA-200c (P= 0.05) and miRNA-141 expression (P= 0.07) had shorter disease-free survival. On Spearman's rank correlation, both miRNA-200c (r= 0.42; P= 0.006) and miRNA-141 (r= 0.46; P= 0.002) correlated significantly with E-cadherin and there was an inverse association between miRNA-141 and ZEB2 expression (r= -0.33, P= 0.03). **Conclusions:** Low expression levels of miRNA-200c and miRNA-141 may facilitate tumor progression in eyelid SGC by promoting EMT and both have emerged as novel potential predictors for survival in eyelid SGC patients.

OR 16: Deciphering the Diversity of Somatic Alterations and *Salmonella* Infection in Gallbladder Cancer by Whole Exome Sequencing

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Introduction: Carcinoma of the gall bladder is relatively a rare lethal malignancy with dismal prognosis. In India there is high incidence (3.9-8.6/1, 00,000) with majority of patients having advanced disease. Recent developments in next generation sequencing technologies has enabled the discovery of new molecular therapeutic targets in many human cancers. **Objectives:**Interrogate the landscape of somatic alterations in Indian gall bladder cancer using whole exome sequencing technology. **Material and Methods:**We interrogated the coding region of 26 Indian gall bladder cancer samples using whole exome sequencing at an average coverage of 100X and above. We further validated the findings using an additional set of 27 FFPE samples. **Results:**Using a bioinformatics filtering approach, we identify 383 somatic alterations across 17 tumors, which includes an average 112 synonymous, 245 missense, 8 nonsense, 8 indels and 8 splice site changes. The average mutation rate considering the paired tumors is about 14 mutations/mb. We found *TP53* (35.2%), *ERBB2* (17.6%), *SF3B1* (17.6%), *ATM* (17.6%)and *AKAP11* (17.6%)mutations in more than two samples by exome sequencing analysis. Furthermore, we examined our exome sequencing data for identifying *Salmonella* sequences as well as presence of 143 HPV types using computation subtraction based on HPVDetector. Based on our evaluation we found association of typhoidal *Salmonella* strains in 11 of 26 gall bladder cancer samples and non-typhoidal *Salmonella* species in 12 of 26 sample, 6 samples were co-infected with both. **Conclusions:**The profiling of somatic alterations and identification of non typhoidal *Salmonella* traces may aid in changing the current treatment paradigm of gall bladder cancer.

OR 17: Modulation of tobacco carcinogen induced early molecular markers by various doses of Polymeric black tea polyphenols (PBPs) in lung and liver of A/J mice

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Rationale: Chemoprevention with phytochemicals is evolving and promising approach for management of lung cancer, a leading cause of death in smokers. We studied the carcinogen induced early molecular changes in lung and liverand its modulation by various doses of, polymeric black tea polyphenols (PBPs) in experimental lung carcinogenesis. **Methodology:** Effect of 0.75,1.5 and 3% black tea derived PBPs onbenzo(a) pyrene[B(a)P] (i.p.) induced molecular changesin lung and liver after 24 hrs. was studied in A/J mice model.Benzo(a)pyrene derived BPDE-DNA adducts in initiated cells and its modulation by various doses of PBPs were studied using immunohistochemical staining. Modulation ofexpression of phase I and IIenzymes (isoforms of CYPs and GSTs) were analyzedusing western blottingwhile theiractivities were studied using specific substrates. **Results:**Administration of various doses of PBPs significantly decreased the B(a)P induced BPDE-DNA adducts in both liver and lung. Significant trend was observed in the decrease in BPDE-DNA adducts over various doses of PBPs used. 1.5 and 3% PBPs showed significant decrease in expression as well as activityof isoforms of phase I (CYP1A1 and CYP1A2) and phase II (GST mu, GST pi, GST alpha) enzymes while0.75% had marginal effect. **Conclusions:**All the doses of PBPs demonstrated anti-initiation effect in the process of carcinogenesis through inhibition of both phase I and phase II enzymes. However, 1.5% PBPswere found to be more effective in the inhibition of both expression and activity of metabolizing enzymes implying the concern of bioavailability in the chemoprevention clinical trials.

OR 18: INPP4A goes nuclear: nucleo-cytoplasmic shuttling of INPP4A regulates cell proliferation and apoptosis

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Introduction: Cancer figures among the leading causes of morbidity and mortality worldwide, with approximately 14 million new cases annually and 8.2 million cancer related deaths in 2012. The number of new cases is expected to rise by about 70% over the next 2 decades. The Phosphatidyl inositol 3-kinase (PI3-K) pathway is a key signaling cascade that is dysregulated in a large variety of human tumors. Inositol polyphosphate 4 phosphatase type I enzyme (INPP4A) is a lipid phosphatase which acts as a negative regulator of the PI3-K pathway by indirectly decreasing Akt activation in the cytoplasm. In this study, we report, for the first time, a novel localization of INPP4A in the nucleus. We have also established that INPP4A shuttles continuously between the nucleus and the cytoplasm, and it is this nucleocytoplasmic shuttling of INPP4A that contributes to critically regulating cell proliferation and apoptosis in the cell. **Objectives:** The aim of the present study is to probe the role of INPP4A in the nucleus. **Material and Methods:** We have used multiple techniques like immunocytochemistry, exogenous expression of INPP4A, immunohistochemistry and western blotting in MCF-7 cells to confirm our initial observation of the novel sub-cellular localization of INPP4A in the nucleus. Cells were fractionated into nuclear and cytoplasmic extracts, followed by western blotting to compare the nuclear levels of INPP4A in various paired cell lines of normal and cancerous origin. We have also corroborated the nuclear levels of INPP4A with the different cell cycle stages, to see if the entry into nucleus is cell-stage dependent. Next, we engineered the wild type INPP4A plasmid such that it expresses predominantly in the nucleus ($Nuclear^{Hi}$), as opposed to in the cytoplasm in the wild type ($Cytoplasmic^{Hi}$), and performed proliferation and apoptosis assays using flow cytometry (FACS) and TUNEL respectively. **Results:** We demonstrate for the first time that enzymatically active INPP4A, apart from being expressed in the cytoplasm, also localizes to the nucleus of various cell lines, as well as in bronchial epithelial cells in murine lung tissues. We further show that nuclear level of INPP4A is dependent on the cell cycle and is highest at the G0/G1 phase. The level of nuclear INPP4A is significantly higher in cells derived from non-cancerous origin, compared to those from cancerous origin. We find that $Nuclear^{Hi}$ INPP4A significantly suppresses cell proliferation compared to $Cytoplasmic^{Hi}$ INPP4A, and sustained presence of INPP4A in the nucleus leads to massive death in the cells. **Conclusions:** Overall, our findings suggest that the level of INPP4A in the nucleus, which is maintained by nucleo-cytoplasmic shuttling, can critically regulate the balance between the extent of proliferation and apoptosis in the normal cell, which is disrupted in a cancer cell.

OR 19: Testis specific heat-shock protein 70-2 (HSP70-2); a novel potential therapeutic target for renal cell carcinoma

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I**ntroduction**: Renal cell carcinoma (RCC) represents one of the most resistant tumors to radiotherapy and chemotherapy. Current therapies for RCC patients are limited because of the lack of diagnosis and therapeutic treatments. Testis specific heat-shock protein 70-2 (HSP70-2), a member of HSP70 chaperone family, has been shown to be involved in various cancers. **Objectives**: In the present study, we investigated the association of HSP70-2 with various malignant features of cancer cells, in order to develop a novel target for RCC. **Material and Methods**: HSP70-2 mRNA and protein expression was investigated in A704, ACHN and Caki-1 cells derived from RCC patients by reverse transcriptionpolymerase chain reaction (RT-PCR) and by Western blotting. Validation of HSP70-2 protein expression was carried out by indirect immunofluorescence (IIF) and flow cytometry for cytoplasmic localization, colocalization in various subcellular compartments and surface localization respectively. Further, gene silencing approach was used to examine the involvement of HSP70-2 with malignant properties of RCC cells. **Results**: RT-PCR and Western blotting data showed HSP70-2 expression in all RCC cells. Flow cytometric analysis and IIF demonstrated HSP70-2 expression on cell surface and organelles. Knockdown of HSP70-2 expression in RCC cells with specific shRNA resulted in significant reduction in cell viability, cell growth, colony formation, migration, invasion and wound healing properties of RCC cells. **Conclusions**: For the first time, we have put forth an evidence of potential role of HSP702 in various malignant properties of RCC cells indicating that HSP70-2 could serve as a novel potential therapeutic target for the RCC.

OR 20: Regulation of p73 and Its Role in Suppressing Metastasis

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Introduction: p73 is a member of the p53 tumor suppressor family, which transactivates p53responsive genes and mediates DNA damage response. Similar to p53, p73 is also maintained at a very low level in non-stressed cells but it rapidly gets induced and activated upon genotoxic insults. But the molecular mechanisms behind differential facet of turnover and activity of p73 under non-stressed and stressed conditions was not known. Furthermore, p73 is emerging as an important player in suppression of metastasis. But how p73 exerts its anti-metastatic function is still unclear. **Objectives**: The objective of our study was to find out novel interactors of p73 and novel downstream targets of p73 which have anti-metastatic functions upon DNA damage. **Material and Methods**: Tandem affinity purification screen: It was conducted on nuclear extracts from cells infected by adenovirus expressing either GFP or Flag-HA-tagged p73 by sequential anti-Flag and HA immunoprecipitation. Quantitative RT-PCR Profiler array, ChIP assay. **Results**: Our differential proteomics screening lead us to identification of many p73-associated proteins. Our results demonstrated that, TRIM28, a RING-type E3 ubiquitin ligase, interacts with p73 under unstressed conditions but not after etoposide treatment. TRIM28 ubiquitylates and targets p73 for proteasome-mediated degradation in normal conditions. However, upon genotoxic stress, phosphorylation of p73 at tyrosine 99 position by c-abl kinase leads to abrogation of its interaction with TRIM28 thereby promoting p73 stabilization. On the contrary end another protein, MED15, only interacts with tyrosine 99 phosphorylated p73 and it serves as a coactivator of p73. Abrogation of MED15 expression leads to decline in p73-mediated transactivation and disrupts p73 tumor suppressor and anti-metastatic functions. Furthermore, to identify novel p73 targets involved in Metastasis suppression, we performed a customized quantitative RT-PCR array analysis. For this purpose, we first generated p73 knockout HCT116p53-/- cell line using CRISPR-Cas technology. RT Profiler PCR Array was performed using Control (Empty vector) and Experimental (p73 knockout) cell line. We identified several novel downstream targets of p73 which have anti-metastatic functions such as Cell Adhesion Molecules, ECM Protease Inhibitors, Microtubule Associated Proteins. **Conclusions**: TRIM28 is essential for homeostasis of p73. MED15 functions as coactivator of p73. Several proteins with anti-metastatic potential are downstream targets of p73. These p73responsive proteins gets upregulated upon genotoxic stress and assist in p73-mediated metastasis suppression. Thus, our work provides extensive insights regarding anti-metastatic role of p73.

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Tanshinone I, a diterpene, in vitro displays cytotoxic and anti-angiogenic effects on Human Myeloma cell line.

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Introduction: Multiple myeloma (MM) remains an incurable malignancy of plasma cells residing in the bone marrow. Though with the advent of various therapeutic modalities like lenalidomide, bortezomib and autologous stem cell transplantation for the majority of myeloma patients,failure is inevitable due to the drug resistance and also imparts huge number of severe side effects.Myeloma cells like other cancer cells display very high proliferation rate and have angiogenesis as one of the hallmarks. Telomerase activity hasalso been found to be very high in the case of myeloma. So, in this study we aim to determine the cytotoxic and anti-angiogenic potential of Tanshinone I, a diterpene found in the roots of *Salviamiltiorrhiza,* on human myeloma cell line. **Material and Methods:** In vitro activities of Tanshinone I was checked on the human myeloma cell line by MTT assay, Propidium Iodide(PI) Assay, Annexin-V binding assay, Western blotting. Telomerase activity was measured using the commercially available kit (Roche). Data was analyzed statistically. **Results:**Tanshinone I showed very high cytotoxic effect on the human myeloma cells with an $IC_{50}$of 1.5μM in RPMI-8226. Significant increase in the sub-G1 phase was observed in the PI assay where as there was higher number of Annexin-V and PI double positive cells were seen in the Annexin-V assay showing apoptosis. Western blot analysis revealed that apoptotic pathway followed by myeloma cells was partially through down-regulation of Bcl-2 and upregulation of Bax. At different doses of Tanshinone I there was significant decrease in the expression of Vegf thus displaying the anti-angiogenic property. Telomerase activity was found to be significantly down-regulated in myeloma cells. **Conclusions:**Our study proved that Tanshinone I has displayed significant cytotoxic potential by induction of apoptosis via down-regulation of anti-apoptotic proteins Bcl-2 and up regulation of proapoptotic protein Bax. Furthermore, Tanshinone I demonstrate significant anti-angiogenic properties (Vegf) displayed by myeloma cells in vitro. Telomerase activity shown by telomerase, which is one of the precursors for malignant transformation of myeloma cells,was significantly down-regulated in the myeloma cell lines. Studies unraveling the pathways involved in mediating the apoptosis and angiogenesis need further evaluation.

The role of Methi (fenugreek) on growth of grafted tumors in experimental animals.

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Introduction: Methi or fenugreek (*Trigonella foenum graecum*) is one of the oldest herb which used for the treatment of multiple diseases in Unani, Ayurvedic and Chinese medicine. Modern studies show that fenugreek seeds and leaves have not only a lot of various health and beauty benefits and also have antitumor properties *in vitro*. However, the mechanisms of antitumor action of fenugreek *in vivo* are still unclear. **Objectives:** To study the role of fenugreek on growth of grafted tumors in experimental animals. **Material and Methods:** We used mature rodents with grafted tumors in mice (Ca755 mammary carcinoma; Lewis lung carcinoma (3LL); ascitic L1210 lymphoid and P388 lymphocytic leukemia) and rats (Guerin carcinoma and substrains, resistant to doxorubicin and cisplatin; Walker 256 (W256) mammary carcinoma; C6 glioma). The seed powder of fenugreek (Fen) obtained from University of the West Hungary. The animals were consumed Fen (250 mg/kg of body weight) from the day of tumor grafting up to sacrifice. All experiments were carried out accordingly to the rules of Ethic Committee. The level of malone dialdehyde (MDA) was measured by thiobarbituric method (535 nm), expression of proteins – by the Western blotting , polyamines (PA) content – by HLPC, blood elements were determined using PCE-210 hemoanalyzer. **Results:** It was found that Fen led to increase lifetime of animals with all experimental tumors by 15-50% ($P<0,05$). The smallest increase (5-8%) we observed in animals with W256 and P388 while antitumor effect of Fen was not educed. However, consumption of Fen inhibited growth other tumors by 25-48% and decreased average volume of the metastases per animal (3LL). We observed that Fen reduced NF-κB (p50/p65) expression, diminished of NF-κB-dependent genes expression (*c-myc, bcl-xl*), decreased level of ornithine decarboxylase *(odc)* (key enzyme of PA biosynthesis). PA are essential for growth and cell proliferation. We found that Fen led to decrease level of main PA (putrescine, spermidine and spermine) in tumor tissue. In addition, Fen decreased level of MDA in all experimental groups, reduced generation of superoxide anion-radicals, increased level of erythrocytes and Hb, does not affect of creatinine, urea, ALT and AST levels in blood serum. These biochemical data are in good agreement with the tumor growth inhibition. **Conclusions:** The obtained results show that Methi has antitumor activity *in vivo*. On the basis of these data we made a hypothesis that fenugreek is perspective for cancer prevention in the cancer risk groups and might be helpful as ancillary agent for treatment of oncological patients.

miR-1# inhibits cell-proliferation by targeting the oncogene CCRG1 in cancer cells.

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Introduction: MicroRNAs are small, endogenous non-coding RNAs that are key regulators of gene expression. Recent reports suggest that miRNAs also control the levels of multiple cell-cycle regulators. A major objective in the field is to identify the oncogenic and tumor-suppressor miRNAs that mediate the degradation of cell-cycle/replication proteins preventing genomic aberrations that promote oncogenesis. **Objectives:** The study aims at identifying novel miRNA:gene pairs regulating DNA replication, cell-cycle and understand the physiology behind this regulation. **Material and Methods:** Microarray-profiling, RT-PCR and/or western blotting was used to identify differentially expressed miRNAs/mRNAs. Putative miRNA targets were determined using TargetScan, miRanda. Luciferase-reporter assay authenticated miRNA:gene pairs. For gain/loss-of-function studies, miRNA mimic/inhibitor was transfected and cell-proliferation was studied using BrdU-FACS, BrdU-immunofluorescence and wound-healing assay. **Results:** Microarray-profiling identified 60 differentially expressed miRNAs in asynchronous, serum-starved and serum-released HCT116 cells. RT-PCR confirmed upregulation of 13 miRNAs in serum-starvation, which restored to normal levels after serum-release. Additionally 25 cell-cycle genes exhibited an opposite expression pattern (downregulated in quiescence and upregulated after serum-release) as seen by q-PCR. We focused our study on miR-1#. MiRNA target-prediction tools displayed one miR-1# binding site in CCRG1 (cell cycle regulating gene 1) 3'UTR. Luciferase-reporter assay confirmed this miRNA:gene pair. Moreover, miR-1# levels were compared in 2 osteosarcoma cells lines: U2OS (rapid-proliferating) and KPD (slow-proliferating). U2OS showed high CCRG1 and low miR-1# expression than KPD. miR-1# overexpression downregulated CCRG1 mRNA and protein levels and reduced cell-proliferation as seen by BrdU-FACS and BrdU-immunofluorescence. Further, wound-healing capability was significantly reduced in miR-1# transfected cells. **Conclusions:** miR-1# was significantly downregulated

in rapid osteosarcoma and inhibited proliferation by targeting CCRG1, demonstrating a tumor-suppressive function that possesses a therapeutic potential.
(miR-1#, CCRG1-*nomenclature as per lab inventory)*

Cytokines in health and diseases-Physiological perspective

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Background: Cytokines are hormone like substances having paracrine action and autocrine function. They are secreted by lymphocytes, macrophages, endothelial cells, neurons and glail cells. Cytokines whose amino acid sequences are known termed as interleukins. Cytokines include interleukines (IL-1 to 13), chemokines, CSF (colony stimulating factor), TNF- α and TNF-β and interferons. Cytokine receptors have three superfamilies- subfamily I (erythropoietin, IL-4, IL-7, growth hormone, prolactin), subfamily II (IL-3, IL-5, IL-6, IL-11, granulocyte-macrophage colony stimulating factor - GM-CSF, ciliary neurotrophic factor, ocostatin, leukemia inhibitory factor), subfamily III (IL-2, IL-4, IL-7, IL-9, IL-15). Another superfamily of cytokines is chemokine family (complements like C5α, leukotrienes, polypeptides). Chemokines attract the substances that attract neutrophils. **Material and method:** A review study. **Results:** Cytokines are involved in regulation of cell growth, angiogenesis and tumor treatment. IL-4 is useful in allergic and parasitic infestations. Erythropoietin increases red cell production. Growth hormone increases growth and development of tissues. Prolactin stimulates milk secretion from breast. Increased IL-6 production occurs in myeloma, Castleman's disease. IL-11 is used as adjuvant in chemotherapy induced thrombocytopenia. GM-CSF is used for treatment of chemotherapy induced neutropenia. Antibodies against TNF are used in rheumatoid arthritis and crohn's disease. Interferons provide immunity against viral infections. **Conclusion:** Cytokines are involved in growth, differentiation and activation of cells. They are increased in cancerous conditions, allergic reactions, inflammation and are used in tumor treatment. Interferons are used clinically in hepatitis B and C, kaposi sarcoma, multiple sclerosis and chronic granulomatous diseases.

Keywords : *Cytokines, interleukins, chemokines.*

Studying the expression of CR1 in specific colon cancer cell lines *in vitro*

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Introduction: Cripto-1 (CR1) is regulatory gene involved in embryogenesis and promotes carcinogenesis by modulating cancer cell proliferation, migration and EMT transition. Metformin is an anti-diabetic drug which has been found to exhibit anti-neoplastic effect. Since cancer stem cells are believed to be a major driving force for the aggressiveness nature of cancer, we want to study how treatment with Metformin affect changes in CR1 expression. **Method:** Colon cancer (HT29) cell lines were cultured *in vitro*. Dose of Metformin used was determined using MTT. HCT116 and HT29 cells were treated with Metformin for different time periods and CR1 expression was studied. To further validate the regulation of expression, CR1 cDNA was amplified and the product was ligated to 1013 vector. Transfected cells were analyzed for CR1 and other related parameters. **Result**: Changes in expression of CR1 were observed on treatment of cells (HCT116, HT29) with Metformin. Specific bands for CR1 were aligned completely to human gene reference sequence in NCBI database. Increased expression of human CR1 were observed in transfected cells. Modulation of gene expression was validated using QPCR. **Discussion:** Initial results indicate an inverse correlation between Metformin doses and CR1 expression patterns. Signals from various growth factors cascade through cardinal signaling pathways like PI3K/Akt and MAPK. We are currently studying the molecular cross-talking between these pathways and their regulatory role in controlling the action of CR1 and their link with the genesis and modulation of cancer.

MicroRNAs and Cell Cycle Regulation

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Cell cycle control is an intricate process involved in the differential expression of genes. It is regulated by both transcriptional and post-transcriptional mechanisms. Although great progress has been made on gene regulation, but during cellular proliferation and differentiation, many regulatory mechanisms remain unknown. Since cell cycle progression requires the presence and activity of multiple proteins that are not expressed in quiescent cell, the regulation of the levels of these proteins is a central issue in the understanding of the control of the cell cycle and its deregulation in human diseases such as cancer. Particularly, miRNAs emerge as a new class of small non-coding RNA regulators of the cell cycle and expression of these specific miRNAs oscillates orderly along with the cell cycle progression. Recently, identified miRNAs have been estimated to control the expression of more than 30% of protein-coding genes and they have emerged as candidate components of oncogene and tumor-suppressor networks. In addition, they are found to play a major role in proliferation, apoptosis, metastasis and even angiogenesis. Due to the relevance of cell-cycle control in tissue homeostasis and proliferative diseases, the modulation of cell cycle entry or progression by miRNAs, and the possible control of miRNA function in a cell-cycle dependent manner are of prime focus of research. Therefore, this review summarizes and highlights the relevance of understanding the connections between the miRNAs and the cell cycle progression.

A novel drug 3-(3´4´,5´-Trimethoxyphenyl)-5-(N-methyl-3´-indolyl)-1,2,4-triazole [NMK-T-057] induces cell cycle arrest, apoptosis and reprogramming of epithelial to mesenchymal transition (EMT) and stemness in breast cancer cells via targeting Notch-1 signaling.

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Epithelial to Mesenchymal transition (EMT) is an important and coordinated series of events associated with tumor metastasis and invasion. Accumulating experimental evidences had shown the importance of Notch-1 signaling in the regulation of EMT, induction of stemness and acquisition of chemoresistance properties in breast cancer. Hence targeting the Notch-1 signaling in breast cancer can serve as an effective therapeutic approach to combat this disease. Indole ring system is one of the most crucial heterocycles that has found versatile pharmacological implication in medicinal chemistry. Many of the natural and synthetic indole-based heterocycles with various functionalities are reported as potential anticancer molecules. Recently, the diverse biological activities of hydrazide-hydrozones have attracted the researchers to develop their heterocyclic analogues as efficient chemotherapeutic agents. In the present study we have reported the anticancer mechanism of a novel 3-(3´4´,5´-Trimethoxyphenyl)-5-(N-methyl-3´-indolyl)-1,2,4-triazole compoundalso known as

NMK-T-057 against the carcinoma of breast. NMK-T-057 was found to be highly cytotoxic against various breast cancer cells such as MDA-MB-231, MDA-MB-468 and MCF-7, while it has negligible cytotoxicity against the non-cancerous MCF-10A. NMK-T-057 significantly induced cell cycle arrest of the BC cells at G2/M phase and initiated mitochondrial-dependent apoptotic signaling. Moreover it was found to alter the mesenchymal morphology of MDA-MB-231 cells and inhibited the EMT process. Further investigations revealed that treatment of MD-MB-231 cells with NMK-T-057 resulted in the drastic inhibition of Notch-1 signaling. Thus we might conclude that NMK-T-057 could be potential drug candidate against breast cancer, which can target Notch-signaling.

Molecular mechanisms of cancer susceptibility associated with the Single Nucleotide Polymorphisms [SNPs] of the Nuclear Hormone Receptor VDR in relation to Breast cancer: An *in silico* approach.

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Introduction: Breast cancer is a multistep process involving multi-factorial involvement of genetic and environmental factors. A number of researchers have shown an association between vitamin D levels and breast cancer. Calcitriol (the active form of Vitamin D) binds to the nuclear Vitamin D Receptor in target organs. VDR forms heterodimers with the Retinoid X Receptor recruiting other transcriptional co-activators that regulate target gene transcription, including those involved in cell proliferation, differentiation, and apoptosis. Genetic polymorphisms of VDR can hence modulate the risk of breast cancer by altering its expression as well as its function in breast cell. **Objectives:** *In silico* exploration of the probable mechanism of increased risk of breast cancer with the related polymorph/s (SNPs). The computational genomic analysis of the SNPs followed by the Mutational Analysis (ΔΔG) of Vitamin D Receptor Protein. To develop the 3D structures of VDR and its Breast Cancer associated SNP variants viz. *Fok I, Taq I, Apa I and Bsm I* by Homology Modelling (using MODELLER 9.10) . To perform the binding affinity analysis of Calcitriol with Wild Type VDR & its variants followed by the binding affinity analysis of Retinoid X Receptor-α (RXR) with liganded Wild Type VDR and its liganded SNP variants. **Material and Methods:** *In Silico* exploration of the SNPs was performed using Sorting Intolerant From Tolerant (SIFT) bioinformatics tool to predict the effect of coding variants on protein function. Primary FASTA sequence of VDR was procured from the Uniprot database and the 3D structure of VDR was procured from the RCSB protein Data Bank. Due to absence of the experimental 3D structures of the variants of VDR, MODELLER 9.10 was used for the Homology Modeling of variants. Ramachandran Plot was used for the validation and selection of the generated 3D structures *(.pdb)*. The structure for Calcitriol (the active form of Vitamin D) was generated using the ChemSketch Software & CORINA online server. Chimera was used for energy minimization and removal of steric collision. To examine the effect of point mutation on the change in protein stability, the difference in folding free energy (ΔΔG) was calculated using the I-mutant program. Molecular interaction & binding analysis was done using Autodock version 4.0. For the protein-protein interaction (PPI) analysis ZDock & PatchDock tools were used in the Microsoft Windows 7 professional Version 2002, Intel (R) i7 processor, 3.30 GHz CPU and 16.0 GB RAM DELL Machine. **Conclusion:** The computational genomic analysis and exploration of the four SNPs of VDR viz. *Fok I, Taq I, Bsm I and Apa I* predicts that Fok I & *Bsm I* are synonymous SNPs and lie in the coding/exonic region while Taq I & *Bsm I* are non-synonymous SNPs and lie in the non-coding/ intronic region of VDR. *Fok I & Taq I* persist their genomic alterations showing amino acid substitution at protein level resulting in decreased protein stability. The binding affinity analysis of VDR variants with Calcitriol (VDR *Fok I* - 6.74 Kcal/Mol & VDR *Taq I* -6.42 Kcal/Mol) shows that these variants have a lower binding energy in comparison to Wild Type VDR protein (-7.39 Kcal/Mol). The binding affinity analysis of Liganded Wild type VDR (VDR+Calcitrol) to RXR (ZDock: 1397.892 & Patch Dock: 15508) and liganded SNP variants of VDR to RXR shows that liganded VDR (*Fok I)* has almost similar binding energy (ZDock-1404.273 & Patch Dock-15558) as wild type VDR & RXR however liganded VDR (*Taq I)* variant has lower binding energy (ZDock-1304.912 & Patch Dock-15302) as compared to wild type VDR & RXR. This indicates that these SNPs may cause the impairment of normal interaction of liganded VDR with its heterodimeric partner RXR at protein level. The liganded VDR-RXR heterodimerization is functionally linked to vitamin D responsive elements (VDRE) binding and functions to recognize the VDREs in the DNA sequence of vitamin D-regulated genes. VDR is known to regulate about 3000 genes in the human genome including genes like hp21 and hFOXO 1 which are involved in cell cycle control (proliferation, differentiation, migration and death). The SNPs in VDR may cause alterations in the major molecular actions of VDR, namely ligand binding, heterodimerization, and transactivation. Ligand-intensified heterodimerization, VDRE binding and co-activator recruitment by VDR appear to be functionally inseparable events that affect $1\alpha,25(OH)_2D_3$-elicited gene transcription.This indicates that breast cancer risk and pathogenesis in females can be influenced by SNPs and the analysis of SNPs in breast cancer research has pleiotropic implications for clinical and public health issues, as well as cancer biology. Computer-based structural & genomic analysis of SNPs may play a significant role in cancer management.

Effect of BMP pathway inhibitor in TNBC cell proliferation

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Triple Negative Breast Cancer (TNBC)is clinically heterogeneous & aggressive form ofbreast cancer with limited treatment options &lacks proven targeted therapy. Limited understanding of molecular pathways involved in TNBC poses challenges in treatment of TNBC. The conventional treatment modality for TNBC involves systemic chemotherapy; however acquired resistance and relapse is of great concern. Increasing evidence has shown that cancer stem cells (CSC) are mainly involved in development of resistance &tumor re-initiation & metastasis,in which BMP signaling pathway plays a crucial role. This pathway regulates various cellular processes including maintenance of cancer stem cells. In the present study we investigated the involvement of BMP pathway inhibitor LDN193189in the proliferation of TNBCcells using MDA-MB231cell lineby cell cytotoxicity, multi-caspase activation,clonogenicity&cell migration assays.LDN193189 exhibited significant cytotoxicity on MDA-MB231 cells with an IC50 value of 1.49uM. Higher concentrations of LDN193189 promoted caspase activation there by implying its role in inductionof apoptosis. Cells exposed tothis inhibitor for longerduration displayed reduced colony formation as indicated by the results of clonogenic assay. These results throw an insight into the possibility of developing LDN193189 as an effective targeted molecule for the treatment of TNBC.

Combined microRNA / mRNA profiling identifies miR-4516 / Ube2N signalling in P53 dependent apoptosis in keratinocytes

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Introduction: Apoptosis plays a crucial role in maintaining skin homeostasis and its imbalance via dysregulated miRNA signaling contributes to skin pathologies like skin cancer, psoriasis etc. Psoriasis is a chronic inflammatory skin disease characterized by hyper-proliferation and decreased differentiation of keratinocytes along with accumulation of immune cells expressing pro-inflammatory cytokines in the epidermis. microRNAs are a class of

endogenous short non-coding RNA molecules that downregulate gene expression at post-transcriptional level, effecting diverse cellular processes. Their functional role in psoriasis pathogenesis has recently been defined. Conventionaltherapy like PUVA (Psoralen plus ultraviolet A) is till date, most effective in clearing psoriasis symptoms, yet mechanism underlining its pro-apoptotic activity is incompletely understood. **Objectives:**Elucidating microRNA/mRNA regulatory pathways underlining PUVA induced apoptosis. **Material and Methods::**miRNome and genome wide expression profiling of PUVA treated keratinocytes was performed using Exiqon miRCURY LNA array and Illumina Human HT12 v4 gene expression bead chip respectively. **Results:**We observed significant differential expression of miR-4516 and 1932 genes in PUVA treated keratinocytes. Pathway analysis of the differentially expressed genes using IPA and PANTHER revealed RIG-1 like receptor (RLR) signaling, apoptosis and p53 pathways to be significantly associated with PUVA mediated effects. Our study for the first time demonstrated that ectopic expression of miR-4516, directly targets E2 enzyme of ubiquitination pathway (Ube2N), by binding to its 3'UTR as confirmed by luciferase reporter assay, and this interaction regulates p53 activation in PUVA induced apoptosis. **Conclusions:**These results highlight pro-apoptotic function of miR-4516 and possible new strategy targeting miR-4516/Ube2N or p53 for therapeutic intervention in proliferative skin disorders.

One-Step Strep-Tag Purification Methods for the Identification and Validation of Proteins-Protein Interaction Complexes Involved in Cancer Promotion.

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The Strep-Tag system is a method, which allows the purification and detection of proteins complexes by affinity chromatography. The strep-tag is a synthetic peptide consists of eight amino acid peptides (Trp-Ser-His-Pro-Gln-Phe-Glu-Lys) that specifically binds to streptavidin, originally selected from a genetic random library. The *Strep*-tag® was originally selected from a genetic random library as an eight amino acid peptide that specifically binds to streptavidin. Streptavidin is a tetrameric protein expressed in *Streptomyces avidini,* showed strong affinity to vitamin h-biotin, Streptavidin is commonly used in molecular biology and biotechnology. Identification and purification of protein complexes is the key to understand protein function, biological processes and signalling pathways. To understand Protein-protein interactions (PPIs) and their cellular function in mammalian cells we develop novel methods. By using the strep tag affinity chromatography method, enabling fast and simple one-step purification, coupled with competitive elution under physiological conditions, we successfully purified a PP2A holoenzyme and PME-1 protein complex from a cultured mammalian cancer cell line. We identified both known and novel interacting proteins for PP2A and PME-1 complex and demonstrate that the purified protein complexes by this method are functional.

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Role of Mammalian Enzyme PON2 In Cell Proliferation And Apoptosis Of Tumor Cells

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Mammalian paraoxonase family comprises three highly conserved enzymes PON1, PON2, and PON3. PON1 and PON3 are present in serum lipoprotein fractions, however PON2 is an intracellular protein found in almost every tissue, particularly in the mitochondria, endoplasmic reticulum and perinuclear region.PONs are important anti-oxidative enzymes and hence detoxifying. Their roles in atherosclerosis, organophosphate degradation, diabetes, obesity and innate immunity have been established. Physiological substratefor PON2 is unknown, although it shows lactonase activity *in vitro*. The cytoprotective effect of PON2 through anti-apoptotic behavior is satisfactorilydocumented. However, the pathway by which PON2 reducesapoptosis is not clear.We have selected human hepatic carcinoma cell line (Huh7) to study the role of PON2 in cell proliferation and apoptosis. The Huh7 cells were grown with and withouthydrogen peroxide (in the range of 50-500 μM) and anti-cancerous drug cis-platin(in the range of 2-20 μM) treatment. The control and treated cells were used to detect the level of PON2 expression by real time PCR. PON2 showed significantly reduced level of expression, which supports the previously reported anti-apoptotic behavior of PON2. To understand the mechanism of anti-apoptotic, PON2 expression are being silenced by transfecting siRNA followed by estimation of apoptotic and cell cycle markers like caspases (3, 8 and 9), pERK and pAkt by using western blotting technique.These studies on PON2 together with the previous reports suggest that PON2 stabilizes tumor cells, which could be a potential target for cancer treatment, however the exact mechanism is yet to be understood.

Mechanistic insights into a novel di-(2-picolyl) amine: 3-(Bromoacetyl)coumarin drug entity: in vitro binding profile with DNA/Cu(II) ions and cytotoxic activity against cancer cells

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Introduction: Cancer is a complex class of disease in which a group of cells divide uncontrollably beyond the normal limit, subsequently intruding into the near or distant tissues (metastasis), ultimately causing cell death. To circumvent such disease, development of new chemotherapeutic agents is required having maximum curative potential and minimal side effects. **Objectives:** Unlike normal cells, cancer cells contain elevated copper levels which play an integral role in angiogenesis. Copper is an important

metal ion associated with the chromatin DNA, particularly with guanine. Thus, targeting copper via copper-specific chelators in cancer cells can serve as effective anticancer strategy. Keeping in view these facts, we synthesized di-(2-picolyl) amine: 3-(Bromoacetyl) coumarin (ligand-L) against malignant cells. **Material and Methods:** Using human peripheral lymphocytes as model system, we assessed lipid peroxidation, protein carbonylation, ROS generation, DNA damage and apoptosis by ligand-L in presence of exogenously added Cu(II) in cells to simulate malignancy like condition. We also used interaction studies (UV and fluorescence spectroscopy) to ascertain its binding with DNA and Cu(II) ions. **Results and conclusions:**Results showed that Cu(II)-ligand-L interaction leads to lipid peroxidation and protein carbonylation (markers of oxidative stress), DNA damage and apoptosis in treated lymphocytes. All these effects induced by ligand-L were attenuated by neocuproine and ROS scavengers. This indicates that ligand-L cytotoxicity is due to redox cycling of copper to generate ROS which leads to pro-oxidant cell death. These findings will provide significant insights into the development of new chemical molecules with better copper chelating and pro-oxidant properties against cancer cells.

Keywords: copper chelation;redox cycling; anticancer activity.

Soy Isoflavone Daidzein Induces Cell Death By Instrinsic Pathway Of Apoptosis In Breast Cancer Cells.

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Introduction: Consumption of soy has been associated with decreased incidence of breast cancer. We have been studying Diadzein, a soy isoflavone for its effect on breast cancer cell lines. **Materials:** In the present study, effect of Diadzein has been investigated on survival of human breast cancer Cell line MCF-7. Sub lethal dose of Diadzein determined by MTT assay was used for subsequent experiments. 50μg/ml of Diadzein in DMSO as vehicle was used to study induction of apoptosis in these cells. Cells treated with DMSO only served as Control. Phenol free DMEM medium supplemented with 10% fetal bovine serum (treated with activated charcoal to strip off any steroid present in serum) was used for isoflavone treatment in these cells. Bax and Bcl-2 were analyzed by Western Blotting. Caspase 3 was analyzed using Caspase-Glo® 3/7 Assay kit. **Key findings:** Treatment of MCF-7 cells with Diadzein leads to a significant increase in Bax expression. However it resulted in significant decrease in Bcl-2 expression. Thereby, Bax:Bcl-2 ratio increased in Diadzein treated cells compared to control cells. Furthermore, an increase in Caspase 3 activity was observed in Diadzein treated cells as compared to control cells. These results indicate involvement of Diadzein induction of apoptosis. **Conclusion:** From the above findings we may infer that Diadzein may have a protective role in breast cancer by inducing apoptosis of malignant cells. These findings may be further corroborated by studying other markers of apoptosis.

INPP4A goes nuclear: nucleo-cytoplasmic shuttling of INPP4A regulates cell proliferation and apoptosis

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Introduction: Cancer figures among the leading causes of morbidity and mortality worldwide, with approximately 14 million new cases annually and 8.2 million cancer related deaths in 2012. The number of new cases is expected to rise by about 70% over the next 2 decades. The Phosphatidyl inositol 3-kinase (PI3-K) pathway is a key signaling cascade that is dysregulated in a large variety of human tumors. Inositol polyphosphate 4 phosphatase type I enzyme (INPP4A) is a lipid phosphatase which acts as a negative regulator of the PI3-K pathway by indirectly decreasing Akt activation in the cytoplasm. In this study, we report, for the first time, a novel localization of INPP4A in the nucleus. We have also established that INPP4A shuttles continuously between the nucleus and the cytoplasm, and it is this nucleocytoplasmic shuttling of INPP4A that contributes to critically regulating cell proliferation and apoptosis in the cell. **Objective:** The aim of the present study is to probe the role of INPP4A in the nucleus. **Materials and Methods:** We have used multiple techniques like immunocytochemistry, exogenous expression of INPP4A, immunohistochemistry and western blotting in MCF-7 cells to confirm our initial observation of the novel sub-cellular localization of INPP4A in the nucleus. Cells were fractionated into nuclear and cytoplasmic extracts, followed by western blotting to compare the nuclear levels of INPP4A in various paired cell lines of normal and cancerous origin. We have also corroborated the nuclear levels of INPP4A with the different cell cycle stages, to see if the entry into nucleus is cell-stage dependent. Next, we engineered the wild type INPP4A plasmid such that it expresses predominantly in the nucleus ($Nuclear^{Hi}$), as opposed to in the cytoplasm in the wild type ($Cytoplasmic^{Hi}$), and performed proliferation and apoptosis assays using flow cytometry (FACS) and TUNEL respectively. **Results:** We demonstrate for the first time that enzymatically active INPP4A, apart from being expressed in the cytoplasm, also localizes to the nucleus of various cell lines, as well as in bronchial epithelial cells in murine lung tissues. We further show that nuclear level of INPP4A is dependent on the cell cycle and is highest at the G0/G1 phase. The level of nuclear INPP4A is significantly higher in cells derived from non-cancerous origin, compared to those from cancerous origin. We find that $Nuclear^{Hi}$ INPP4A significantly suppresses cell proliferation compared to $Cytoplasmic^{Hi}$ INPP4A, and sustained presence of INPP4A in the nucleus leads to massive death in the cells. **Conclusion:** Overall, our findings suggest that the level of INPP4A in the nucleus, which is maintained by nucleo-cytoplasmic shuttling, can critically regulate the balance between the extent of proliferation and apoptosis in the normal cell, which is disrupted in a cancer cell.

Cytotoxic activity of some medicinal plants on A549 cell line

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Introduction: Medicinal plants play a central role in the healthcare system of the large proportions of the world's population. Plant derived compounds are an important source of several clinically useful anticancer agents. Cytotoxicity screening models are the preliminary methods for selection of active plant extracts against cancer. **Materials & Methods :**Cytotoxic activity of active extracts of the plants-P.vulgaris, T.bucatta and A. lappa was carried out against human lung cancer(A549) cell line at eight different concentrations to determine the IC50 (50% growth inhibition) by MTT assay &caspase 3-7 assay. Each sample was assayed in triplicate and control samples include cells without plant extracts. **Results:** Results demonstrate that the percentage of growth inhibition increases with increasing concentration of test compounds. The P.vulgaris extracts induced significant cytotoxic effects on the A549 cancer cell line and these effects were stronger than the other selected plant extracts. **Conclusion:** Extracts which exhibit substantial antiproliferative & apoptic activity may represent a source for novel natural anticancer entities.

Keywords: A549, P.vulgaris, T.bucatta, A.lappa.

Interplay of nuclear and mitochondrial encoded miRNAs in Cervical Carcinogenesis

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Background: Infection with human papillomavirus (HPV) is the major etiological agent of cervical cancer. However, infection alone is not sufficient for tumorigenesis. In this direction, we hypothesize that additional aberrant genetic and epigenetic changes in both host and HPV genome and their interplay is expected to impact progression to cervical carcinogenesis. Recent studies have also suggested the import and export of miRNAs encoded by both nuclear and mitochondrial genome within and outside the cells. However, such a possibilities are less explored in histpathologically confirmed cervical cancer samples. Hence in the present study, we intended to identify the crosstalk of miRNAs encoded by mitochondrial and nuclear genome within the cells which might facilitate the development of cervical cancer. **Materials and methods:** Differentially expressed known and novel nuclear encoded miRNAs were identified using next generation sequencing using Ion torrent platform in normal (N), premalignant (P) and malignant (T) samples (n=15, each). We have constructed the small RNA which is enriched using biotin-streptavidin method. Data generated was analyzed by mapping to human genome (hg19) which was subsequently aligned to miRBase19 and analyzed using CAP-miRSeq tool. *Insilico* functional analysis was performed using various bioinformatic tools such as miRDB, PITA, TargetScan, DIANA MICROTv3.0 and miREval. Computational analysis also predicted the novel mitochondrial sequences. Selected miRNAs were validated using Taqman real time PCR. **Results:** We identified a total of 423,410 and 414 differentially expressed miRNAs in P vs N, T vs N and T vs P respectively. Further 2 novel nuclear encoded miRNAs were also identified and predicted to target genes involved in p53 pathway, Wnt signaling pathway and Ras pathway. We have identified 1 mitochondrial encoded miRNAs and predicted its targets. hsa-miR-21 was shown to be 2- fold upregulated in cervical cancer samples and novel-1 and novel-2 nuclear encoded miRNAs was shown to be downregulated and upregulated in cervical cancer samples respectively. **Conclusion:** Our results demonstrated that nuclear and mitochondrial miRNAs could act as agent that can act dynamically to the changing microenvironment at cellular level in cancer. Our findings are expected to facilitate the development of these deregulated miRNAs as biomarker for cervical cancer.

Keywords: miRNA, Mitochondria, Next Generation Sequencing

Role of specimen imaging as a reliable tool to assess the margin status following surgery for breast cancer

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Background: Assessment of margins after surgery for breast cancer and especially when breast conservation surgery (BCS) is contemplated is an essential part of the management. Various modalities/techniques like frozen section or imprint cytology are in use and have their limitations in the fact that the structural histological evaluation is not feasible. This leads to false negatives and also has limitation in that it is operator dependent. In order to obviate these shortcomings various centers are already using specimen imaging (Mammography and ultrasound). **Aims and objectives**: The aim of the study was to assess the accuracy of specimen imaging in assessing the margin status after surgery(MRM, lumpectomy) for breast cancer as compared to the frozen section . **Materials &Methods:** 30 biopsy proven patients with breast cancer were evaluated in this prospective study at a tertiary cancer care center. The specimen(lumpectomy or mastectomy) was sent for specimen ultrasonomammography and later for frozen section . The final histopathology served as the gold standard. **Results:** Specimen ultrasonomammography was observed to be superior to frozen section in providing detailed assessment of margins and multicentricity specially in patients undergoing breast conservation. Specimen mammography could also detect additional cancers that frozen may miss especially the *in situ* cancers

Simulation Lumpectomy to assess the feasibility of Breast Conserving Surgery(BCS) following Neoadjuvant chemotherapy(NACT) in Locally Advanced Breast Cancer(LABC).

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Background: Obtaining negative margin is critically important for local control of breast cancer , failure of which results in re-excision. The response of NACT in LABC patients offers the chance for breast conservation. The effort is therefore here to find out whether the so called Lumpectomy(BCS) in LABC would be safe/optimal and margins could be free after NACT . **Materials &Methods:** 30 LABC patients after complete routine and metastatic work up were subjected to trucut biopsy and posted for three cycles of NACT, followed by surgery(MRM) . Subsequently Simulation Lumpectomy were performed on the mastectomy specimen with the margin of 1-2 cm all around the palpable tumour. The margins were then reassessed with intraoperative ultrasonomammography and histopathological examination.. Statistical Analysis done. **Results:** A statistically significant correlation was observed between Imaging, Frozen and HPE analysis of specimen(Simulation lumpectomy and the parent specimen). All 30 patient showed response to NACT and in all the patient simulation lumpectomy specimen margins were free of tumour. **Conclusions:** Breast conserving surgery is feasible in LABC after neo-adjuvant chemotherapy . It was also observed during the study that response of breast conserving surgery is better in those patient in whom the size of lump is less than 3.

Randomized Clinical Study to assess the outcome following modified radical mastectomy with half suction drain between hospitallized and patients managed at home with drain in situ.

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Background: Management of drain after surgery (modified radical mastectomy) is one of the essential components which cannot be neglected. The quality of life of patient depends upon drain output. It was observed in this study that patient who weans off early from drain have better outcome in terms of quality of life(in terms of less flap necrosis, less infection rate, Enhanced recovery after surgery, Almost nil seroma formation) **Materials &Methods:** 30 LABC patients after complete routine and metastatic work up were taken up for modified radical mastectomy. After the surgery based on computer generated randomization patients were grouped under two categories. One group were discharged with drain in situ and the other group of patients were managed in the hospital. Both groups were then studied for drain output, seroma formation, flap necrosis etc. . **Results:** A statistically significant difference was observed in drain output between both the two groups of patients. It was seen that patients who were discharged with drain in situ showed a significant reduction in the time before drain removal.The drains were removed after the drain output reduced to less than

25ml in 24 hours. **Conclusions:** It was observed in this study that discharge patient of MRM wean off earlier from drain in comparison to hospitalised patient and hence have better quality of life .

ULTRASOUND GUIDED FNAC OF AXILLARY LYMPH NODES Vs SENTINEL LYMPH NODE BIOPSY IN EARLY BREAST CANCERS :A INSTITUTIONAL PROSPECTIVE STUDY

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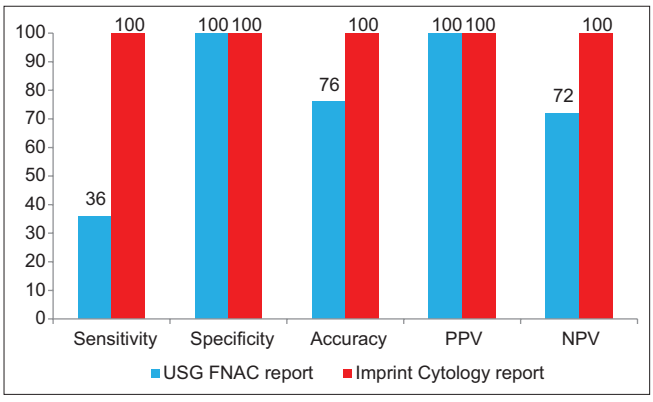
Background: Both USG guided FNAC and sentinel lymph node biopsy have been useful to avoid a morbid axillary dissection in early breast cancers . The main purpose of study is to compare the accuracy between the two procedures. **Materials:** Place of study: Meenakshi Mission Hospital and Research Centre. Duration of study : 12 months, Sample size (n): 44 patients, INCLUSION CRITERIA: clinically node negative breast cancers undergoing MRM & BCT. **Exclusion Criteria:** Palpable axillary lymphadenopathy Pregnancy Prior axillary surgery Prior non oncologic breast surgery Study method: After history ,examination and mammography ,patients who fit into the Inclusion criteria are selected. An informed consent is obtained. USG of breast & axilla is done . Lymph nodes which are round or oval in shape, short axis more than 5 mm in size are selected and FNAC is done with 21g needle. SLNB is done using methylene blue followed by frozen section analysis.Axillary lymph node biopsies are then compared with those from the USG guided FNAC and SLNB. Statistical Analysis Plan: Finally the entire data is tabulated.Data analysis was done with the help of computer using SPSS statistical package- Version 17. **Results:** USG FNAC : USG FNAC could not be done for 2 cases.No nodes -29(69%). Nodes -present & Malignancy -positive-7(16.7%). Nodes & Malignancy- positive -6(14.3%). **Slnb- Frozen Section:** No evidence of Malignancy (Negative)-28(64.1%),Positive for Malignancy (Positive) -16(35.9%). Final Histopathology report-axillary nodes,Positive for Malignancy (Positive) -16(35.9%). No evidence of Malignancy (Negative)-28(64.1%).

Comparative Efficacy of USG FNAC report and SLNB with Histopathology as Golden standard

Parameter	Values For	
	USG FNAC Report	Slnb- Frozen Section Analysis
Sensitivity	36	100
Specificity	82	100
Accuracy	76	100
Positive Predictive Value (PPV)	100	100
Negative Predictive Value (NPV)	72	100



In this study, the sensitivity of USG FNAC was found to be 36 % and that of SLNB was found to be 100%. The specificity of both the studies was found to be 100 %. Accuracy of USG FNAC was found to be 76% and SLNB was 100 %. The positive predictive value and negative predictive value of USG FNAC was 100% and 72 % and SLNB was 100% and 100 % respectively. **Conclusion:** We could derive the following conclusions from the analysis of our prospective controlled study, which included 44 patients.Both USG FNAC and SLNB are excellent alternatives in order to avoid a morbid axillary dissection.Compared to USG FNAC, SLNB has better sensitivity, accuracy and negative predictive value.

DOES AXILLARY TUCKING DURING MODIFIED RADICAL MASTECTOMY REDUCE SEROMA FORMATION? - A RANDOMIZED CONTROL TRIAL IN 100 PATIENTS.

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Background: Seroma formation following breast surgery continues to be a major concern for the surgeon and the patient. The reported incidence of seroma formation varies widely between 3% and 85%. Surgical techniques to reduce the dead space following surgery have been shown to reduce the incidence of seroma. Wide variation exists in the surgical techniques practiced by surgeons based on their individual beliefs & training. The optimal ways to reduce the incidence of seroma are still unknown.Primary objective was to find whether axillary tucking during modified radical mastectomy helps to reduce seroma formation. Secondary objective was to evaluate factors affecting drain amount & seroma formation. **Materials and Methods:** This prospective randomized study was done in a tertiary care center between September 2013 and February 2015. First 100 consecutive adult patients clinical node positive breast cancer patients planned for primary modified radical mastectomy were randomized into axillary tucking (T) & no tucking (NT) groups. The total drain volume, date of drain removal, seroma formation & aspiration data were recorded by perioperative evaluation and patient's drain charts on follow up. Statistical analysis was done using Chi square & T test methods. Association of clinical factors (age, Body mass index, stage, grade, number of removed lymph nodes and number of metastatic nodes), surgical factors (duration of surgery, operating surgeon, blood loss etc.) with the seroma amount was correlated within respective groups and with the other group. Patients undergoing sentinel lymph node biopsy, breast conservation surgery, reconstructive surgery and those who had neoadjuvant therapy were excluded. **Results:** Out of total 100 patients, tucking group (T) (n= 50) & no tucking group (NT)(n= 50) None of the clinical factors and operative factors like number of lymph nodes dissected or positive lymph nodes, operative blood loss or duration of surgery had any effect on persistent seroma formation either within their groups or when compared with the other group. Level III nodal dissection was significantly associated with more drain volume in both the groups as compared to level II dissection. The mean drain volumes were 700 & 776 ml for tucking & no tucking groups respectively. Significantly greater proportion of patients in tucking group had drain volume < 500ml (p=0.017). The mean number of drain days were 10.16 & 11.8 days respectively for T & NT groups (p= 0.005). No significant difference was found in the number of seroma aspirations between the two groups (p=0.42). **Conclusions:** Obliterating dead space by axillary tucking decreases total drain volume & causes early removal of drain however the number of aspirations for seroma was not significantly altered.

Clinicopathological features and prognostic factors of pregnancy associated breast cancer from a north Indian cancer centre

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Background: Pregnancy-associated breast cancer (PABC) is defined as thedevelopment of breast cancer during pregnancy or duringthe 12

months following delivery or anytime during lactation. It occurs in 1/3000 to1/10,000 pregnancies. Itis often diagnosed at an advanced stage and its prognosis is worse compared to non-PABC.PABC data from developing countries like India are scarce. Our objective was to analyze the findings of PABC from a tertiary care cancer centre in India. **Material and Methods:** A retrospective review of breast cancer patients treated from 2010 to 2015 from departmental computerized database was performed and pregnancy associated breast cancer were identified and data were analyzed. **Results:**A total 22 patients were identified as PABC. Mean age of patients was 28.6 years (range 19- 34 years). Majority of patients (72.7%) were diagnosed during lactation period. Six patients were detected during pregnancy, among them one patient in first trimester who underwent termination of pregnancy, three patients in second trimester and two cases in third trimester. Majority of patients (90.9%) presented with lump in breast and mean duration of symptoms was 4.2 months. Family history of breast or ovarian cancer was seen in 13.6%.High resolution ultrasound was performed in majority of patients. Two patients had bilateral synchronous breast cancer. Inflammatory breast cancer was seen in 9% cases. Stage wise distribution was as stage I (4.5%), II (13.6%), III (63.6%), and IV (18.1%). Among distant metastasis 9% cases had liver and similar number of cases had skeletal metastasis at presentation. Treatment modalities were upfront surgery (18.1%), neo adjuvant chemotherapy (63.6%), palliative chemotherapy (18.1%), and adjuvant radiotherapy (72.7%). Histopathological features were as high grade tumor (54.4%), node positivity (68.1%), estrogen or progesterone receptor negativity (59%) andHER2neu receptor positivity (33.3%). Median follow up was 22 months (range 2 months- 5.2 years). Approximately 44.4% cases had recurrence and most common sites were bone followed by liver. Overall survival and disease free survival at 2 years were as 72.7% and 55.6% respectively. **Conclusion:**Pregnancy associated breast cancer is very rare occurrence. Majority of patients present in advanced stage with worse outcome. In comparison to non-PABC these patients have more frequent poor prognostic factors like node positivity, higher grade, ER/PR negativity, and Her2neu positivity.

Clinicopathological Profile of Basal and Non-Basal subtypes of Triple Negative Breast Cancer

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Introduction: Triple-negative breast cancer (TNBC), defined by the absence of estrogen receptor, progesterone receptor and human epidermal growth factor receptor-2 overexpression, constitutes one of the most challenging groups of breast cancers. The western literature uniformly indicates that basal-like (BL) subtype of TNBC shows a more aggressive behavior with poor prognosis. There is paucity of reliable data in Indian setting and the aim of this study is to bridge the lacunae. **Objectives:** (1) To identify TNBCs and categorize them into basal-like and non-basal-like (NBL) subtypes. (2) To compare the treatment outcome between two subtypes of TNBC. **Materials and Methods:** The patients of TNBC diagnosed and treated at Rajiv Gandhi Cancer Institute and Research Centre during January 2012 to December 2012 were identified. The subjects befitting the inclusion criteria of study were differentiated into BL and NBL subgroups using immunohistochemistry with three basal markers 34βE12, c-Kit and EGFR. The detailed data of subjects were assembled from clinical records. The clinicopathological characteristics as well as treatment outcomes were compared between two subtypes of TNBC. **Results:** The present study observed 27% breast cancer patients to be TNBC. The BL and NBL subtypes comprised of 63% and 37 % respectively of all cases included in the study. Statistically significant association of basal subtype with premenopausal status (p=0.020) and high grade of tumor (p=0.004) was found. Among early breast cancer patients, significant association of basal subtype with more lymph node positivity (p=0.010) and higher pathological lymphnodal stage (0.050) was seen. Despite having observed association of BL subgroup with parameters pertaining to aggressive behavior, the disease free survival and overall survival was found to be higher in comparison to NBL subgroup. **Conclusions:** The study proves that TNBC is not a single entity but it is a heterogeneous disease. The BL subtype of TNBC is seen more in younger premenopausal patients, associated with a high grade histology and higher nodal stage.

Two years experience in a genetic counseling clinic at a tertiary care cancer centre in North India

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Background: Genetic counseling is a communication process, which aims to help individuals, couples and families understand and adapt to the medical,psychological, familial and reproductive implications of the genetic contribution to specific health conditions. During this process the individuals at risk for a genetic disorder are educated regarding the consequences of the condition. We analysed the data collected within a period of two years in the genetic counseling clinic at Rajiv Gandhi Cancer Institute and Research Centre at Delhi. **Materials and Methods:** 91 probands came to our clinic for counseling.They were explained about hereditary cancers, their pedigree analysis done and they were told whether they should proceed for testing or not according to their risk assessment. 18agreed to proceed for testing. Saliva samples were collected and sent to Strands Life Sciences, Bangalore for testing by extraction of DNA and usingNext Generation Sequencing. The probands who came positive by testing were offered post test counseling along with their family members. **Results:**Out of the 18/91 i.e 20% subjects who went in for testing, 13 (14.3%) were tested for Hereditary Breast and Ovarian Cancer (HBOC) syndrome while 5 (5.5%)were tested for Li Fraumeni syndrome. 7/ 13(53.8%) tested for HBOC syndrome came out to be positive for various mutations in the BRCA1 and BRCA2 genes while 4/13 (30.8%) were negative and 2/13 (15.4%) were variants of unknown significance. In case of Li Fraumeni syndrome, 1/5(20%)subjects tested positive for mutations in the P53 gene, while 1/5 (20%) was negative and 3/5 (60%) had variants of unknown significance. **Conclusion:** More subjects who are at high risk need to go in for testing. Most of the probands coming to our clinic are for HBOC syndrome followed by Li Fraumeni syndrome. Further research needs to be initiated to identify the variants of unknown significance and the role which they may play/not play in the pathogenesis of the disease.The probands who underwent testing and came positive were advised about their prevention measures and follow up regimes along with their families.

Rare Tumors of the Breast : A Road Less Travelled

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Introduction: Breast tumors constitute a diverse group of morphological phenotypes and specific histopathological types with particular prognostic and clinical characteristics. Rare tumors of the breast constitute less than 2% of all breast cancers. Given the rarity of these tumors, the literature primarily contains case reports, small series and population based studies. The paucity of these cases has made large trials difficult, leading to lack of consensus regarding optimal treatment and management protocols. **Objectives:**1) Identification of the rare histological subtypes of breast cancer 2) Comparative analysis of clinical and pathological variables, management and response to treatment with respect to overall survival (OS) and disease-free survival (DFS). **Material and Methods:**All patients diagnosed with breast malignancy during 2008-2012 at Rajiv Gandhi Cancer Institute and Research Centre (RGCI and RC) were screened. The rare histological subtypes were identified among all screened cases. The clinical records of all identified cases were retrospectively reviewed for pathological diagnosis, clinical parameters, epidemiological details, and management protocols.

The treatment outcomes were determined by calculating DFS and OS at average 4 yrs follow -up after the completion of treatment using Kaplan-Meir method. **Results:** We retrieved 96 cases of rare subtypes from the RGCI and RC database representing 4.15% of the total 2240 breast cancer cases. The most common morphology observed in the series were mucinous carcinomas (36.5%), papillary neoplasms (14.6%) and medullary carcinomas (13.5%). The other relative frequencies of each subtype are elaborated in Table 1. The tumors of rare histologies presented mainly as early stage disease (79.2%) with 87.9 % of the patient cases at the age of ≥50 yrs. The average tumor size was 7.0 cm (Range 0.40-15.0). Also, these early stage cancers showed a higher degree of lymphnode negativity (94.7%) and Estrogen receptor/Progesterone receptor positivity (60.4%). The triple negative tumors constituted 27.1% of all the tested cases with majority occurring in medullary and metaplastic subtypes.Median OS in this study group was observed to be 53 months. However, median OS in subgroup early breast cancer treated only with surgery was 60 months and was found to be statistically significant ($p<0.0001$) in comparison with patients treated with a combination of surgery, chemotherapy and RT wherein the median OS was 37 months in the same subgroup. **Conclusions:** Rare tumors of the breast pose significant challenges right from inception. Hence, systematic evaluation of patient with detailed histopathology will aid accurate diagnosis. The present study hopes to add to the current understanding of diagnosis and management of this small percentage of cases.

Table 1: Breast Tumors of Rare Histologies

Type of Tumor	Frequency	Proportion
Apocrine	5	5.2
Cribriform	3	3.1
Fibroepithelial	5	5.2
Medullary	13	13.5
Metaplastic	9	9.4
Mixed	4	4.2
Mucinous	35	36.5
Neuroendocrine	2	2.1
Paget's disease	3	3.1
Papillary neoplasm	14	14.6
Pleomorphic variant of lobular carcinoma	2	2.1
Tubular	1	1.0
Total	96	100

Tumor Biology of Breast Cancer in Nepalese Young Women

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Purpose: Breast cancers in <40 years of age group usually presents with aggressive biology and has poor prognosis. The aim of this study was to see clinic-pathological and hormone receptors of breast cancers in young women and compare with ≥40 year age group. **Methods :** Prospective observational study of 335 women with breast cancer out of total 366 patients over a period of 8 years (2007 Jan to 2014 Dec) was carried out at the Department of Surgery, Tribhuvan University Teaching Hospital, Kathmandu, Nepal. All patients with hormonal receptors and HER2 reports were included in the study. **Result:** Out of the total breast cancer women, 87 patients were <40 years of age (23.8%). Mean tumor size was larger in younger women (5±2.5 vs 4.5±2.4 cm). Locally advanced disease was higher in younger patients (55% vs 47%). Lymphatic and vascular invasions were higher (63% vs 35% and 40% vs 25%).Grade II and III tumors were higher (56% vs 25%).ER, PR and HER2 positivity was detected in 46.9%, 48.9% and 23.3%, respectively.Significant lower ER/or PR expression (34.5% vs 54%) was seen in younger women, p=.002.Triple negative tumors (ER-, PR- and HER2-ve) was proportionately higher in younger patients (23% vs 13.7%, p=.043). **Conclusions:**Young Nepalese women presents one quarter of all female breast cancers,more frequently locally advanced with aggressive tumor biology like ER/PR negative and triple negative breast cancers.

Per operative brachytherapy in Accelerated Partial Breast radiation.

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Background: Per operative brachytherapy plays a major role in accelerated partial breast irradiation. In this method, the brachytherapy catheters are implanted during the time of breast conservation surgery. The advantage of peroperative technique is the precise determination of the location of the tumor and its cavity visible during surgery, a need for only one general anesthesia (implantation of applicators takes place during surgery), resulting in reduced overall treatment time. **Materials and Method:** 10 patient diagnosed with early breast carcinoma from May 2014-Nov 2015 with ER PR positive, clinically and imaging wise node negative were selected for per operative brachytherapy. At the time of lumpectomy the flexible catheters were put in the tumor cavity with margin of 3cm.The catheters were implanted in 2 planes one in superficial and other in deep plane. CT simuation was done for all patients. cavity was contoured as CTV with 3 cm margin and the brachytherapy HDR plan was approved according to ABS recommendation with 90% dose should be received by 90% of the target,V150<70cc,V200<20cc and skin dose <100% with a dose prescription of 34Gy in 10 fraction. **Results:** All 10 patients who underwent breast conservation surgery in their post operative histopatholgy had T1&T2 size tumour,margin negative and all nodes negative by axillary dissection. Dosimetric analysis of all the 10 patients plan were done. The mean CTV coverage of the target is 83%.The mean V150 (volume receiving 150% of the dose) is 62cc.The mean V200(volume receiving 200 % of the dose) is 34cc.The mean homogeneity index was 0.4. The mean skin dose is 119cGy. Except for CTV coverage all the other parameters were within normal limits of ABS recommendation. CTV coverage is less because of dose optimisation done near skin to avoid high dose to the skin. There were no acute or chronic skin toxicity in these patients. **Conclusion:** Peroperative catheter implantation for APBI is more advantageous compared to postoperative APBI. In future peroperative catheter implantation will be the standard of care for APBI

Prognostic factors determining the progression of disease of patients with Her2 targeted therapy and toxicity profile of Her2 targeted agent (Trastuzumab) in Indian Breast Cancer Patients: A single institute experience from India

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Introduction: Invention of trastuzumab has changed the treatment of breast cancer and lives of many patients all over the world. Despite patient getting benefitted from the drug, a few were non-responders. **Materials and Methods:** This is a retrospective analysis of breast cancer patients presenting to a tertiary care cancer centre in Southern India from 2007 to2011. All early and locally advanced breast cancer patients, who were Her2neu 3+ on IHC are included in the study. Patients with upfront metastatic disease and Her2neu 2+on IHC or negative on FISH were excluded from the study. Chemotherapy regimens used were-,FAC 6 cycles, and AC 4 cycles, followed by 12 cycles of weekly paclitaxel . Trastuzumab was given after 6 cycles of FAC or weekly with paclitaxel followed by 3weekly maintenance until 1 year. **Results:**A total of 185 patients were eligible for evaluation. The median age at presentation was 49 years. Early and locally advanced breast cancer patients

accounts for 122(65.94%) and 63(34.05%) respectively; 48(25.94%) patients were hormone receptor positive. A total of 72 patients received trastuzumab along with their chemotherapy. 5year disease free survival(DFS) in patients receiving trastuzumab arm were 90.21% and patients not receiving were 45.37%. 6 out 7 patients who progressed on trastuzumab had lymphovascular invasion and SBR Grade III. Cardiotoxicity was recorded in the form of diastolic dysfunction and decrease in ejection fraction(10-20% decrease from baseline)was seen in 7(9.72%) patients. Cardiac function reversal to normal was observed over 6-22 months and no cardiac related mortality observed. All patients who developed cardiotoxicity were hormone receptor negative. **Conclusion:** Trastuzumab with chemotherapy improves the DFS in Her2neu positive patients. Lymphovascular invasion was a poor prognostic marker indicating nonresponsiveness to trastuzumab therapy or aggressive disease. Patient who were hormone receptor negative and Her2neupositive, receiving trastuzumab were at increased risk of cardiotoxicity.

Epidemiological study of Triple Negative Breast Cancer patients in North Indian population

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Introduction: Breast cancer is the second most common cancer among women worldwide and the most common cause of death in women in developed countries. Triple Negative Breast Cancer refers to any breast cancer which does not show the expression of Estrogen receptor (ER), Progesterone receptor (PR) and Her2/neu. TNBC accounts for 10-25% of all breast carcinomas. This makes it more difficult to treat since most chemotherapy targets one of these receptors, so triple-negative cancers often require targeted therapies. **Objectives:** To investigate the prevalence of TNBC in study of North Indian population and to compare various clinicopathological characteristics of TNBC with non-TNBC. **Material and Methods:** The study was carried out in the Department of General Surgery in collaboration with the Department of Pathology, Institute of Medical Sciences, Banaras Hindu University, Varanasi, India, from January 2013 to December 2015. 103 patients were included in the study that underwent modified radical mastectomy. The procedure of immunostaining procedures were performed using formalin-fixed, paraffin-embedded tissue sections. These sections were stained by immunohistochemically for estrogen receptor (ER), progesterone receptor (PR) and human epidermal growth factor receptor 2 (HER 2 Neu) by using ready to use monoclonal antibody and HRP polymer detection system with 3'-3' diaminobenzidine hydrochloride (DAB) as chromogen. **Results:** Of all 103 patients; 35 (34%) were triple negative. The average age of patients of TNBC and non-TNBC group was found as 44.16 and 40.73 years respectively. Numbers of patients of post-menopausal state were greater than the premenopausal patients in TNBC (22/35; 62%) and non-TNBC groups (45/68; 66%). Further, TNBC patients reported at clinically early stage of I and II (18/35; 51.4%) while non-TNBC patients predominantly reported at later stage of III and IV (44/68; 64.7%). It was also observed that breast tumor size in majority of the patients in both the groups lies between 2 cm to 5 cm (TNBC=23/35; 65.7% and Non-TNBC=35/68; 51.5%). Pathological lymph node metastases were noted in 51.5% (18/35) cases in TNBC group and 64.7% (44/68) cases in Non-TNBC group. **Conclusion:** In conclusion, despite the limitation of less number of breast cancer cases, we analyzed that TNBC tumors have an aggressive clinical values than that of non-TNBC as shown by OR, though having no statistically significant difference between the prognostic clinical parameters of two groups.

Prognostic Value of Breast Cancer Subtypes Based on ER/PR, Her2 Expression and ki-67 Index in Women Received Adjuvant Therapy after Conservative Surgery for Early Stages Breast Cancer

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Introduction: Breast cancer is the most common malignancy in women, accounting for 29% of all female cancers. it accounts for <1% of all cancer cases in men. In a population based cancer registries in Gharbia, Egypt, breast cancer was the most frequent cancer among Egyptian females. Prognostic information for the individual patient is based on the analysis of biological markers in the primary tumour including (ER), (PR), (HER2) and Ki67, together with age, tumour size, histological grade and lymph node involvment. Molecular subtyping of breast cancer may provide additional prognostic information regarding patient outcome. **Objectives:** To evaluate the prognostic effect of breast cancer subtypes on local relapse rates, distant metastases, and survival in women underwent breast conservative surgeryfor early stages breast cancer. **Material and Methods:** Data of 100 patients affected by early stage breast cancer and treated with breast-conserving therapy were reviewed. Patients were grouped, based on the basis of receptor status and HER-2 status, patients were grouped, as: luminal A (ER + and/or PR+, Ki67 low and HER2-), luminal B (ER + and/or PR+, Ki67 high and/or HER2+), HER2-positive (ER-, PR- and HER2+) and triple negative (ER-, PR, HER2-). Distribution of variables among subtypes was evaluated with Pearson's test. Survival rates were calculated with life tables; Cox regression stepwise method was used to identify predictive variables of survival. **Results**: Median age was (range 18-50) and median follow up time of 40 months (range 36.83-43.17).Breast cancer specific survival and distant metastases rates were different among breast cancer subtypes (both outcomes P= 0.001) , there was significant difference regarding local relapse rates (P= 0.002). Axillary nodes status (P= 0.007), adjuvant therapy (P= <0.001) and breast cancer subtypes resulted prognostic factors of breast cancer specific survival; axillary node status (P= 0.007) and breast cancer subtypes had an impact on distant metastases. **Conclusions**: In our study, breast cancer subtype seems a prognostic factor of breast cancer specific survival and distant metastases rates & of local relapse rate. Patients could be submitted to conservative surgery, if feasible, but considering the differences in survivals, patients with worse prognosis should receive more aggressive adjuvant treatment.

The role of age at menarche and at menopause on breast cancer risk: a hospital based study from eastern India

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Background: In the general population, breast cancer risk is related to several reproductive factors. Specifically, risk increases with early age at menarche and late age at menopause. Our aim was to establish a relationship between early menarche and late menopause with the Bengali women of Eastern India. **Material and methods:** A hospital based case-control study was conducted among breast cancer patients during Aug 2010 to October 2012. 231 female breast cancer patients were selected from the Oncology Unit of NetajiSubhash Chandra Bose Cancer Research Institute (NCRI), Kolkata, India. 69 healthy age matched females without any family history of any cancer and none of whom had used menopausal hormone therapy, were included in the analyses were selected for the control group. **Results:** Average age of the screened patients was 48.40±11.32 years (range: 26-77 years). The age of menarche below 13 years in 58.87% patients and above 13 years in 31.60% patients were observed.In the present study, there was a significant increase in the patients with menarche before 13 years of age ($p<0.01$, OR: 2.39; CI: 1.26-4.29) and the mean age of menarche of patients was 13.1 years. Premenopausal women had a greater risk of breast cancer than postmenopausal women of an identical age (45-53 years, $p<0{\cdot}001$). Height and obesity were independent risk factors for breast cancer among post-menopausal but not pre-menopausal women; post-menopausal women of average height (~165.3cm) had 17% higher risk of breast cancer than pre-menopausal women.The effect of menopause in women of an identical age and trends by age at menopause were stronger for ER−positive disease than for ER-negative disease ($P < 0.01$). **Conclusions:**From the study it was confirmed that early menarche increases the risk of having breast cancer. The data on early menarche suggest that early-onset regular cyclic ovarian

function is related to the increased risk of breast cancer that is associated with this category of women.Women who go through menopause later in life have an increased risk of breast cancer compared to women who go through menopause earlier.

A Paradigm Shift in Clinicopathological Profile of Carcinoma Breast Amongst North Indian Women

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Background: Survival in carcinoma breast has been linked to a variety of clinical, pathologic and molecular features viz., histologic type, grade, tumor size, lymph node metastases and hormone receptor status. Reportedly, the disease in younger women tends to be more aggressive with unfavorable biological markers. **Material and methods:** Thisprospective study was conducted on 143 cases of histologically proven carcinoma breast treated between December 2011 -January 2016 in Jawaharlal Nehru Medical College, A.M.U., Aligarh. Data was collected regarding clinical profile including parity, histological type, grade and hormone receptor status of tumors. **Results:** Mean age of patients was 46.4±11.8 years. Majority of patients were between 31-50 years of age (58.8%), with a substantial number of patients (40.6%) being below 40 years of age. The disease was most common in multiparous (90.9%) and pre-menopausal women (58.0%). Most patients had LABC i.e., Stage III (44.1%); of these maximum (50.8%) were in stage IIIA followed by stage IIIB (47.6%). Infiltrating/invasive ductal carcinomas not otherwise specified were the most common type of tumor (90.2%). Tumors with HER-2/neu overexpression were the most common subtype (32.9%), followed by Triple negative tumors (28.7%%), and Luminal A (24.5%). Amongstpatients ≤40 years of age, HER-2/neu overexpression (40.0%%) were most common type of tumor, followed by Luminal A subtype (26.7%%), and and Triple negative tumors (20.0%). A statistically significant relationship was observed between age and tumor stage (p=0.003) with a higher frequency of advanced carcinoma being observed in women >40 years of age (48.4%) compared to those younger (46.8%) However, no significant relationship was observed between tumor grade (p=0.141) and age. No significant relationship was observed between either tumor stage (p=0.165) or grade (p=0.051) with menopausal status. No association was found between age and ER positivity (p=0.603),PR positivity (p=0.176) or HER-2/neu receptor status (p=0.649). No significant association was observed between hormone receptor based subtypes of carcinoma breast and either age (p=0.447) or parity (p=0.380) or menopausal status (p=0.486). No significant association was observed betweeneither stage of breast carcinoma and ER/PR status (p=0.154) or between lymph node metastasis and ER/PR status (p=0.092) or HER-2/neu positivity (p=0.714). **Conclusion:** Breast cancer is more common in multiparous as well as premenopausal women. Women older than 40 years havea higher frequency of advanced carcinoma. There is no association between either stage of breast carcinoma or lymph node metastasis with ER/PR status or HER-2/neu positivity

Sentinel lymph node biopsy in node negative early breast cancer patients with Methylene blue dye only method- A Preliminary Experience

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Introduction: The combination of both isosulphan blue and the radioactive sulphur colloid gives the best result and is the standard procedure for performing Sentinel lymph node biopsy (SLNB) in node negative early breast cancer to stage the axilla. Isosulphan blue is costly and nuclear medicine facility is not widely available. An affordable, equally efficient alternative could be the use of methylene blue dye alone for doing SLNB. **Materials and Methods:** Of the 56 node negative early breast cancer patients included in the study, 24 were subjected to the combination method of methylene blue and radioactive sulphur colloid and 32 to methylene blue only for carrying out SLNB. All the patients were subjected to axillary lymph node dissection (ALND) following SLNB. Median follow up of the patients were 2.3 years. **Results:** Sentinel lymph nodes were identified in all the 56 patients. Five and 8 patients were SLNB positive for malignancy in combination method and blue dye only method respectively. One patient from the combination method with a negative SLNB report was positive on ALND. All other results were concurrent. Sensitivity and specificity of the blue dye only method was100% and combination method was 83.3% and 100% respectively. None of the patients had any major complications pertaining to methylene blue dye injection. On a median follow up of 2.3 years, none had axillary recurrence. However, 2 patients had recurrence at the breast scar site. **Conclusion:** The results of methylene blue dye alone are comparable to the combination method for SLNB. When nuclear medicine facilities are not available, the use of blue dye alone could be justified to carry out SLNB to avoid ALND when not necessary. However, this needs validation by further studies in large numbers.

Possible role of GPNMB in patients with breast cancer

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Introduction: Glycoprotein non-metastatic B (GPNMB) is a type I transmembrane protein, which is isolated from differential expression assay using metastatic melanoma cells. The physiological function is very little known but may be supposed to be associated with cell invasion and motility particularly in breast cancer cells. **Objectives:** Here we investigated the role of GPNMB in breast cancer. **Material and Methods:** We checked expression of GPNMB by RT-PCR,western blot and immunohistochemistry in several cancer cell lines followed by establishment of GPNMB measurement by ELISA.Next we evaluated serum GPNMB in patients with breast [n=164; primary 119, metastatic 43), gastric (n=38), and colorectal (n=50) cancer in our institute from 2011.9-2014.2. We further investigated relationship between GPNMP and HER2 *in vitro*. **Results:** GPMNB expressed in breast (5/6:83%), gastric (3/6:50%), colon (1/7:14.3%) cancer cell lines. Of breast cancer cell lines, GPNMB was highly expressed in SK-BR3 (HER2 positive), BT474 (HER2/ER positive), MDA-MB-157 (Triple negative) cells. Shed GPNMB in culture medium was measurable and correlated with expression of each cell lineby colorectal cancer patients (p=0.018). Of breast cancer patients, GPNMB for HER2-type patients was higher than those for Luminal type and DCIS patients (p=0.0386, p=0.0195, respectively). Those for triple negative patients was also higher than those for DCIS patients (p=0.0459). Blockage of GPNMB induced not only HER2 but also EGFR expression. On the other hand, inhibition of HER2 by trastuzumab (Tra) increased expression of GPNMB. Depletion of GPNMB increased sensitivity of Tra, suggesting that GPNMB may play an important role in crosstalk of signal transduction for breast cancer. **Conclusions:** BPNMB may work as a novel therapeutic strategy to overcome HER2 positive breast cancer.

Characteristics of Benign and Malignant Breast Masses on Shear Wave Elastography

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Introduction: Shear wave elastography (SWE) is a novel technique of ultrasound used to characterize breast masses based on tissue stiffness. **Objective:** To identify the most useful SWE parameter in characterising the breast masses and illustrate the SWE patterns of benign and malignant breast masses. **Methods:** Ethics clearance from the Institute committee was taken and an informed written consent was obtained from participants. Patients with suspected breast masses were studied. A detailed history was obtained and a

physical examination followed by B mode Ultrasound (US) of the breast was performed. Appropriate Breast Imaging Reporting and Data System (BI-RADS) category was assigned to each mass. SWE was performed on BI-RADS 3 and 4 masses. Qualitative (Ecolor, Eshape, Ehomogeneity) and quantitative SWE parameters (Emax, Emin, Emean, Eratio) were recorded. Ultrasound guided core biopsy of the mass was performed and results were correlated with the SWE parameters. **Results:** One hundred and nineteen patients with a single breast mass each and of mean age 42.3+ 13.6 years, were enrolled. Those diagnosed with malignant breast mass (MM) were older (48.8±11.9 years), had larger sized mass (mean 2.9±1.32 cm) with shorter duration of symptoms (4+2.2months) as compared to patients having a benign mass(BM), whowere of mean age 35.2+11.7 years, had mean mass size of 2.5+1.5cm and longer duration of symptoms (7.2+6.4 months, p 0.001). On histopathology, 57 were BM and 62 MM. SWE characteristics of the two categories of masses were significantly different. BM were oval (50.8%), homogenous (66.7%) and blue in color (77.1%) while MM were irregular (93.6%), inhomogenous (92.1%) and red/orange (90.5%) in color. Best differentiating qualitative parameter was Ecolor [specificity 84.2% and sensitivity 91.9%, p 0.001) Elasticity of BM were low (Emax=72.6+/-60.6 kPa, Emean=47.9+/-44 kPa, Emin=28.5+/-33.4 kPa) while that of MM were significantly higher (Emax=215+/-64.1 kPa, Emean=163+/-51.6 kPa, Emin=99+/-48.7 kPa, p 0.001). E ratio was also higher for MM (14.7+/-8 vs 5.8+/-5.1, p 0.001). Emax (cut-off of 140kPa) and Emean (cut-off of 102kPa) emerged as the best quantitative parameters. **Conclusion:** Patients with benign and malignant breast masses have distinct demographic profile and SWE characteristics. Various qualitative and quantitative SWE parameters prove useful in characterization of breast masses

Keywords: Breast masses, Shear wave elastography, ultrasound guided biopsy

Assessment of response to Neo-adjuvant Chemotherapy in Breast Carcinoma using Shear Wave Elastography _ Pilot work

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Introduction: Pre-operative neo-adjuvant chemotherapy (NACT) has become a standard of care even in operable breast cancers (Br Ca). NACT response assessment in Br Cainvolves clinical examination and imaging (conventional and functional).Shear wave elastography (SWE)is a novel technique which has the potential to assess NACT response in Br Ca. **Objectives:** To evaluate post NACT response in patients of Br Ca using SWE. **Materials and Methods:** Histopathologically proven Br Ca patients listed for NACT in the form of FEC (5 Fluorouracil, Epirubicin and Cyclophosphamide), were studied. Their clinical history, general & breast examination findings were recorded.SWE of the breast mass was done prior to the start of NACT (baseline) and post NACT (within one week after receiving each cycle of NACT).SWE qualitative features of shape(Eshape), homogeneity(Ehomo),color (Ecolor)as well as the quantitative parameters of tissue stiffness - maximum(Emax),minimum(Emin),mean(Emean) and ratio(Erat) were evaluated.SWE results were correlated with NACT response assessed by B mode ultrasound based on RECIST criteria (gold standard). **Results**: Four patients with four breast masseswere evaluated. Two masses showed partial response (PR) denoted by reduction in longest dimension (>30% reduction each). With regard to their other baseline qualitative SWE parameters of Ecolor- red and E shape-irregular , and Ehomo- heterogeneous, a change was noted following NACT. The E shape- remained irregular but the homogeneity and color changed to reasonably homogenousand green color respectively in one mass while the second mass showed changed Ecolor to light blue indicating softness (response)of the tissue. Two tumors in the other two patients depictedstable disease(SD),denoted by<30% reduction in longest dimension. The baseline qualitative SWE parameters of both the masses were E shape-irregular), E homo- heterogeneous and E color-red. Post NACT, these qualitative parameters remainedunchanged in both. The quantitative changes (table 1) depict 60-70% drop in the stiffness values of masses showing PR whereas it was10-20%drop in masses showing SD. The drop in stiffness is visibly larger in patients with PR, than in patients with SD. **Conclusion:** SWE is a promising technique for assessment of response to NACT in patients with breast carcinoma. Large prospective studies need to be undertaken for further validation of results.

Keywords: Breast carcinoma, Shear wave elastography, Neo-adjuvant chemotherapy

Surgical management of breast cancer patients under local anaesthesia : Surgeon's perspective

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Introduction: Along with breast cancer, some patients presented with some coexisting diseases and consultant have to face difficulties to treat such kind of patients.Despite advances in anaesestetictechniques, some patients have relative or absolute contraindications to general anaesthesia. We describe a safe and simple technique for the performance of simple mastectomy or breast conservative surgery under local anaesthesia allowing the patient to receive optimum treatment. **Objective :**The aim of the study was to assess the feasibility of local anaesthesia in breast cancer surgery in those patients who are unfit for general anaesthesia. **Materials &Methods:** All diagnosed breast cancer patients from the year 2008 to 2015 were assessed physically and then relevant investigations were done. Patients who were declared as unfit by anaesthesistsor not willing to go for operation under general anaesthesia due to significant risks described by anaesthesists, offered operation under local anaesthesia. Proper counseling of the patient done to reduce anxiety and to build confidence. Day before operation patient was allowed to take anxiolytic drug at night. Before starting operation both narcotic and non narcotic analgesics was given through parenteral route. During procedure 2% Lidocaine HCL USP with 0.0005% Epinephrine USP was used. **Results :**Total 11 cases under went breast cancer surgery from the period between 2008 to 2015. Among the patients six underwent lumpectomy and 5 mastectomy. Axillary dissection was done in 5 patients out of 11. In all patients the method was successful in producing adequate anaesthesia and allowed the performance of the surgery without significant deviations from usual technique. All the patients were between the age of 52 to 77 years; the average age of patients was 64.72years.The tumour stage was : T1 (01) & T2 (10). The total volume of Lidocaine required for surgery was less than 7.0mg/kg. Surgery were completed under local anaesthesia in all patients, that means no patients require conversion from local to general anaesthesia. The time taken for the performance of the procedure (anaesthesia plus Surgery) was no longer than conventional general anaesthesia plus surgery and the average time was 62.7 minutes (range 30 to 90 minutes). Per operative blood loss was low in all patients and collection from drain tube did not exceed more than 300ml in any patients. There was no surgical haematomas of the resected site, which would require needle drainage. There was also no surgical morbidity in terms of wound infections, necrosis of skin flaps and no side effects of lidocaine. **Conclusions:** As because surgery plays main and important role in the management of breast cancer patients and it can be feasible by local anaesthesia even the patient have significant co-morbidities. So, it is necessary to do more practice in patients who are not fit for general anaesthesia and thereby establish the precise criteria and determine the efficacy as well as tolerability.

Surgical management of the axilla in women with operable breast carcinoma: A protocol based approach from a tertiary centre in India.

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Background: Although well established protocols exist to address the axilla in the West, there is a dearth of evidence from the Indian Subcontinent.

This study evaluates the management of axilla in a protocol based approach in accordance with accepted guidelines. **Methods:** Aprospective cohort of 227 women, with either EBC or LABC after neo adjuvant chemotherapy (NACT), was studied. Axillary ultrasound (AUS) and guided FNAC/biopsy, SLNB, low axillary sampling (LAS) and ALND were used in a systematic way to address the axilla and adjuvant therapy was given where indicated. **Results:** AUS guided FNAC identified 80 patients (35.24%) suitable for ALND without SLNB. AUS had a sensitivity and overall accuracy of 81.4% and 77.2%. 147 SLNBs were performed with 73 in EBC and 74 in LABC post NACT, with identification rates of 93.15% and 82.43% respectively. 40 had positive sentinel nodes and underwent ALND. 18 patients without sentinel nodes identified, underwent LAS which yielded positive nodes in 5 and no nodes in 2 patients and were subjected to ALND. 81 patients had positive nodes on ALND with 58% of positive nodes confined to level I only. The incidence of seroma in axilla was 36.2% with a mean increase in upper limb volume of 64 ml at 3 months.With a median follow up of 18 months 3 axillary recurrences occurred in patients with a negative SLNB (3.3%) **Conclusion:** This study shows that well established guidelines to address the axilla can be incorporated into clinical practice in developing countries like India.

Keywords: Axilla, AUS, SLNB, ALND.

Platinum in Triple negative carcinoma breast . A study from Indian Subcontinent

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Introduction: Standard treatment of locally advanced cervical carcinoma (CC) is actually represented by concomitant chemoradiotherapy followed by brachytherapy. However, in spite of good local control rates after treatment, local and regional relapses still a major cause of failure treatment.). We performed study to evaluate whether (Cisplatin) CDDP-based doublet therapy improves survival compared to weekly CDDP plus RT (Radiotherapy) in these patients. **Methods and Materials**: From 1 January 2011 to 31 December 2013 we prospectively selected series of consecutive 40 patients with clinical stage II -III carcinoma Uterine Cervix . Primary and secondary objectives included the rate of response , safety, predictive factors of relapse , overall survival and progression free survival. Patients received 2 cycles of neoadjuvant Paclitaxel (175 mg/m^2) and Cisplatin (75 mg/m^2) once 3 weekly. All patients underwent Radiotherapy external beam and bachytherapy . Then another 4 cycles of CDDP- doublet combination.. They were followed up till June 2014 in our Oncology unit at Sri Ramachandra University and Hospital. **Results:** Progressions occurred in 2 patients (5 %) with an average of three months as they defaulted treatment. Recurrences occurred in 5 patients (12.5%) with an average of 15 months. The overall treatment failure rate was 17.5%. Thirty-two (82.5%) of treated patients were in good locoregional control with a median follow of 24 months (36-8). **Conclusion:** Relapses of cervical cancer have a poor prognosis and long-term survival remains very poor. The suitable treatment of the primary disease, respecting essentially therapeutic times, is one guarantee of a good prognosis.Paclitaxol when added to first-line chemotherapy,for locally advanced CC, concurrent RT and with CDDP-based doublet chemotherapysignificantly has now been shown to improve overall survival among women ,it is **s**afe and effective for more then 80 % patients with locally advanced disease treated with curative intent in a developing country. The addition of Taxol to established therapies for locally advanced cervical cancer is an area of evolving research and a potential strategy toward improving historically suboptimal outcomes for women with advanced disease.

Use of Cisplatinum in Triple negative carcinoma breast . A study from Indian Subcontinent

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Introduction: There is no effective clinical therapy yet for triple-negative breast cancer (TNBC) and this subtype have a poor prognosis due to inherent aggressiveness and the lack of targeted therapeutics.Our hypothesis of a better OS among platinum treated TNBC patients compared to conventionally managed TNBC patients. **Objectives:** The progression free survival and over all survival with use of Platinum for all cases of triple negative breast cancer. **Material and Methods:** Methods and Materials: From 1 January 2011 to 31 December 2014 we prospectively selected series of consecutive 50 patients with clinical stage II-III operable carcinoma breast TNBC . Primary and secondary objectives included the rate of response , safety, predictive factors of relapse , overall survival and progression free survival. All patients underwent surgery . Patients received 4 cycles of adjuvant anthracyclin and cyclophosphamide post Radical Mastectomy and axillary dissection. Then another 4 cycles of Paclitaxel (175 mg/m^2) and Cisplatin (75 mg/m^2) 3 weekly. They were subjected to Chest wall radiation and drainage areas based on the high risk features. They were followed up till December 2015. **Results:** 50 patients with a median age of 55 years were analyzed. Stage II was diagnosed in 35 % of patients and 65 % had stage 3. Forty-five patients (90 %) completed study treatment and 80.6 % received at least 6 treatment cycles. No patients developed any grade 4 toxicity. 35 patients(70 %) are live and in remission as on the date of followup . Median Overall survival 24 months. 10 patients had progression and relapse due to treatment delays, younger age and incomplete treatment. **Conclusions:**The 4 drug combination therapy with a platinum incorporated in adjuvant therapy is effective and safe, offering a high 70 % survival rate in TNBC. This study suggests a modest benefit of adding Platinum in TNBC. More importantly, this trial design is feasible and lays the foundation for additional studies for this treatment-refractory disease.

Role Of Post Mastectomy Radiotherapy In T1,T2 Lesions With 1-3 Positive Axillary Lymph Nodes - A Retrospective study of 101 Cases.

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Introduction: Post mastectomy radiotherapy (PMRT) reduces loco-regional recurrence (LRR) and improves overall survival [1], [2] and [3]. There is international consensus to recommend PMRT for patients with tumour size ≥5 cm (T3), tumour invasion of the skin, pectoral muscle or chest wall (T4) and patients with ≥4 positive lymph nodes (LN) [4], [5] and [6]. However, the role of PMRT for patients withT1 ,2 disease with 1–3 positive LN is still controversial. The side effects of radiotherapy and its associated morbidity have to be considered in the risk benefit ratio , thus difficult to arrive at consensus in early breast cancer.In a developing country like India, factors such as patient education, level of awareness, financial aspect, long term follow up, limitation of resources have to be balanced and tailored according to the indication and need of the patient. **Objectives**: 1.Empirically explore whether it is advisable to carry out radiation when there are 1-3 nodes. 2..Whether Perinodal extention in this subgroup is an important parameter to consider for radiotherapy. **Material and Methods:** We collected data after approval from our institutional board review committee and analysed case files of patients who presented and were treated at our governmental tertiary referral centre from a period between 2007-2012.Of the 691 patients who underwent mastectomy, we short listed 101 cases for our study who fulfilled our basic inclusion criteria of T1,2 N1 on final histopathology. The inclusion criteria for this analysis were: (1) Female patients with unilateral breast cancer and no distant metastasis at initial diagnosis who underwent mastectomy and axillary lymph node dissection; (2) postoperative pathology indicated T1–2 and 1–3 positive axillary lymph nodes (T1–2N1M0) disease, at least 10 lymph nodes removed by axillary dissection; (3) complete surgical resection of the tumor and negative margins; (4) complete estrogen receptor (ER), progesterone receptor (PR) and human epithelial growth factor receptor family 2 (Her2) status; (5) No neoadjuvant chemotherapy was administered before surgery and endocrine therapy was performed based on the hormone receptor status. In order to study the research questions, we formulated hypotheses as follows,1. Radiotherapy does not have any impact on recurrence post mastectomy.2. There is no influence of Peri nodal extention on recurrence. The above hypotheses were tested using chi-square test. **Results:** On applying chi

square test we found out the observed and the expected value Radiotherapy was given in 60 patients and 41 were not given .Recurrences were obtained in 9 amongst radiotherapy and without radiotherapy in 16.When chi square was appliedwith 1 degree of freedom , the value was highly significant at 0.006 with 99% CI.Hence our hypothesis was rejected. Also in case of PNE with recurrence and radiotherapy,8 had PNE with radiotherapy and recurrence and 27 had no recurrence,on computation degree of freedom was 3 and p value was 0.013% hence highly significant. **Conclusions:** Radiotherapy should be strongly considered in patients with 1-3 nodes post mastectomy as it decreases the chances of recurrence and also if PNE is present chances of recurrence are increased , hence radiotherapy be considered.

The relationship between the polymorphisms of -2548 G/A of leptin Gene, Q223R, K109R of leptin receptor gene and risk of Breast Cancer in a cohort of sporadic breast cancer patients in Sri Lanka.

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Background: Currently breast cancer is the most common cancer in Sri Lankan women with a cumulative incidence rate of 2.456%. Several epidemiological studies have reported that obesity is a major risk factor for sporadic breast cancer. Obesity is associated with increased plasma leptin levels. Potential association of circulating leptin, LEP gene and LEPR gene polymorphisms with breast cancer have been proposed but are inconsistent. We have previously reported that circulating leptin level are significantly higher in sporadic breast cancer when compared to age and Body Mass Index (BMI) matched controls. To determine the effect of the polymorphisms of leptin gene (LEP)-2548 G/A (rs7799039), leptin receptor (LEPR) gene Q223R (rs1137101) and K109R (rs1137100) on the breast cancer susceptibly in sporadic breast cancer patients in Sri Lanka. **Method:** Here we investigated genetic variations in LEP gene (-2548 G/A) and LEPR gene (Q223R, K109R) in 80 matched pairs of newly diagnosed unilateral sporadic breast cancer women and healthy controls matched for age and BMI. Blood samples from patients were collected before or a few days after surgery but before commencement of chemotherapy / radiotherapy from breast clinics or in wards of National Cancer Institute Maharagama, Sri Lanka. Controls had no personal or family history of breast cancer or any other cancer, and no clinical evidence of breast cancer. From collected blood samples DNA were extracted by manual method. Further, diluted DNA samples were amplified with target specific PCR primers designed in-house and the amplified products were purified using Wizard® SV Gel and PCR cleanup system. Genotyping was performed by ABI PRISM® SNaPshot™ Multiplex assay with in-house designed SNaPshot primers. Sizing and genotyping data generated using ABI 3500 DX instrument was further analyzed and confirmed with GeneMapper® v4.1software of Applied Biosystems®. Genotype distributions were compared using Mc Nemar's test. **Results:** Mc Nemar Chi square values (Odd Ratio) for -2548G/A, Q223R, K109R genotypes were 0.25(3) P=0.617, 3.368(.357) P=0.0665, 14.049(4.125) P=0.002 respectively. **Conclusion:** LEPR gene K109R showed an extremely significant association with sporadic breast cancer whereas LEPR gene Q223R polymorphism and -2548 G/A LEP gene polymorphism had no effect.

Supported by National Research Council Grant NRC 11-018

Level III axillary lymph node dissection in carcinoma breast

Arpan Chaturmohta

As the trend is towards conservative surgery for the breast carcinoma, the necessity of the complete axillary dissection is being questioned much more today. In this study,we have aimed to analyze the frequency of level III lymph node metastases, contributing risk factors and recurrence rate after complete axillary dissection. This is a retrospective study. Hundred and four female,histopathologically proven breast carcinoma patients underwent modified radical mastectomy and complete axillary dissection in the Department of Surgical Oncology,GCRI, ahmedabad are included in the study.Age, menopausal status, tumor location, histopathologicaltype,grade, pathological T and N stage, estrogen (ER) and progesterone (PR) receptor status, multicentricity, total metastatic lymph nodes in level I+II, lymph node capsule invasion are analyzed as the risk factors. Their relationship is studied with level III lymph node metastasis and recurrence rate and incidence of arm edema after complete axillary dissection was analyzed.

Adenomyoepithelioma- a rare breast neoplasm – case study of two cases

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Background: Adenomyoepithelioma of the breast is a rare benign breast neoplasm characterized by biphasic proliferation of epithelial cell(luminal cell) and myoepithelial cell. Histopathologic heterogeneity is quite common in these tumors and recognition of adenomyoepithelioma is challenging. The knowledge of heterogeneity in the various patterns of adenomyoepithelioma in combination with immunohistochemistry(IHC) , always allows the correct diagnosis of adenomyoepithelioma. Total surgical excision with clear margins is the treatment of choice. If incomplete excision is done, local recurrences are common and may present with more aggressive behavior and hematogenous spread. Therecognizationof the various patterns of adenomyoepithelioma and use of IHC in making the correct diagnosis to incorporate the correct treatment for the patient is very necessary. **Material And Method:** We describe the two patients with breast lump. A 40 yr old female patient, excision of lump was done. Another 63 yr old female patient, trucut biopsy was done and specimen was received in the Department of pathology, IMS, BHU. The tissue was processed and blocks were made. Hematoxylin and eosin (H& E) stain was done on the slides. IHC was performed on the selected blocks. **Result:** The histopathological features showed a biphasic tumor comprised of tubules having inner columnar to cuboidal epithelial cell sorrunded by clear cells of myoepithelial origin. No cytological atypia was noted. IHC was performed. The luminal cells were positive for epithelial membrane antigen(EMA) showed strong cytoplasmic and membranous positivity. The myoepithelial cells were highlighted by smooth muscle actin (SMA). **Conclusion:** Adenomyoepithelioma is a rare benign entity of breast and the diagnosis of adenomyoepithelioma is solely depends upon the ability of pathologist to recognize the varying histopathological patterns in combination with IHC for epithelial and myoepithelial component.

Keywords: Adenomyoepithelioma, Immunohistochemistry(IHC)

Adenolipoma of The Breast : A Clinicoradiological Entity And Pathologist

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Introduction: Breast hamartoma are benign lesion composed of variety of normnal breast components arranged in disorganized manner. These are rare and described as adenolipoma, fibrolipoma,adenifibrolipom etc. clinically these present as painless well circumscribed , mobile lumps of breast. Incidence and etiology remain obscure due to its rarity. These have been described in women in their fourties or fifties. Mammographically they appear non homogenous mass with circumscribed fatty masses. Histologically they appear as circumscribed masses with variable amount of fat,fibrous and glandular tissue. Here we are presenting adenolipopma developing in preexisting

fibroadenoma in a 29-year-old women with review of literature.Case report A 29 year unmarried premenopausal lady presented to Rajeev Gandhi cancer institute with self detected pain less lump breast of 4 year duration with clinical diagnosis of fibroadenoma. She noticed sudden enlargement in size for last 6 month. On physical examination a firm, rounded, mobile lump of 8*9 cm size of with defined margin at upper outer quadrant of left breast. No palpable axillary lymphadenopathy on left side. Contra lateral breast and axilla unremarkable. On evaluation MR mammogram showing a huge 9.8*9.1*5.8 cm well circumscribed fatty mass predominantly in outer quadrants with enhancing thickened septae and small irregular soft tissue component showing type 1 (persistent) kinetics suggestive of hamartoma. Her trucut biopsy from lump showing stromal and adipose tissue hyperplasia. Stromal tissue composed of spindle cells in collegenousstroma with no evidence of nuclear atypia or mitosis suggestive of benign phylloides tumor.She underwent lumpectomy though axillary route in view of scar. Specimen on gross appearance showing encapsulated yellow soft measuring 9*9 cm. on pathological examination on cut section a solid homogenous and lobulated mass with white streaks throughout. On miocroscopic examination well circumscribed with psuedocapsuelesion composed of mature adipose tissue , breast duct and lobules surrounded by fibro collegenous tissue. Features suggestive of a hamartomatous lesion adenolipoma. **Discussion:** Hamartomas were first described in 1971 by Arrigoni*et al* in a study of 10 patients whose breast tumors clinically and grossly resembled fibroadenomas. The majority of these lesions occur in females >35 years old. At clinical examination, hamartomas are usually occult, but they may manifest as large, mobile, soft to firm masses .Tumors as large as 17 cm have been reported . Breast hamartomas have become more frequently diagnosed due to the increased use of mammography, but they may be mistaken for neoplasms.ss Breast hamartomas are rare benign lesions that are composedof varying amounts of glandular, fibrous, adipose and smoothmuscle tissue. They are reported to have an incidenceof 0.1-0.7. It is known that hamartomasresult more from improper development in the organ ratherthan from tumorous process.The most characteristic histological feature of hamartomas is thepresence of lobules within a fibrotic stromacoincidental malignancy, very rarely, can occur in mammary hamartomas.However, it is still not clear whether malignant lesion derivesfrom the hamartoma itself, or is an incidental finding, that initiatesgrowing nearby and extends into the hamartoma afterwards. Surgical removal is the curative method for breast hamartomas.If there is a coincidental epithelial malignancy in the lesion, there is a potential for recurrence . Excision and histological examination is necessary for a differential diagnosis and also for any epithelial lesions of the hamartoma. Fibroadenomas are benign fibroepithelial neoplasms of the breastcomposed of both stromal and epithelial components.Association of fibroadenoma and hamartomamay be due to either hormonal imbalances and/or developmentalabnormalities. Ourpatient did not have any additional treatment after surgical excision.

A Rare Case of Matrix producing Heterologous Metaplastic Breast Carcinoma- Masquerading as Benign Mass on Mammography

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Introduction: Mammography is an established screening tool for detecting breast cancer. Benign and malignant masses can be reasonably differentiated on mammography. However the morphological characterisation of abnormalities on mammography is not always specific and it is imperative to understand this limitation to avoid erroneous diagnoses. Malignant matrix forming tumors, which can be primary extraskeletal or metaplastic carcinomas are exceedingly rare in the breast and can be mistaken for a benign mass in the presence of calcification. It is thus important to familiarizewith this unusual, misleading entity mimicking a benign morphology on mammography and histopathology clinching the diagnosis. **Materials and Methods/Results:** A 32 year female was referred to our mammography unit with complaints of painless lump in the right breast for two years. Bilateral mammography revealed a heterogeneously dense breast with a round, circumscribed mass in the retroareolar region of the right breast showing extensive, coarse calcifications, with no skin or nipple changes. These chunkycalcifications were thought to represent benign popcorn calcifications associated with an involuting fibrodenoma and a BIRADS 2 category was assigned.Patient returned one year later with marked increasein size of the lump and an excision biopsy was performed. Histopathology revealed features of carcinoma with areas of chondro-osseous differentiation, as well as areas of cartilage and bone formation and malignant spindle cell component. Overall features suggested heterologous metaplastic carcinoma with matrix production. Limited literature is available on the clinical presentation, imaging and management of the metaplastic matrix producing tumors of the breast. Theseslow growing metaplastic tumors with extensive matrix mineralisation as in this case, can be misleading and lead to a delay in diagnosis and wrong management.It may be wise to consider this diagnosis when the finding of dense and bizarre nature of the calcificationsare encountered in a breast mass on mammography which could also be an outcome of matrix production by the malignant tumor. **Conclusion**: Heterologous metaplastic matrix forming breast carcinoma is a rare entity. It should be suspected when a mass with a dense, extensive calcification is detected on mammography and the final diagnosis is confirmed on histopathology.

Axillary Ultrasound in - an alternative for Sentinel Lymph node Biopsy?

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Axillary lymph node status is the single most important prognostic factor in breast cancer and therefore accurate of staging of axilla is of paramount importance. Sentinel lymph node biopsy (SLNB) represents the standard of care to accurately stage the axilla. If we can find alternative non-invasive methods to stage axilla then patients can be spared of staged procedures of SLNB. We determined the accuracy of clinical examination & ultrasonography in predicting axillary lymph node metastases pre-operatively by correlating them with histopathological results in breast cancer patients undergoing Modified Radical Mastectomy. **Methods:** 40 patients with proven breast malignancy were prospectively studied. They underwent clinical and sonographic assessment of ipsilateral axilla and their accuracy were determined by comparing with final Pathological results (HPR). **Results:**USG had a higher sensitivity, specificity, positive predictive value and negative predictive value as compared to clinical exam alone. CE+USG had a 100% sensitivity and npv in premenopausal age which was higher than in postmenopausal age group. False negative rate in our study was 2.5%. **Conclusion:** USG added significantly to CE in predicting metastatic axillary lymph nodes pre-operatively in breast cancer patients.The results can be further improved by adding USG-guided FNAC and increasing the frequency to >12 MHz Therefore High resolution USG with USG-guided FNAC could obviate the need for SLNB as a tool for axillary staging in breast cancer patients with no palpable axillary lymphadenopathy.

Accuracy of CE and USG (Overall)

Parameters	CE	USG	P value
Sensitivity	90.9	95.45	<0.001
Specificity	44.44	89	0.01
PPV	66.7	91.30	<0.001
NPV	80	94.11	<0.01

Development and validation of a broadly distributed IHC based test for optimal treatment planning for Stage 1 and 2 IDC of breast patients: Beyond ER, PR, Her2 and Ki67

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Introduction:'Breast Cancer' recurrence risk in early stage patients is currently assessed using clinical parameters and biomarker based tests including Oncotype DX and MammaPrint. Such tests are useful but insufficient as they apply only to a limited set of node negative patients and are largely prognostic with restricted chemopredictivity. Additionally these tests are also prohibitively expensive for patients in India and SE Asia.There is an unmet need for a broadly distributed, cost-effective and'predictive' test which will: i) Accurately estimate the 'risk of recurrence' and enable optimum treatment planning for a broader set of patients ii) Offer new 'targeted drugs'. **Objectives:** Molecularly defined tests based on signaling pathways other than proliferative/hormone dependent pathways (viz: ER/PR/Her-2-neu) would be of tremendous help in finding 'predictive biomarkers' which are indicative of not only risk of recurrence, response to chemotherapy but helpful in development of new targeted drugs.In specific, our approach is to develop test based 'predictive/targetable' biomarkers to overcome the limitations of the existing tests by being useful for assessing risk of recurrences and offer targeted therapy. 1) To develop and validate a test based on 'predictive biomarkers' for ER+/PR+/Her2-or+ breast cancer patients in Stage 1 & 2 to assess risk of recurrence and usefulness of chemotherapy. 2) License the 'predictive biomarkers technology' to a Pharma to develop new drugs. **Material and Methods:** ~40 key biomarkers from multiple molecular pathways critical in pathogenesis of Breast Cancer including apoptosis, self-renewal, angiogenesis selected from literature review were analyzed by IHC on a training set comprising 400 samples as a retrospective study. Inclusion criteria: IDC, Stages I-IIIc Age <74, ER+/PR+, Her2+/-, with minimum 5-year follow up and known clinical outcome. Oncopathologists graded the slides for percentage of tumor stained and staining intensity. The IHC data was analyzed using a Statistical model developed using SVM based method, which is a robust predictor of outcome. The "OncoStem Score" that was developed stratifies patients into low or high-risk for recurrence based on a combination of 6 best biomarkers. **Results:** As per EGAPP recommendations the robustness of our assay was first confirmed in analytical validation experiments by comparing Inter-pathologist, Inter-operator, Inter- tumor block and Inter-laboratory site variation. While minor changes in 'OncoStem Scores' were observed, none of the variables tested had any effect on the 'outcome prediction/accuracy' of risk stratification. Importantly, when comparing Inter-pathologist variation, the Intra-class correlation (ICC) is 0.933, indicating almost perfect correlation between both Pathologists' scoring patterns.Retrospective clinical validation on additional 450 cases shows 90% accuracy in predicting risk of distant recurrence in breast cancer patients with Stage 1, 2 & 3A with ER+/PR+/Her2- or + disease. The NPV of the test is 95%. We also analyzed the 'Stage and grade' distribution of low risk patients predicted correctly. Overall ~60% and 33% patients classified as 'low risk' belonged to Stage 2 and 3 respectively. Majority patients in 'low risk' had Grade 2 and 3 disease over Grade 1. We found no correlation between the OncoStem Score and Ki67 expression. Interestingly, a small head-to-head study (N=35) shows that the OncoStem assay is superior in predicting outcome compared with Oncotype Dx. **Conclusions:** We have developed a robust IHC based 'prognostic and predictive' cost effective and 'broadly distributed' test- more suitable for Stage 1&2 patients in India and SE Asia. Our test will spare many node positive patients from excessive chemotherapy and will offer targeted drugs in future to high risk individuals in a highly cost effective manner.

Involvement of CD44 and associated molecules in pathogenesis of Urothelial carcinoma of bladder

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Introduction: Bladder cancer is the 9th most common cancer and 13th most common cause of cancer death worldwide. The Extra-cellular matrix (ECM) acts as a physical scaffold to which cancer cells attach and migrate and thus is crucial for the regulation of cell motility, proliferation, invasion and metastasis. CD44 is a multistructural and multifunctional cell surface molecule, which is best characterized as the Hyaluronic Acid (HA) receptor, and it is involved in cellular proliferation, differentiation, migration and angiogenesis. **Objectives:** In the present study implication of CD44 variants and associated molecules (HAS1 & HAS2) has been observed in Indian patients of urothelial carcinoma of bladder (UBC). **Material and Methods:** In this study, 30 patients with urothelial carcinoma of bladder were enrolled to determine the circulatory levels of CD44, HAS1 and HAS2 in tissue lysates by ELISA. Expression of CD44, HAS1 and HAS2 was also confirmed by Immunoblotting (WB), Q-PCR and Immunohistochemistry (IHC) in tumor tissues and adjacent normal tissues. Variant specific expression of CD44 in tissues was quantified by real-time PCR. **Results:** The circulatory levels of HAS2 and CD44 were found to be elevated in patients as compared to controls. Levels of HAS2 and CD44 were also found to be significantly ($p<0.001$) higher in tissue lysates. Molecular expression of HAS2 gene was significantly ($p<0.05$) elevated in tumor tissue of patients as compared to HAS1 and positively correlated with CD44 expression. Variant analysis of CD44 showed significantly ($p<0.001$) augmented expression of Variant 3 and Variant 6 in tumor tissue as compared to adjacent normal tissue. **Conclusions:** Our study shows potential role of CD44 glycoprotein, specifically its Variant 3 and Variant 6 in the pathogenesis of UBC. In Indian cohort of UBC, HAS2 isomer is primarily involved in HA synthesis and helps in formation of extracellular matrix surrounding tumor and concurrent downstream signalling cascade mediated by CD44 receptor. Further, silencing of CD44 and/or its specific variants will broaden our understanding of CD44 mediated signalling in development of UBC.

Preferred Mode of Presentation: Poster

Prostate Cancer: Promise and Potential of Chemopreventive Strategy

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Prostate cancer (PCA) is the second most frequently diagnosed cancer and sixth leading cause of cancer death among men worldwide. The PCA mortality results from metastasis to the bone and lymph nodes, and the progression from androgen-dependent to androgen-independent PCA growth. Since advanced stage of PCA growth and development is androgen independent rendering androgen ablation therapy ineffective, control of PCA at this stage through chemoprevention and intervention is both practical and translational. This involves the use of natural or synthetic agents, either alone or in combination, to prevent the development of invasive malignancy by inhibiting early stages of carcinogenesis and suppression or reversal of pre-malignant lesions. Various studies have shown that besides many vegetables, fruits and grains, some phytochemicals from non-dietary sources also offer significant protection against several cancers. Lifestyle and dietary habits are vital factors in reducing cancer risk as evidenced by epidemiological and laboratory studies as well, since there are remarkable differences in globally human cancer incidence and mortality. In this aspect, various cancer chemopreventive agents would be superior and effective towards preventing, retarding or reversing the process of carcinogenesis. A number of these agents have shown promising results in preclinical studies while many others are in clinical trials. Details will be discussed during the presentation.

Key-words: Prostate Cancer, Cancer Chemoprevention.

Invivgensome: Intra vas deferens Lumen assembly of nanoparticle drug for Prostate Cancer Prevention

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Introduction: Prostate cancer is the most common form of cancer in the male with the incidence of the latent form going beyond 60% in the age group above 70 years. It is known that there are interchanges of products between the prostate and the material flowing along the vas deferens. Since sperms are continually being produced and flowing along the vas deferens an opportunity of intervention at the level of the prostate by means of using the sperm flow opens up. **Objectives:** The aim of the study was to evaluate the potential of vas deferens being used as a novel route for the dual modalities based targeted and localized drug delivery to prostate gland mediated by Invivgensome, a phenomenon of *in-vivo* generation of liposome by an polyelectrolytically charged polymeric implant for the treatment of Benign Prostate Hyperplasia (BPH), which is a non-cancerous growth of the epithelial as well as the stromal cells of the prostate gland. **Material and Methods:** The new drug gives a means of assembling in the vas deferens a nano particle based drug on a continual basis with one single intervention of implantation. Low molecular weight SMA combined with high molecular weight SMA and DMSO. The high molecular weight SMA is antimutagenic. Low molecular SMA will act as cleavage centers for the high molecular weight SMA and so nano particle of High molecular weight SMA produced **Results:** The drug has such a property that it targets onto the secretory epithelium of the prostate gland. Further the antimutagenic drug inhibiting the tendency of an epithelial cell from undergoing mutation and becoming cancerous form. **Conclusions:**Recent studies points to the exciting possibility of arriving at a variant of RISUG which implanted in the vas deferens releases nanoparticles which form antimutagenic liposomes. These liposomes reach the prostate and seem to have a protective action to prostatic functions with the scope of inhibiting random mutations which are one of the important causes of prostate cancer

Keywords: Styrene maleic anhydride, phospholipids, vas deferens, prostate cancer, liposome, sperm

Observational Study of Cone Beam Ct Based Interfractional Urinary Bladder Filling Variation During Igrt in Pelvic Malignancies.

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Background: One of the major factors limiting the precision of radiotherapy for pelvic malignancies is organ motion. The inter- and intra- fractional movement of the bladder can be as much as 3 cms due to changes in volume of bladder and adjacent organs. The greatest challenge for radiation oncologist is to observe and correct these intrafraction and interfraction changes, to achieve higher tumor dose homogeneity in pelvic malignancies by following strict bladder filling protocol. **Material and Methods:** All patients of pelvic malignancies undergoing IGRT (Image guided radiotherapy) with curative/ adjuvant treatment having urine holding capacity of at least half an hour were included in the study. Patient with Carcinoma urinary bladder, patients earlier having received pelvic radiotherapy and having metastatic disease were excluded from the study. This prospective study was conducted between August 2014 and January 2015. The bladder protocol was followed from the planning day and then on daily basis before treatment. The CBCT data set was fused to the original planning CT and was used to characterize the bladder each day. Bladder contouring was done on all planning CTs and treatment CBCT images by the same oncologist. The volumetric changes of the bladder were compared and its volume was measured to analyse the interfractional filling variation after bladder protocol. Total 300 CBCT was contoured in 26 patients and were compared with the planning CT to see the average bladder filling and standard deviation in transverse, anterio-posterior and longitudinal diameter. **Results:** Volume of the bladder, Transverse diameter, Anterio-posterior and Longitudinal diameter were measured in maximum dimension. The mean bladder volumes was 182 cc (range, 72–292) and SD was 110cc. The maximum movement of the bladder during treatment was seen in longitudinal dimension with mean 5.6 cm and SD was 2.08 cm (Range, 3.52-7.68) then in anterio-posterior dimension with mean 6.69 cm and SD was 1.34cm (Range, 5.35-8.03) and followed by transverse diamension with mean 8.36 and SD 1.21 (range, 7.15- 9.57). **Conclusion:** This study has basically shown that interfraction bladder movement occur even after following strict bladder protocol. Our finding are consistent with the other studies published in literature. So, we strongly recommend bladder protocol to be followed in pelvic malignancies patients.

Transmural Invasion In Patients With Rectal Cancer At Thin Section Magnetic Resonance Imaging

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Background: The extramural tumour spread is an important factor to influence the prognosis in carcinoma rectum. The preoperative therapy is very less likely to be beneficial who have minimal extramural spread in comparison to more extensive extramural spread. The modalities used in current provide little information about the relationship between the tumor and the circumferential resection margin, and they have not been shown to enable accurate measurement of the local depth of tumour spread. MR imaging has not been widely adopted for these applications. **Objective:** To evaluate the accuracy of MR imaging in illustrating the extramural depth of tumor invasion in rectal cancer patients, with the histopathologic results as standard. **Material and Methods:** Pathologically confirmed on biopsy rectal cancer patients at our institute during the period of January 2012 to July 2015 included in our study. All patients informed and written consent has been taken to involve into the study. All patients underwent MRI and maximum transmural depth has been measured and compared with standard, defined at histopathologic analysis as the distancefrom the outer edge of the longitudinal muscularispropriato the outer edge of the tumour. **Results:** Tumor EMD measurements obtained at both MR imaging and histopathologic analysis were available for 48(85%) of 56 patients after primary surgery. Mean EMDs were 3.65mm±3.60(SD) and 3.78 mm±4.08 at MR imaging and histopathologic analysis, respectively.The mean difference between the MR-derived and histopathologicallyderived EMDs was -0.09mm±3.55(95%CI-0.67mm, 0.51mm). Therefore, MR and histopathologic assessments of tumor spread were considered equivalent within 0.75mm, comparable to the results of MURCURY trial.

Keywords: Rectal cancer; transmural spread; magnetic resonance imaging

A Comparison Between Minimally Invasive and Open Esophagectomy In Cancer Esophagus

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Background: For potentially curable esophageal cancer patients, therapeutic options are varied, including primary surgical resection, surgical resection after neoadjuvant chemotherapy or chemoradiotherapy (CRT), or nonsurgical treatment using definitive CRT. Surgical resection has traditionally remained the treatment of choice for carcinoma esophagus. It can be performed by both traditional open i.e, transhiatalesophagectomy, transthoracic esophagectomy or minimally invasive methods i.e, VATS esophagectomy, laproscopictranshiatalesophagectomy. Esophagectomy is associated with high morbidity and prolonged post operative recovery periods. Minimally invasive can improve post operative outcomes. **Objectives:** To compare the post operative outcome of minimally invasive versus open esophagectomy at a regional cancer centre in south india in last two years. **Material and Methods:** From June 2013 to May 2015, 17 patients who underwent minimally invasive esophagectomy are compared to 30 patients who underwent open esophagectomy. Statistical analysis is performed using stata 11 software. **Results:** Minimally invasive as compared to open esophagectomy , took slightly longer operative time (188 minsvs 171mins; p=0.002), less blood loss (111 ml vs 241 ml; p<0.05), shorter ICU stay (4 vs 6days; p <0.05), shorter hospital stay (8 vs 11days; p<0.05), less pulmonary and cardiac complications (1/17 vs 3/30 patients; p=0.62), less anastomotis leak (2/17vs 4/30 patients; p=0.87), more lymph node yield(13vs 11; p=0.17),slightly higher R0 resection(15/17 vs 26/30 patients; p=0.87).

Keywords: carcinoma oesophagus; oesophagectomy; minimal invasive

Laparoscopic surgery for carcinoma rectum- single institution experience from India

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Introduction: Laparoscopic surgery for management of carcinoma rectum is still not widely considered the standard of care. Therefore we analyzed results of our laparoscopic surgery for carcinoma rectum. **Patients and Methods:** Retrospective analyses from prospectively maintained database of 110 patients of carcinoma rectum operated with laparoscopic approach between April 2010 and March 2015. Analyses was done for intraoperative parameters,post operative complications, morbidity and mortality, oncological outcomes and disease free survival and overall survival. **Results:** The mean blood loss was 159.90±76.48 ml and mean operating time was 3.21±0.53 hours. Mean ICU stay and day of discharge was 2.44±0.95 and 6.76±1.46 days respectively. Twenty three percent patients had post operative morbidity with only one postoperative death. Complete mesorectal excision was done in 90.9% of patients and CRM was negative in 90% of the patients. Mean lymph node harvest was 11. Twenty six (23.6%) patients were lost to followup. Thirteen (11.8%) patients had recurrence and 70 (63.6%) patients are alive. The median disease free and overall survival is 23 and 28 months respectively. Results of our study show acceptable post operative outcomes, oncological adequacy and survival. **Conclusion:** There is a learning curve associated with laparoscopic procedures. Our study shows that laparoscopic approach for management of carcinoma rectum isoncologically adequate and safe procedure.

Peri-operative Outcomes of Pancreatoduodenectomy in GCRI: A 5-Year Experience

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Background: Pancreatic cancer is one of the leading cause of cancer-related death worldwide. Surgical resection is the only curable treatment. Historically, resection of pancreas was regarded with scepticism. However, advanced knowledge and widening indications for pancreatic resections have led to greater expectations with regard to patient outcomes. The objective of this study is to examineperi-operative outcomes in patients posted for pancreatoduodenectomy (PD) in a high volume cancer centre. **Materials and Methods:** A retrospective analysis of hospital records was done on 141 patients (90 males and 51 females) who underwent PDs at Gujarat Cancer and Research Institute, Ahmedabad within 5-years period from January-2008 to January-2013. **Results:** Between January 2008 and January 2013, a total of 141 PDs were performed in our institute. The median number of PDs performed per year was 28.2%. The overall morbidity and mortality rate was 35.5% and 4.96% respectively. The most common age group affected was 50-59 yrs which had 64 patients (45.4%). Among clinical presentations, jaundice was the most common (72%) presenting complain. Rate of complications was inversely proportional to the level of albumin. Rate of complication was higher in cases with pre-operative stenting (60%) as compared to patients without pre-operative stenting (40%). Classical PDs were performed in 91 patients, in rest (50 patients) pylorous preserving pancreatoduodenectomy (PPPDs) was done. The mean duration of surgery was 6.7 hrs. Mean duration of hospitalization was 14.3 days. **Conclusions:** Pancreatic cancer has a poor prognosis with <5% alive at 5 yrs, despite active surgical treatment. This single institution, high-volume experience indicates that pancreatoduodenectomy can be performed safely for pancreatic head and periampullary region tumours with improved outcomes thereby supporting the idea of centralization of pancreatic resectional surgery.

Keywords: Pancreatic cancer, pancreatoduodenectomy (PD), stenting.

Locally advanced gastro-esophageal junction carcinoma- evaluation of two modalities of treatment at a tertiary care center

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Introduction; The incidence of Gastroesophageal junction (GEJ) adenocarcinoma is increasing rapidly. Data separately on GEJ tumors management is rare. **Objectives:** to evaluate the clinicopathological characteristics of GEJ tumors. To compare two modalities of treatment- Neoadjuvant treatment followed by surgery (group-N) and upfront surgery (group-S) in GEJ tumors in terms of recurrence and survival patterns.**Materials and Methods:** Records of all the patients diagnosed as GEJ tumors as per Siewert classification, between 2005-2013 were reviewed. Patients who underwent either of the treatment modality with curative intent having age above 18 yrs, ECOG PS 0,1,2, clinical, radiological, endoscopic and histologically proven GEJ tumor which is limited loco-regionally included. Patients medically and surgically unfit and patients with metastatic disease at presentation were excluded. Kaplan-Meire graph utilized to calculate survival and recurrence pattern. Chi-square(X2) test used to assess association between clinico-pathological parameters with the outcome. The comparison of survival and recurrence rate between two groups computed by log rank test. **Results:** Total 68 eligible patients were evaluated. Group-S were 43(63.2%) and group-N 25(36.8%). Adenocarcinoma was the predominant histology (85%each). All the patients in group N were AJCC stage II (100%) and 95% in group S were stage III. Group-N received either neoadjuvant chemotherapy-19(76%) or concurrent chemoradiation-6(24%). Surgical technique in both groups was Ivor-Lewis 52(76.4%) or Minimally invasive Mckeowns technique 16(23.6%). Median follow-up period was 21 months. In group-S, high grade tumors had worse survival (OS-grade III 20 months Vs grade I,II 36 months. *p*-0.015). No clinico-pathological factors affected outcome in group-N. In group-N 5/25(20%) had grade 3 toxicity. Severe postoperative complications occurred 10(23%) in group-S and 4(16%) in group-N. Group-N has higher DFI (17.5months) and OS (30.5 months) compared to group-S (DFI 14months; OS 21.5months) but without statistical significance (*p*-0.56 and *p*-0.83 respectively.) **Conclusion:** Improved recurrence free period and survival with Neoadjuvant treatment over primary surgery group is not reflected statistically. Further prospective randomized studies required to assess the effect of neoadjuvant therapy in GEJ tumors.

Is faecal diversion mandatory for rectal cancer patients undergoing low anterior resection after neo-adjuvant chemo-radiation?

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Background: Neoadjuvant therapy amongst other factors is considered as a risk factor for leak following low and ultra low anterior resection for rectal cancer patients . Faecaldiversion significantly reduces the leak rates. Aim of the study was to assess the utility of the triple test, namely a negative air leak test, complete integrity of the surgical doughnuts and an intact anastomosis felt on digital rectal examination, in foregoing faecal diversion in rectal cancer patients undergoing low and ultra low anterior resection (post CTRT). **Materials and Methods:** The study period was from August 2009 to August 2014 (60 months). The study includes rectal cancer(post CTRT) patients not undergone diverting stoma following low or ultra low anterior resection. Decision of foregoing stoma was made on basis of triple test. The patients who satisfied the criteria did not undergo a stoma. Patients were followed for anastomotic leak. Correlation of patient and the procedure related factors with the anastomotic leak was also done. **Results:** The study included 200 patients. 14 patients developed anastomotic dehiscence. No perioperative mortality . Age more than 50 years and end-to-end anastomosis were found to be significantly associated with leak. **Conclusion:** No reason to recommend routine faecal diversion in these patients. 'TRIPLE TEST', can be used to decide on requirement of faecal diversion . Age more than 50 years and end-to-end anastomosis were found to be significantly associated with anastomotic leak and routine faecal diversion can be considered in these cases.

Early experience of laparoscopic single port onco-surgery in Nepal

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Purpose: The aim of this study is to compare the Conventional Laparoscopic Surgery (CLS) and homemade Transumbilical Single Port Laparoscopic Surgery(SPLS). **Study Design:** Bhaktapur Cancer Hospital,Nepal , from 2013-01-01 to 2015-07-30,28 cases of sigmoid colon and upper lying rectum cancer patients underwent Transumbilical Single Port Laparoscopic Surgery(SPLS) and 34 cases of sigmoid colon and rectum cancer underwent of Conventional Laparoscopic Surgery(CLS), and the retrospective analytical study was done. Homemade Trocar Inserter was made by surgical glove, cutting a plastic suction tube to make a circle and inserting trocars in cut fingers of glove. In both SPLS and CLS radical resection was done as Dixon's Procedure. The difference in SPLS group was the incisions of 1-2 cm below the umbilicus to insert the laparoscopic instruments.

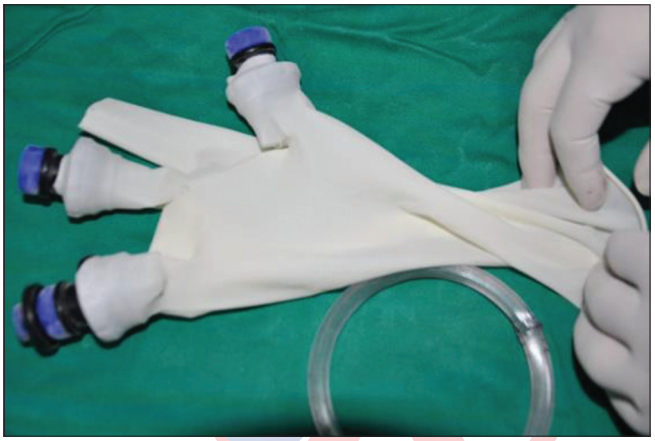

Fig. Handmade intsrument introducer

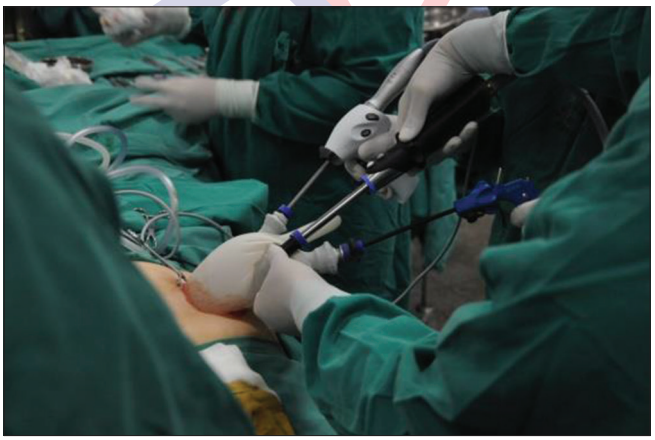

Fig. Single Port laparoscopic Surgery

Results: Out of 28 cases of SPLS, 1 case was converted open, 27 cases were operated and in other group 34 cases underwent CLS successfully. In SPLS group, the mean operating time 117.8min, mean blood loss 62.7ml. In CLS group, mean operating time 145.9min, blood loss 40.6ml. SPLS operating time was slightly longer than CLS which was statistically significant while there was no statistically differenence in blood loss between two groups .In SPLS group, mean time of first passage of flatus

2.6 days, mean first defecation time of 4.4 days, mean hospital stay of 10.5 days and In CLS group, 3.0 days, 5.4 days, 9.7 days respectively. In SPLS group, 5 patients and in CLS group 6 patients had postoperative complications,. In SPLS group the average distance of tumor from proximal/distal resected margin is respectively 5/6cm and mean 15.85 lymph nodes harvested and In CLS group 5.6cm/5.97cm and 13.88 lymph nodes respectively..There was no significant statistic difference between two groups for their postoperative histopathological value. As in CLS the drainage tubes are kept, but in SPLS no drains are kept, it also results in better cosmetic appearance

Parameters	SPLS	CLS	t value	P value
Operating time(min)	117.78±11.90	145.85±19.89	-2.37	P=0.021
Blood loss ml	64.81±24.18	40.59±18.74	1.58	P=0.120
Drainage tube No.	0.37±0.21	1.82±0.13	-11.41	P=0.000

Conclusion: Transumbilical Single Port Laparoscopic Surgery for sigmoid colon and rectum cancer can be successfully and safely performed, and has better benefits over Conventional Laparoscopic Surgery for reduced incision, less postoperative pain and improved cosmetics and can be alternative to traditional laparoscopic surgery.

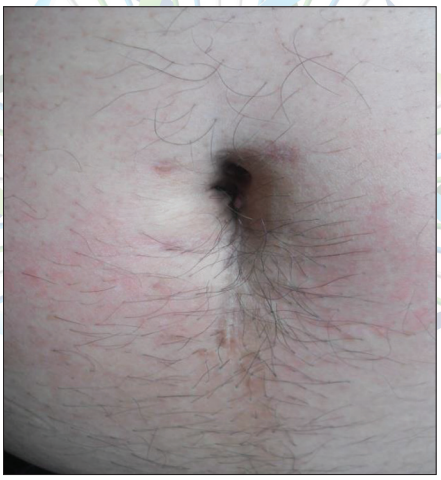

Fig. SPLS

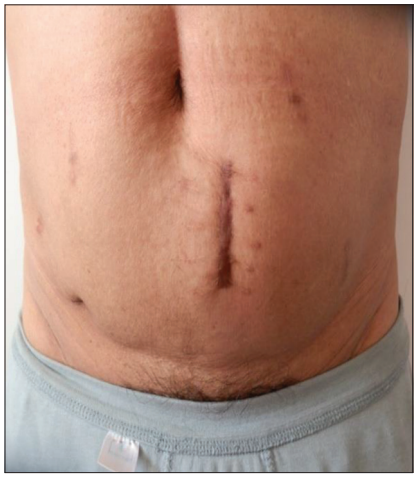

Fig. CLS

Assessment of Tumour response and resection rates in unresectable metastatic colorectal liver metastases following cetuximab with neoadjuvant chemotherapy

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Background: Surgical excision of colorectal liver metastases (CLM) is potentially curative. Liver metastasis presents in approximately 50% of colorectal cancer patients, of whom 80% will be inoperable at diagnosis. Only a minority of patients with liver metastases is amenable directly to surgery (20%). Therefore, efforts have been made to increase the resectability of patients with initially unresectable colorectal liver metastases. The patients with unresectable colorectal liver metastases (CLM) have a dismal survival and is a common clinical challenge. Historically, palliative treatment of metastatic colorectal cancer with fluorouracil (FU) and leucovorin (LV) yielded response rates of only 10% to 20%, with a median overall survival time of approximately 6 to 12 months. **Materials and Methods:** This is a prospective, randomized study of 152 patients with non-resectable, synchronous or metachronous colorectal liver metastases between Feb 2010 to January 2016 were enrolled. Patients with KRAS wild-type non-resectable liver metastases (technically non-resectable due to size or location or ≥5 metastases) were randomly assigned to group A or B. 76 patients in group A, received cetuximab with FOLFOX6 (54 patients) or FOLFIRI (22 patients) and 76 patients in group B, received FOLFOX6 (46 patients) or FOLFIRI (30 patients). Computerized tomographic assessment for resectability was performed after every 4 cycles by the multidisciplinary team. Patients with resectable disease were offered surgery. The primary end point was response rate evaluation according to Response evaluation criteria in solid tumors (RECIST) criteria. Secondary end points were R0 resection rate of liver metastases, perioperative morbidity and mortality. **Results:** An objective response rate was noted in 48 (63.1%) patients in group A, and 34 (44.7%) patients in group B (difference 11%, 95% CI −8 to 30; odds ratio [OR] 1.62, 0.74—3.59; P < 0.01). Eight (10.5%) patients had radiological complete response (CR); 40 (52.6%) patients had partial response (PR) in group A; in group B, none had CR and all 34 (44.73%) patients had PR. The most frequent grade 3 and 4 toxicities were skin toxicity (12 patients in group A, and 2 patients in group B), neutropenia (12 patients in group A and 17 patients in group B) and neuropathy (7 patients in group A and 4 patients in group B). The R0 resection rate was higher in group A than in group B [32 (42.1%) vs 22 (28.9%) patients] (difference 11%, 95% CI −8 to 30; odds ratio [OR] 1.62, 0.74—3.59; p<0.001). The most common postoperative complication was liver failure and was similar in both groups (12.5% in group A and 18.1% in group B). Postoperative mortality was similar in both groups; 5.3% in group A and 2.6% in group B (difference 11%, 95% CI −8 to 30; odds ratio [OR] 1.62, 0.74—3.59; p=0.45). The median follow-up was 28 months, Median OS from initiation of neo adjuvant therapy were 25.7 in group A and 22.3 in group B (difference 11%, 95% CI −8 to 30; odds ratio [OR] 1.62, 0.74—3.59; p=0.91) and and the PFS was 13.9 months in group A and 11.5 months in group B (difference 11%, 95% CI −8 to 30; odds ratio [OR] 1.62, 0.74—3.59; p=0.014). **Conclusion:** The study revealed that combination chemotherapy plus cetuximab resulted in high response rates, rapid tumour shrinkage with a 100% R0 resection rate. The objective response rate was 63.1% with a partial or complete response noticed in 52.6% and 10.5% of the patients, respectively. In addition a further 26.4% of patients had stable disease. Complete resection of previously unresectable colorectal liver metastases can be performed with minimal morbidity and mortality.

Systematic review and meta-analysis of recommended second-line therapies for advanced gastric cancer

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Background: With several approaches to treatment of patients with gastric cancer (GC) after first-line therapy, a meta-analysis was conducted to compare outcomes among these options. **Materials and Methods:** Electronic databases and relevant congress abstracts were systematically searched. Inclusion criteria included English-language, randomized controlled trials (RCTs) of adult patients who received prior chemotherapy for GC or gastroesophageal junction cancer, published through 28 May 2014. Interventions were limited to those in National Comprehensive Cancer Network or European Society for Medical Oncology guidelines. For all outcomes, Bucher indirect comparisons were conducted. A fixed-effect Bayesian network meta-analysis was conducted for overall survival (OS). Risk of bias and heterogeneity were evaluated. **Results:** Ten RCTs met eligibility criteria and evaluated best supportive care (BSC), docetaxel, FOLFIRI, irinotecan (IRI), IRI+cisplatin, paclitaxel (PAC), ramucirumab (RAM) and RAM+PAC. Two studies were excluded from the base-case analysis of OS due to design or reporting limitations but were included in a sensitivity analysis. Two studies were excluded from the analysis of discontinuations (DCs) due to adverse events (AEs) owing to design or lack of data. Table 1 reports results for these outcomes relative to BSC. Results were consistent across all sensitivity analyses. Sources of heterogeneity included geographic participation, primary tumor site and dosing regimen; however, a formal test of heterogeneity was not feasible as single studies were used for almost all treatment comparisons. **Conclusions:** Compared to BSC, OS was significantly improved for all interventions, and DCs due to AEs were significantly higher for all interventions except RAM. Results should be interpreted with caution due to limited number of studies, wide confidence intervals and between-study heterogeneity. Odds ratios could not be reliably estimated due to data scarcity and should be interpreted relative to each other, not in terms of absolute values.

Table 1: Bucher method base-case OS and DCs due to AE results relative to BSC

	OS (N=1804)		DCs due to AEs (N=1852)	
Intervention	**Hazard ratio vs BSC**	**95% CI**	**Odds ratio vs BSC**	**95% CI**
Docetaxel	0.67	0.49-0.92	53.8	3.2-906.6
FOLFIRI	0.40	0.17-0.94	37.4	1.2-1193.2
IRI	0.48	0.25-0.92	53.8	2.5-1165.7
IRI+cisplatin	0.44	0.22-0.88	135.1	5.7-3192.8
PAC	0.42	0.21-0.86	32.0	1.2-824.1
RAM	0.77	0.60-0.98	1.8	0.8-4.4
RAM+PAC	0.34	0.17-0.71	33.5	1.3-893.6

AEs, adverse events; BSC, best supportive care; CI, confidence interval; DCs, discontinuations; FOLFIRI, folinic acid, fluorouracil and irinotecan; IRI, irinotecan; OS, overall survival; PAC, paclitaxel; RAM, ramucirumab

Disclosures: This study was funded by Eli Lilly and Company, Indianapolis, IN, USA. This is an encore of an abstract presented at the European Society for Medical Oncology – ESMO Asia Congress 2015, 18 – 21 December 2015; Singapore.

Key words: systematic review; second-line therapies; advanced gastric cancer.

Short and long-Outcomes of Laparoscopic Gastrectomy: A Single-Center Safety and Feasibility Study

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Background: Indications for laparoscopic gastrectomy (LG) for early stomach cancer have spread worldwide, and evaluation of short-term outcomes has been favorable. The present study aimed to evaluate both technical feasibility and safety of LG and short-and long-term outcomes after LG. **Patients:** The study group comprised 348 patients who underwent LG during the period August 2001 through December 2014 at Gifu University School of Medicine. **Results:** Concomitant resection of other organs was performed in 27 (7.7%) of the 348 patients, and conversion to open surgery was performed in 6(1.7%) patients. Final clinical stage of patients according to the Union for International Cancer Control classification was stage IA in 269(77.3.%), stage IB in 44 (12.6%), stage IIA in 16(4.6%), stage IIB in 8 (2.3%), stage IIIA in 7(2.0%), stage IIIB in 3 (0.9%) patients, and stage IIIC in 1 (0.3%) Average values of total blood loss and operation time were 109.9±161.7 ml and 311.1±80.1 minutes, respectively. Postoperative complications were detected in 44 patients (12.6%), and one patient died. According to the Clavien-Dindo classification of surgical complications, the rate of severe complications of grade ≥3a was 23 patients(6.7%) and that of grade ≥3b was 5 patients (1.4%).There were no significant differences in complications in relation to clinicopathological or operative procedures. Cancer recurrence was detected in 2 (0.5%) patients. In the patient with peritoneal dissemination, tumor size and macroscopic type were critical. One recurrence each was detected for Stage IA and Stage IIB cancers. **Conclusions:** The present study showed LG to have a safe postoperative course and to benefit oncologic outcomes.

Evaluation of the Following in Gastric Cancer

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Background: The laparoscopic approach in the management of gastric cancer is applied with increasing frequency nowadays. Laparoscopy is a valuable technique in staging stomach carcinoma and has an important role in the detection of occult extensive intra-abdominal or metastatic disease not detected by conventional radiological staging. The diagnostic laparoscopy for staging of gastric cancer ensures the avoidance of unnecessary laparotomy in one-third of the cases, given that in these patients exists intra-abdominal disease stage M1 (metastases to peritoneum, liver or non-local lymph nodes) that cannot be detected radiographically by modern imaging techniques. Studies suggested that imaging methods of evaluating the pre-operative status of hepatic and peritoneal metastases have two effects : 1) avoiding unnecessary laparotomy; 2) assessing the effectiveness of neoadjuvant protocols in the absence of histopathological confirmation.. Abdominal CT can demonstrate not only the stomach wall and the adjacent tissue, but also the presence of distant metastases by providing rapid and high spatial resolution imaging.But ,the flaw being in its sensitivity to detect subcentimetric nodes and sometimes falsely predicting irresectability. In Japan and Korea, following the en bloc dissection of the stomach and lymph nodes, the surgeon dissects out the individual nodal stations from the surgical specimen, allowing the pathologist to examine and report the number of positive and negative lymph nodes for each nodal station ,meaning , more interest has been shown in this aspect,as it has its own I ndependent impact on survival.Though few landmark trials have compared D1 VERSUS D2 Gastrectomy, not many of them still favoured one over the other.With this background, we have evaluated the number of nodes dissected and its POSITIVITY rate and its impact on prognosis. **Methods:** Totally 73 patients

have been evaluated over the period of 2 years,,Diagnostic laparoscopy have been done in 32 cases..And in all cases, role of imaging and lymph node yield and its impact on prognosis have been evaluated. **Results:** Diagnostic laparoscopy did change the plan of management in 54.5% of patients.Imaging was not supportive in predicting resectabilty/operability.Higher the lymph node yield did have significant impact on prognosis,with average lymph node yiels being 19 and 80% of patients who underwent curative gastrectomy with extended lymphadenectomy are on follow up. **Conclusions:** Diagnostic laparoscopy did play an important role in treatment planning.Imaging was not very supportive in predicting resectability and operability.Though, the absolute curative theory do not propose standard D2 gastrectomy , higher the lymph nodes dissected did have significant benefit on survival.

PET/MRI in Pancreatic and Periampullary Cancer: Correlating with tumor stage and progression-free survival.

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Purpose: To correlate the clinical stage and prognosis of pancreatic or periampullary cancer with the imaging biomarkers at diffusion-weighted imaging (DWI) and glucose metabolic activity derived from integrated positron emission tomography/magnetic resonance imaging (PET/MRI). **Materials and Methods**: This prospective study was approved by the institutional review board and informed consent was obtained. Sixty consecutive patients (mean age,62.7± 12.8y; range,24–85 y; 45 men, 15 women) with pancreatic or periampullary cancer underwent PET/MRI before treatment. The imaging biomarkers were the minimal apparent diffusion coefficient (ADCmin), standard uptake values (SUV), metabolic tumor volume (MTV), and total lesion glycolysis (TLG) of the tumors. The relationships between these biomarkers with clinical TNM stage were evaluated using Pearson and Mann–Whitney U tests. The differences in the imaging biomarkers relative to early recurrence/progression within 6 months after treatment were compared with the Student *t* test.The area under the receiver operating characteristic curve (AUROC) was used to evaluate accuracy. The correlation between the imaging biomarker and PFS (progression-free survival) was investigated by using the Cox proportional hazards model. **Results:** ADC_{min} correlated negatively with TLG (r = -0.284, P = 0.014) and was significantly lower in N1 (P = 0.027) and TNM Stage 3+ tumors (P = 0.043). TLG was significantly higher in T3+ (P = 0.008), N1 (P = 0.033) and TNM Stage 3+ (P =0 .022) tumors. MTV was significantly higher in T3+, N1, M1, and TNM Stage 3+ tumors (all P <0 .05). The MTV/ADC_{min} ratio exhibited the highest AUROC for predicting T4, N1, M1, and advanced TNM stages tumors.Patients with early recurrence/ progression had higher MTV/ADCmin ratio than those without (P = 0.048).Univariate analysis revealed that advanced tumor stage (P = 0.004) and high MTV/ADCmin ratio (P = 0.021) were poor prognostic factors for PFS, but age, sex and tumor size were not. Cox multivariate analysis revealed that MTV/ADCmin ratio remained an independent predictor of PFS (hazard ratio, 1.036; 95% CI, 1.008-1.066, P = 0.018) after adjustment for age, sex, tumor size, and stage. **Conclusion:** Combining DWI and PET data provided complementary information on tumor characteristics. The imaging biomarkers from integrated PET/MRI may predict clinical stage and PFS in patients with pancreatic or periampullary cancer.

Keyword: PET/MR; pancreatic cancer; progression-free survival

Tumorigenesis involves CSC like cells with elevated B-catenin and hTERT protein

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Introduction: Cancer stem cells are documented in a variety of solid tumors and differ distinctly from bulk of cells in the tumor and are said to possess all the qualities of stem cells. The Wnt/B-catenin pathway has been reported to interact with hTERT and Shelterin group of components which are essential in telomere end protection and in DNA damage response. As such dysregulated Wnt/B-catenin has been linked to epithelial stem cell self-renewal leading to formation of chemotherapeutic resistant spheroidal CSC like cells called colonospheres. **Objectives:** To characterize the stem cell like characters of colon carcinoma using cell line HCT116, and to comparatively analyse the expression levels of b-catenin, hTERT and related components in a resistant spheroidal colonospheres with respect to normal cancer cells. **Material and Methods:** DFA was used to determine the extent of stem cell like characteristics in the development front, qRT PCR for relative gene expression, immune-FACS for percent stem cell positive population and ICC for comparative protein analysis. **Results:** We observed increase in stem cell like population at the developing woundfront. Also b-catenin, hTERT and related genes showed significantly higher fold increase in the spheroidal population compared to parental. FACS showed increased stem cell positive population in spheroids. **Conclusions:** We conclude that tumorigenesis results in concentration of stem like cells at the developing front. Also increased levels of b-catenin and related markers in spheroidal population are indicative of the involvement of b-catenin in maintenance of the spheroidal phenotype and might be involved in chemotherapeutic resistance of cancer stem cells

Selective Lateral Pelvic Lymphnode Dissection for Persistent node after Neoadjuvant treatment (NACTRT) in Locally Advanced Carcinoma Rectum (LARC) : Intermediate Outcomes

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Background: 15 % to 25 % of LARC present with lateral pelvic lymph nodes (LPN), especially with rectal tumors below the peritoneal reflection. Lateral pelvic lymph node dissection (LPND) is done for LPN persisting even after administration of neoadjuvantchemoradiotherapy (NACTRT). We compared survival between those who underwent TME with or without LPND to evaluate whether LPND is worth the effort. **Methods:** From July 2013 to March 2015, patients with LARC within 10 cm from anal verge with suspected pelvic nodes metastasis on MRI were selected. All patients received NACTRT and were followed up with TME. LPND was performed when pelvic node persisted following NACTRT. Clinicopathological and perioperative details were recorded and survival was compared for those who underwent TME with LPND (TMPLND) withthose without LPND (TME). **Results:** Of the 362 patients operated with curative intent for LARC, forty (11%) had LPN on presentation and twelve (3 %) had persistent lateral pelvic nodes following NACTRT. Four out of twelve patients showed residual disease in the lateral pelvic nodes (33 %). Median follow up for TME was 24 months (7-42months) vs 19 months (13-29 months) for TMPLND. Five patients each in TMPLND (41.7%) and TME (20%) developed recurrence. The disease free survival at 19 months was 90.7 % (TME) vs 71.3% (TMPLND). **Conclusion:** LARC presenting with lateral pelvic nodes are treated with CTRT. The outcome of patients with persistent LPLN after CTRT and undergoing LPLND is less favorable than those with no persistent node after CTRT and LPLND may not eliminate all local recurrences.

Colorectal Cancer at Presentation in Indian Subcontinent, Young vs Old : A Comparative Study.

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Background: Increasing incidence of colorectal cancer (CRC) has been documented in younger population. Many studies have suggested grim prognosis in young patients while others contradicts this belief. We aimed to compare the effect of age on the histology, stage, response to neoadjuvant treatment and its effect on resection rates. **Methods:** Retrospective analysis of 779 consecutive patients of CRC registered at Tata Memorial Hospital from1 July 2013 to 31 July 2014 was done. Patients were divided as per age at the time of registration into Young(<45 yrs) and Old(>45 yrs) age groups. Both groups were compared with respect to demographic and treatment related factors. Statistical analysis was done with SPSS software. **Results:** Mean age in our study was 47 years with 45.1% being Young and 54.9% being Old. Young patients had higher incidence of rectal cancers(60.70%)as compared to colonic cancers (39.3%) (p=0.03) ,while in Old group both subsiteswere equally distributed. Pathologically, Signet Ring type (20.5%) and Mucinous types(20.5%) are significantly more common in Young as against the Old (signet ring(7.7%)&mucinous(13.8%).Young patients had higher incidence of poorly differentiated histology than Old patients(38.6% vs21.1%). Young patients had higher incidence of locally advanced disease at presentation (53.84% vs 45.56%,p=0.046). There was a higher rate of nodal positivity in Young group(81.19%) vs old group(65.72%), (p=.000). There was no significant difference in relation to resection rate, TRG and margins in both groups. **Conclusion:** Young patients present more commonly with advanced disease and poor histological types, though they respond equally well to neoadjuvant treatment.However impact of age at presentation on survival needs to be evaluated by assessing the long term treatment outcomes.

Keywords: Colorectal Cancer, Epidemiology, Demography

Peritoneal Metastasesfrom Colorectal Cancers – Outcomes from Indian Subcontinent

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Background: In India there is dearth of literature regarding demographics/presentation of peritoneal metastases(PM) from colorectal cancers(CRC). The aim of our study was to ascertain demographics, presentation andsurvival of patients with peritoneal metastases in Indian subcontinent. **Methods:** A retrospective analysis of patients diagnosed with PM of CRC origin from august 2013 to july 2014 was performed. PM was classified as limited (Peritoneal Carcinomatosis Index - PCI < 10) and widespread (PCI> 10). Data regarding follow up was obtained from electronic case records/telephonic interviews. All patients received systemic chemotherapy(SC) with/without surgery. **Results:** Of 800 registered patients with CRC, Information regarding site of metastases was available in 720 patients. 70/720 i.e. 9.7%patients had peritoneal metastases (median age 47 years).6.25% (45/720) patients had peritoneum as the only metastatic site. 53 patients had synchronous presentation. Resections were performed in 23 patients (19 underwent R0 resection and 4 were R+). At median follow up of 11 months, the median OS was 14 months. Patient with PCI < 10 had significantly better survival (41 mths) as compared to those with PCI > 10(15 mths). Patients undergoing R0 resection had better survival (27.8 mths) as against those with R+ resection (18 mths). Survival of patient receiving only SC was 11 months. **Conclusion:** 10% patients with CRC present with PM and have a median OS of 14 months. Select group of patients who undergo R0 resection of only disease portion had median survival of 27.8 months.

Pet/Ct For Gastro-Intestinal And Hepatopancreaticobiliary Malignancies: Does It Really Help?

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Introduction: PET/CT plays an important role in management of GI cancers. It is the best modality for identifying distant metastases, but we studied if it can alter the line of management. **Objectives**: To evaluate whether PET/CT change the decision making in GI malignancies. **Material and Methods**: Study was conducted at MDTC of Army Hospital (R&R), New Delhi. 202 patients with GI and Hepatico-Pancreatico-Biliary(HPB) cancers received during 2013-14 were studied. After initial work up, treatment plan was formulated. All patients underwent PET/CT. Findings were analysed comparing with CT findings and Intra op findings. Diagnostic accuracy was evaluated. All statistical analyses were performed using SPSS V.22. **Results**: 202 patients with GI and HPB cancers were eligible for study. On PET/CT, 40 cases were found metastatic, declared Major Change in Intent, shifted to Palliative therapy. 28 cases had locoregionally advanced disease, declared Minor change, shifted to Neo-adjuvant therapy. 144 cases continued as per initial plan. 82 cases received NACT/NACCRT. PET/CT for response assessment was done. 18 cases had progressive or unresectable disease. 126 patients finally underwent surgery. 81 cases had corroborative findings. 40 cases had metastatic disease not picked up on PET/CT. 15 cases with Post Neoadjuvant PET/CT showingmCR had corroborative pCR. **Conclusions**: PET/CT can serve as means of de novo diagnosis of GI tumours. For T- staging, modalities like USG, CT or MRI are better, as they provide better anatomical assessment of disease. It definitely alters management in N+ Carcinoma Rectum which merits NACCRT. Post neoadjuvant PET/CT can serve as an early and accurate means of predicting response and directing changes in therapy, helping to avoid morbidity and expense of chemo and radio therapy. In post neoadjuvant progressive disease, it avoids unwarranted surgical morbidity. In cases of GIST, PET/CT is standard of monitoring response to chemotherapy and is recommended. **Summary:** We analysed whether advising PET/CT in cases of Gastro-Intestinal malignancies is Cost beneficial or Not.

Salvage chemotherapy for poor responders to chemoradiotherapy (CTRT) in locally advanced rectal cancers (LARC)improves outcomes

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Introduction: Management of LARC includes CTRT followed by assessment for surgery after 6 to 8 weeks in patients where R0 resections possible. Mercury group identified high negative predictive value of MRI in this situation. Patients where R0 resection is not possible are offered palliative chemotherapy. The primary aim of our study was to assess the role of Salvage chemotherapy for poor responders to chemoradiotherapy in terms of achieving R0 resection. **Material and Methods:** All patients with LARC undergoing CTRT had a MRI scan at presentation and 6-8 weeks after CTRT (MRI 2).Those patients where R0 resection was doubtful were then selected to undergo chemotherapy. Post 4 cycles of chemotherapy all patients underwent restaging MRI (MRI3) and reassessed for surgical resection. **Results**: Between June 2012 and December 2014, 50 patients received salvage chemotherapy with CAPOX regime 19(38%) or FOLFIRINOX 31 (62%) after CTRTR. Median number of chemotherapy cycles received was 4 (range 2-8). MRI 3 revealed further radiological downstaging in 26 (52%) of the patients and 18 patients underwent R0 resection (1 exenteration). 6(12%) patients in this group defaulted treatment to avoid permanent stoma. Of 24 patients with poor or no radiological down staging, 13 underwent

R0 resection 11 being exenterative procedures. So overall 34 (68%) patients underwent exploration and 31(62%) had R0 resection.The median time to surgery following chemoradiation was 5 months (range 3-18 months). **Conclusion**: Patients with poor response to CTRT can be downstaged using salvage chemotherapy so as to achieve R0 resection.

Keywords: Locally advanced rectal cancer, chemoradiation, Salvage chemotherapy,

Laparoscopic versus open approach for intersphincteric resection - Results from a tertiary cancer centre in India.

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Introduction: Intersphincteric resection (ISR) is a sphincter-preserving surgery for patients with very low lying rectal cancer.Over last 2 decades a number of studies have shown that ISR is technically feasible and safe, with no compromise in the oncological outcomes. Althoughlarge RCTs comparing laparoscopic surgery with open surgery for rectal cancer have established oncological safety of the laparoscopic rectal cancer surgery,very few studies have specifically looked at the subset of patients who have undergone ISR . We looked at our short term results of ISR comparing open surgery with laparoscopic surgery. **Material and Methods:** This is a retrospective review of a prospectively maintained database including all patients undergoing ISR for carcinoma of the rectum in the Division of Colorectal Surgery at the Tata Memorial Centre, Mumbai between July 1st 2013 and July 31st2015. The oncological outcomes (distal resection margin, circumferential resection margin (CRM) involvement and number of nodes harvested)and the clinical parameters (operating time, estimated blood loss, lengthof hospital stay and 30 day perioperative morbidity and mortality) was compared between the open and laparoscopic groups. **Results:** 72 cases of ISR were performed during the study period. Five patients underwent robotic ISR and were excluded from the final analysis. Of the 67 cases included in the final analysis, 39 cases underwent open ISR (OISR) and 28 laproscopicISR(LISR.). CRM involvement was seen in 10% patients in the OISR group and none in the LISR group (*p* value 0.081). Median distal resection margin was 1 cm in OISR and 1.5 cm in LISR. Two patients in OISR group had involved distal resection margin and hence underwent APER. Other oncological parameters including the number of retrieved nodes as well as histology were comparable between the 2 groups.Although median blood loss was higher in OISR group compared to LISR, it didn't reach significance (p value – 0.239). Median hospital stay was comparable between the two groups. In the LISR, there were no conversions to open surgery. **Conclusion:** Laparoscopic Intersphincteric resection is safe and can be performed with low conversion rates for selected patients with low rectal cancer.

Keywords: ISR, Laroscopic, Rectal cancer

Abstract For Oral Presentation

Role of intraluminal brachytherapy boost in cancer esophagus patients; an institutional experience

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Aims of Study: To evaluate the localcontrol,overall survival, recurrences and late toxicities in patients of cancer esophagus of middle one third treated with EBRT and boost by intraluminal brachytherapy. **Materials and Methods:**All proved cases of middle third of cancer esophagus (stage T3-T4 N0N1 M0) having histology sq. cell carcinoma including all ages, both sex reporting to regional cancer centre, Kamala Nehru Memorial Hospital for a period of 2011 to 2015 with the minimum follow up of six months. Study area includes all the patients reporting to KNMH, dist. Allahabad and other adjacent areas.Total 25 patients were treated by intraluminal boost with curative intent. All patients were considered as per inclusion criteria. All patients were treated with EBRT dose of 40Gy/20 fr/ 4wks along with weekly cisplatinfollowed by a gap of two weeks, patients were re-assessed for local response and radiation toxicities as per RTOG criteria and after that intraluminal brachytherapy 5Gy/fraction in two sittings with one week interval has been given. **Results:** Median follow up period was 30 months. Among 25 patients treated with EBRT + ILRT boost 6 patients are surviving till now (4 are locally disease free and 2 developed recurrence after5 years) and 13 patients died of recurrence and distant metastasis. Local recurrences were seen in 10 patients (4 at same site and 6 at distant site). Distant metastasis noticed in 5 (20%) patients with in period of 6 to 20 months after treatment. Sites of distant metastasis includes liver, lung, spine, pelvic bone.6 patients lost follow up during this period. 5 year OS was 24%, death rate 52%. Among late toxicities stricture noticed in 20% patients, ulceration in 8% and TOF in4% patients. **Conclusion:** Data compiled from above studies shows that cancer esophagus an aggressive disease. Combined modality treatment with EBRT and ILRT boost may improve survival and quality of life of patients. Thusit can be opt as the preferred mode of treatment in advanced stages of cancer esophagus in selected patients.

Key words: Brachytherapy, Intraluminal, Toxicity.

Survival Benefit of Cytoreductive Nephrectomy (CN) Validated in Indian Cohort

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Background: Cytoreductive nephrectomy (CN) has been shown to improve survival in metastatic renal cellcancer (mRCC). Some studies have documented its benefit continuing in the era of targeted therapy. Indian data is sparse regarding benefits of cytoreductive nephrectomy, hence we performed this study to see if CN impacts survival in Indian cohort of patients. **Material and Methods:** Case records of patients presenting with upfront mRCC at our centre were retrospectively analysed. Baseline characteristics, histopathological information and survival outcomes were assessed. Overall survival (OS) was calculated from the time of diagnosis to death due to any cause. Multivariate analysis using Cox regression was done to adjust for confounding variables such as age, performance status, systemic treatment and number of metastatic sites. **Results:** A Total of 130 patients with upfront metastatic disease were analysed.Median age was 52 years (range 18-80 years). Twenty nine patients were females (22.3%) whereas 109 were males (83.7%). Clear cell was most common histological subtype (69.2%) followed by papillary type 1 (8.5%). Lungs (59.2%) followed by bones (51.9%) and non-regional lymph nodes (31.5%) were most common sites of metastases. Thirty two patients (24.6%) underwent cytoreductive nephrectomy. Median OS was 18.7 months inthe group with nephrectomy and 8.3 months in the nephrectomy group which remained statistically significanteven after adjusting for age, performance status, number of metastatic sites and targeted therapy administration (hazard rate: 4.123, 95% confidence interval: 1.71-7.312, P=0.028). **Conclusion:** Cytoreductive nephrectomy should be attempted in patients with metastatic RCC wherever feasible. Our study validate the benefits of this procedure in Indian cohort.

Laparoscopic versus total robotic rectal cancer surgery: A single centre experience from a tertiary cancer referral centre from India.

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Purpose: Minimal access surgery has shown equivalent oncological outcomes and better peri-operative outcomes for rectal cancer surgery. But literature comparing laparoscopic and robotic rectal cancer surgery is scarce. We have analyzed the same at a tertiary cancer referral centre from India. **Material Methods:** This is a retrospective study. We used da Vinci Xi system with single docking and single phase technique for total robotic rectal surgery. Analysis was performed with SPSS 21. **Results:** 181 consecutive patients (145 Laparoscopic and 36 Robotic) undergoing curative intent surgery for rectal cancer in colorectal services from October 2013 to September 2015 were assessed. Groups were similar with respect to age, sex, ASA status and BMI. Conversion rate (2.7%) and sphincter preservation rates were similar (64%). Robotic group had higher T3/T4 (88% vs 54%, p<0.0001), lower rectal tumors (63% vs 57%, p=0.09) and neoadjuvant chemoradiation rate (75% vs 49%, p=0.004). Both the groups (laparoscopy and robotic) were similar regarding operative time (263 and 280 minutes), blood loss (200 And 100 ml) and hospital stay (7days). They were also similar with regards to circumferential resection margin involvement (2.12% vs 2.7%, p=0.48) and median lymph node harvest (12 vs 10, p=0.56). **Conclusion:** Laparoscopic and robotic approaches for rectal cancer surgery have equivalent peri-operative and short term oncological outcomes. Robotic rectal cancer surgery can be performed safely for locally advanced, low rectal tumors undergoing neoadjuvant chemoradiation. Further evaluation of functional outcomes is needed. Socio-economic parameters and surgical expertise should guide the most optimum approach for rectal cancer surgery.

End-To-Side Pancreatico-Jejunostomy— Early Postoperative Outcomes In 65 Consecutive Cases Of Whipples Procedure

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Background: To evaluate the impact of Heidelberg technique of pancreatico jejunostomy in relation to early postoperative outcomes

in 65 consecutive cases of Whipple procedure. **Materials and Methods:** 65 patients who underwent whipples procedure for the following .The pancreatico –jejunal anastomosis was done by by surgeons trained at Heidelberg university, Germany .An End to side duct to mucosa anastomosis is being followed and the Sutures used are -4-0/5-0 PDS for all layers.The pancreatic remnant is handled gently and anastomosis is done with absence of tension and no distal obstruction after ensuring a good blood supply, the average time taken for Whipple's 250 minutes,average time taken for P-J 45 minutes. **Results:** Classical Whipple's procedure was done in- 40 patients and pylorus preserving in 25 patients. the patients were evaluated for early postoperative complications.. Periampullary carcinoma -38 ,carcinoma Head of pancreas-15 patients ,malignant Terminal CBD stricture -9 patients, Duodenal carcinoma-3 patients . There was no postoperative mortality,and class A leak was seen in 3% patients. Except for wound infection there is no significant difference in total complication rate in patients with pre-op biliary stents. **Conclusion:** Pancreatic leak is a life threatening complication. A meticulous duct –mucosa anastomosis is more reliable in preventing post operative pancreatic fistula.In high volume centers pancreatic fistula rate have ranged from0- 17%.In our study pancreatic fistula rate is 3% and there is no mortality. The procedure has to be performed by experienced hands and the surgeon is the most important prognostic factor.

Salvage of human colorectal adenocarcinoma HT-29 cells from oxidative stress using ascorbic acid and niacin.

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Introduction: Colorectal cancer is the second most common cause of cancer deaths in the world. Accumulating evidence suggests that reactive oxygen species leads to the metastasis of colon cancer. Hence in this study antioxidant activity of ascorbic acid and niacin was evaluated on the cancer stem cells (CSC), cancer non-stem cells (non-CSC) and wild type (WT) of population human colorectal adenocarcinoma HT-29 cells. **Objectives:** 1. Isolation of cancer stem cells (CSC-CD44+) and non-stem cell (non-CSC, CD44-) populations from a standard human colorectal adenocarcinoma HT-29 cell line using fluorescence activated cell sorting. 2. Evaluation of basal levels of oxidative stress in all three populations (WT, CD44+ and CD44- of the HT-29 cancer cell line. 3. Evaluation of the correction of oxidative stress using ascorbic acid and niacin on all the three populations of HT-29 cell line. **Material and Methods**: Human colon cancer cell line, HT-29 was obtained from the National Centre for Cell Science, Pune India. The cells were cultured in Dulbecco's Modified Eagle Medium (high glucose) supplemented with 10% fetal bovine serum and 1% Penstrep in 5% CO_2. The CD44+ and CD44- were sorted using fluorescence activated cell sorting (Biorad S3e sorter). All the three cell populations (WT, CD44+ and CD44-) were assessed for their respective oxidative stress and salvage in response to ascorbic acid and niacin using qPCR for standard genes involved in oxidative stress such as superoxide dismutases (SOD1, 2, 3), mitochondria-derived reactive oxygen species controller uncoupling protein 2 (UCP2), and oxygen transporters that protect against hypoxia such as cytoglobin (CYGB) gene. Also, the cells (WT, CD44+ and CD44-) were assessed for their proliferation using MTT assay before and after treatment with various concentrations of niacin and ascorbic acid and phase contrast images were captured. **Results:** A dose dependent reduction in oxidative stress was found in the WT, CD44+ and CD44- HT-29 human colon adenocarcinoma cells, in response to various concentrations of ascorbic acid and niacin. **Conclusion:** The study may give some key findings for newer therapeutic strategy for human colon cancer.

Keywords: Colorectal Adenocarcinoma, niacin, ascorbic acid, CD44

The clinical feature of c-Met high expression Hepatocellular carcinoma

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Backgrounds: Today, c-Met (HGF receptor) is recognized as a target of treatment for hepatocellular carcinoma (HCC). Clinical application of c-Met inhibitor is attempted and c-Met has been noted. However, the clinical features of c-Met-positive HCC are not yet sufficiently clarified. Thus, we will consider the c-Met high expression hepatocellular cancer features and we tried to investigate the clinicopathological significance. **Material and Methods:** 108 HCC cases underwent hepatectomy in our department in 2004-2013. We studied about c-Met positive rate in HCC cases was evaluated by immunohistchemistry of resected specimens in four strength levels of 0-3. Then, we examined statistically for the patient background and c-Met positive rate, the relationship between c-Met and the clinicopathological factors and the relationship between c-Met expression and the prognosis. **Results:** The positive rate of c-Met (IHC strength level1, 2 or 3) was 69.4% of 108 cases.(including 5 repeat hepatectomy cases and 6 evaluation impossible cases) In the c-Met high expression (IHC strength level 2 or 3) hepatocellular carcinoma, TAE not enforcement, tumor diameter of 30mm or less and less than BMI 22.4 was a significant related factors with c-Met positive HCC cases. c-Met high vs low expression cases of the 50% recurrence free survival was 833 days v.s. 533 days. (=0.41) 5 years overall survival rate was 69,3%vs68.8%(p=0.80). The degree of expression of c-Met didn't have any significant effect on recurrence and prognosis. **Conclusion:** c-Met expression can be not necessarily relevant with malignancy, tumor progression and prognosis in HCC.

Clinicopathological features, hormone immunoexpression, and loss of ATRX and DAXX expression in pancreatic neuroendocrine tumors

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Introduction: Neuroendocrine tumors of the pancreas (PanNETs) are rare neoplasms, and not much is known about their pathogenesis. **Objectives:** We aimed to evaluate ATRX/DAXX immunoexpression in PanNETs a cohort of well-characterized PanNETs. **Material and Methods:** PanNETs diagnosed over a 10-year period were retrieved and clinicopathogical features reviewed. Immuohistochemistry for pancreatic hormones, and for ATRX and DAXX was performed. **Results:** Sixty-eight PanNETs were included (30 males and 38 females) with median age of 39years. Histologically, there were 37 Grade 1 (54.4%), 27 Grade 2 (39.7%) and 4 Grade 3 (5.9%) cases. On immunostaining for hormones, insulin expression was most frequent (22 cases; 38.6%), followed by gastrin (7 cases; 12.3%); twenty-five cases (43.9%) were negative for all hormones. Loss of ATRX/DAXX immunoexpression was noted in 18 cases (39.1%), and was significantly more frequent in tumors larger than 5cm. Lymphovascular invasion, infiltrative borders and infiltration of adjacent organs were also more frequent in tumors with loss of ATRX/DAXX immunoreactivity. Majority of tumors with ATRX/DAXX loss showed negative immunostaining for all hormones. **Conclusions:** Loss of ATRX/DAXX expression is frequent in PanNETs, indicating a role in their pathogenesis. As ATRX/DAXX loss is more frequent in larger tumors, and in those with lymphovascular invasion, adjacent organ infiltration and infiltrative borders, this suggests that loss of ATRX/

DAXX expression confers an aggressive phenotype. Immunohistochemical detection of ATRX/DAXX loss should therefore be incorporated into routine pathological evaluation of PanNETs, as it provides prognostic information beyond tumor grade and stage.

Key words: ATRX; DAXX; immunohistochemistry; neuroendocrine tumor; pancreas

Post operative outcomes after oesophagectomy: A risk analysis

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Background: The study was aimed to identify pre and intraoperative factors that potentially influence morbidity and mortality after oesophagectomy for oesophageal carcinoma and its relation to the tumor subtypes. **Materials and Methods**: 371 patients underwent oesophagectomy for carcinoma oesophagus between January 2007 and January 2011 were analysed. of these 241 patients underwent transhiatal oesophagectomy,27 patients underwent VATS oesophagectomy,103 patients underwent transthoracic oesophagectomy.pre operative,intraoperative risk factors and tumor subtype were included in the risk analysis to asses their influence on postoperative morbidity and mortality. **Results:** Multivariate analysis identified the surgical procedure as the most important risk factor for postoperative morbidity and mortality with the trans thoracic technique having a higher risk. Patients with poor pulmonary reserves had a significant impact on the outcome.the rate of general complications were significantl,length of postoperative intensive care and mortality was significantly higher amongst patients who had squamous cell carcinoma. **Conclusion:** the profile of Indian patients differ from that of the west and the choice of surgical procedure has a significant effect on the outcome with respect to postoperative complications and mortality rate. The 3 and 5 yr survival is similar irrespective of the tumor subtype.

Clinicopathological Spectrum and Cd10 Immunohistochemical Expression In Urothelial Carcinoma Of Urinary Bladder

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Background: Carcinoma of the urinary bladder rankssixth in worldwide cancer incidence. Urothelial carcinoma is the commonest type accounting for 90% of all primary tumors of the bladder. As per Indian Cancer Registry data, it is the 9th most common cancer accounting for 3.9% of all cancers. The prognosis depends largely on the histological grade and stage of the tumor at diagnosis. There is noreliable parameter predicting the risk of recurrence or progression, hence molecular and immunologicalmarkers may be required to estimate the individual prognosis of patients as well as for effectivediagnosis and treatment. **Materials and Methods:** The study was carried on TURBT (transurethral resection of bladder tumour) biopsies and cystectomy specimens received in the Department of Pathology, Adesh Institute of Medical Sciences and Research, Bathinda from January 2015 to January 2016.Hematoxylin-eosin (H&E) stained sections were evaluated histopathologically according to WHO 2004 grading system. Selected cases were also studied by IHC and a semiquantitative scoring forCD10 expression was done based on the percentage of positive cells. **Results:** 26TURBT biopsies and 3 radical cystectomy specimens (total 29 cases)were studied, and urothelial carcinoma were classified according to WHO /ISUP (2004) classification. The most common age group was 51-60 years constituting 51.7% of all the cases with Male to Female ratio of 4.8:1. Mean and median age was 56.52 and 56 years respectively. Most common histological type was high-grade papillary urothelial carcinoma (41.4%) followed by low-grade papillary urothelial carcinoma (24.1%) papillary urothelial neoplasm of low malignant potential (10.3%), papilloma (10.3%), adenocarcinoma (6.9%) and squamous cell carcinoma (6.9%) Overall CD10 expression was significantly correlated with high histologicgrade. **Conclusion:** Urothelial carcinoma is more common in males. High grade papillary urothelial carcinomas is the commonest histological type. CD10 expression is strongly correlated with high tumor grade and stage in urothelial carcinoma of the bladder, and that CD10 may be associated with tumor progression inbladder cancer pathogenesis.

Folfirinox Chemotherapy In Metastatic Pancreatic Cancer –A Prospective Study to Evaluate Safety and Efficacy In Indian Patients

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Background: Metastatic pancreatic cancer is one of the most aggressive and highly lethal malignancie. FOLFIRINOX (leucovorin, fluorouracil [5-FU], irinotecan, and oxaliplatin) is the first combination chemotherapy which significantly improved survival .In india compared to western population there is lower incidence of pancreatic cancer and Gemcitabine is a standard of care with insufficient data for FOLFIRINOX . The purpose of this study was to evaluate efficacy and safety of FOLFIRINOX through its response on clinical symptom and disease progression in metastatic and Locally advance pancreatic cancer in Indian patients. **Methods:** This is single centre, prospective trial conducted over the period of 2 years. Total 33 patients between age group of 18 to 65 yrs with an ECOG score0,1 or 2 to receive FOLFIRINOX (oxaliplatin, 85 mg per square meter of body-surface area; irinotecan, 180 mg per square meter; leucovorin, 400 mg per square meter; and fluorouracil, 400 mg per square meter given as a bolus followed by 2400 mg per square meter given as a 46-hour continuous infusion, every 2 weeks along with growth factor support (G-CSF). chemotherapy was recommended until disease progression, unacceptable toxicity or patient refusal. The primary objective was to determine Clinical Benefit Response (CBR) and secondary objectives were assessment of response rate (ORR), duration of clinical Benefit response (CBR), 6 month progression free survival (PFS) and safety throughout the study. **Results:** Out of 33 patients total 18 (61.5%) patients showed clinical benefit response by their primary measures. The median time to achieve a clinical benefit response was 4.29 weeks.The mean duration of clinical benefit was 22.40 weeks (12.1—65.1 weeks). 1 (3.03%) patient achieved CR after 6 cycle and he was further consolidated with CT+RT. Response rate (PR+CR) was 36.30%, and the disease control rate was (PR+CR+ SD) 66.50%.The median time to response was 33.8 days (range, 25–60), and the median duration of response was 170 days (range, 156–196). The median progression free survival was 6.7 months ranging (3.3 months to 25.3 months) and eleven (33.3%) patients had 6month progression free survival. Most common haematological toxicity was neutropenia , total 28 patients were suffered from neutropenia (84.8%), thrombocytopenia developed in 19 (57.5%), and anemia 15 (45.45%). Neutropenia and febrile neutropenia occurred frequently, and the patients were treated with additional G-CSF to control these toxicities. **Conclusions:** In terms of clinical benefit response(CBR), the FOLFIRINOX regimen appears to be effective in Indian patients with relatively rapid and sustained improvements in all parameters of CBR .Although this regimen is associated high incidence of neutropenia and neurotoxicity it can be adequately controlled by primary prophylaxis of GCSF ,appropriate dose reduction and careful observation and appropriate supportive care. Thus, FOLFIRINOX can be used as the standard treatment for Indian patients with good performance status (ECOG PS 0 or 1,2) in locally advanced and metastatic pancreatic cancer.

Dose Limiting Structures In Irradiation of Carcinoma Prostate: A Closer Look At Lumbosacral Plexus

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Background: IMRT allows limitation of radiation dose to nearby normal organs at risk, while allowing delivery of high doses to the tumor and regional

lymph nodes. Although, the incidence of side effects have been minimized but they still do exist. Urinary, rectal and bowel toxicities have been described in literature and taken care of, since a long time. But, lumbosacral plexus has been an unattended organ at risk and dose escalation in malignancies like prostate cancer further enhances the risk of complication in the form of plexopathy. Patients present with lower limb weakness, numbness and paresthesia. Presentation is from 3 months to years after completion of radiation. Neurologic deficit is irreversible and no effective therapy other than supportive care has been found. Lumbosacral plexus (LSP) is not routinely delineated or given dose constraints during IMRT and it may lead to excessive dose dumping in this structure. A retrospective evaluation of the dose distribution in lumbosacral plexus in patients of carcinoma prostate treated with Intensity Modulated Radiation therapyhas been done in this study. **Materials and Methods:** Fifteen patients of prostate cancer, who were treated with IMRT technique, were included in the present study. Lumbosacral plexus was delineated in every patient from L4-L5 interspace to the level of sciatic nerve on planning CT scan of 2 mm thickness by Radiation Oncologist with assistance of Radiologist using anatomic atlas and Yi et al protocol. No dose limitation was placed for this organ during planning. After delineation, based on each patient's Dose Volume Histogram, total LSP volume, mean dose, maximum dose and volume percentages of LSP receiving 30, 40, 50, 60 Gy were calculated. **Results:** Dose to the primarysite was 76Gy/38fr and nodal drainage was 62.7Gy/38fr. Mean LSP volume was 59.6cc (range, 42.9-81.3cc), mean dose and maximum dose to LSP were 53.2Gy (range 46.5-56.4Gy) and 71.78Gy (range 65.9-77.6Gy) respectively. Mean volume percentages of the LSP 30Gy, 40Gy, 50Gy, 60Gy were 87%, 83.2%, 74.8% and 59.2% respectively. **Conclusion:** Radiation induced lumbosacral plexopathy (RILSP) is a rare but known complication of pelvic irradiation.Dose escalation has become a practice in prostate cancer in past few years. LSP delineation is not performed routinely in IMRT for pelvic malignancies and dose dumping may lead to increased rates of toxicity if this structure remains undelineated in future treatment plans. Mean dose lower than 45Gy, V_{40} lower than 55%, V_{50} lower than 30%, V_{55} lower than 5% during IMRT planning can reduce the risk of RILSP.

Keywords: Lumbosacral plexus, pelvic irradiation

Outcome of High risk prostate cancer treated using Simultaneous Integrated Boost (SIB) IMRT with hypofractionation

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Background: We aim to evaluate the biochemical failure free survival (BFFS) and morbidity in high risk prostate cancer patients treated with long term androgen deprivation therapy (ADT) and hypofractionated SIB IMRT. Recent advances in techniques enable us to deliver a higher dose of radiation to the prostate with limited dose to the adjacent rectum and bladder. Earlier studies have estimated prostate cancer to have low α/β of 1.5. Thus hypofractionated schedules in theory should confer better local control and cancer specific survival (CSS). Due to the long natural history of prostate cancer it becomes imperative to reduce rectal and bladder morbidity. Also BFFS has shown to be a predictor of CSS. Most of the studies with whole pelvic RT and long term ADT have used conventional fractionation schedules. **Materials and Methods:** We retrospectively analysed 100 high risk prostate cancer patients treated at our institute between 2010-2012. All patients received SIB IMRT with 70Gy in 28 fractions to the prostate and seminal vesicles (if involved) and 50.4 Gy in 28 fractions to the pelvic nodal stations with neoadjuvant hormonal therapy for a duration of 3-6 months prior to radiation and adjuvant hormonal therapy for a duration of 24-36 months. They were followed up with serial PSA values and clinical examination. Biochemical failure was defined as serum PSA >nadir + 2 (ASTRO Phoenix definition). Acute rectal and bladder toxicity was scored with the RTOG toxicity criteria. Chronic rectal toxicity (proctitis) and chronic bladder toxicity (cystitis) were assessed using the CTCAE 4.0. Patients without biochemical failure were censored at last follow-up/last PSA check or death. BFFS was calculated by the Kaplan-Meier method

Results: At a median follow up of 45 months (20-87 months), there were 13 cases of biochemical failure among the 100 patients analyzed (13 %) . 5 year BFFS was 78.6%. .There was no Grade 3 or 4 acute rectal or bladder toxicity .Chronic toxicity has been listed in the table below.Urethral stricture developed in 7 patients, of whom 6 had prior TURP showing significant correlation (6/15,p<0.001).

	Grade 2	Grade 3	Grade 4
Proctitis	12	2	0
Cystitis	7	0	0

Conclusion: This study therefore concludes that long term ADT and SIB IMRT provides a feasible alternative to conventional radiation therapy with good biochemical control and acceptable toxicity. Longer follow up of these patients would provide data on cancer specific survival and late morbidity.

Robot Assisted Retroperitoneal Lymph Node Dissection of Post Chemotherapy Residual Mass in Testicular Tumor – A Single Center Experience of 10 Patients

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Background: Retroperitoneal lymph node dissection (RPLND) is a well established treatment for post chemotherapy residual mass in non-seminomatous germ cell tumor (NSGCT). RPLND has the diagnostic as well as therapeutic advantage in post chemotherapy residual mass. Although the open RPLND is gold standard, but it has high postoperative morbidity and poor cosmesis due to long midline abdominal incision. In order to reduce postoperative morbidity and to fasten recovery, Rukstalis et al described laparoscopic retroperitoneal lymph node dissection(L-RPLND). The proposed advantages of L-RPLND are good cosmesis, shorter hospital stay, less post-operative pain and reduced compilation rate. L-RPLND has been used in post chemotherapy cases but it has steep learning curve, and difficulty in dissection at retro-aortic and retro-caval spaces. Robotics has been able to combine open surgical skills to laparoscopy approach because of its advanced feature like 3D visualization and 7^0 movements with tremor filtration. Surgeons are much more comfortable doing complex procedure like radical prostatectomy, radical cystectomy and RPLND with robotics. We describe our experience of robot assisted retroperitoneal lymph node dissection (RA-RPLND) in patients of testicular tumor with post chemotherapy residual mass. Our objectives are to evaluate the outcome of RA - RPLNDin term of surgical, pathological and oncological outcome. We evaluated patients for operating time, blood loss, intra -op and post op blood transfusion, conversion rate, hospital stay along with number of dissected lymph node. **Materials and methods:** A total of 10 patients underwent RA - RPLND between January 2012 to August2015 in our Institute. Study was started on January 2015 so data were collected retrospectively and prospectively regarding demography of patients, tumor characteristic and surgical, pathological and oncological outcomes. Short term and medium term outcomes were also recorded. **Results**:-Mean age of patients was 25.9 years and mean body mass index was 20.44 kg/m^2. RA - RPLND was successfully completed in all 10 patients. Mean operative time, estimated blood loss and length of hospital stay were 216.5 min, 238 ml and 3.6 days respectively.The mean yield of lymph node was 26.87. Matted lymph nodal mass was found in one patient and one patient had only single large retroperitoneal para-aortic mass of size 9x6x4.5 cm. In 9 patient modified RPLND was done and in 1 patient only large para-aortic post chemotherapy mass was excised. Out of 9 patients 7 patients underwent nerve preserving RPLND. Only 5 patients

of nerve preserving RPLND have antegrade ejaculation.Histopathological examination revealed necrosis in 7 patients whereas mature teratoma was noticed in 3 patients with one of these showing sarcomatoid differentiation too. After mean follow up period of 21.3 months, no retroperitoneal recurrence was reported. Three patients developed chyle leak in immediate post-operative period, of these two patientswere managed conservatively and another one underwent exploratory laparotomy and ligation of cysternachyli. **Conclusion:** RA - RPLND is safe and feasible for post chemotherapy residual mass with acceptable complication rate. Ours is a largest reported series till date. In literature authors have mentioned series of 7-8 cases. Though larger studies are required to establish its diagnostic and therapeutic utility.

Keywords: Testicular cancer, Retroperitoneal node dissection, Post chemotherapy residual mass

Short-term endpoints of laparoscopic assisted surgery in patients with colorectal cancer

Background: Laparoscopically assisted surgery was first conducted in 1990 for patient undergoing colectomy for cancer. A recent increase in the number of reports, retrospective analyses, and trials has now provided sufficient data to support the role of laparoscopy in colorectal cancer surgery. We, here by present our experience regarding a the feasibility, safety, short –term outcomes following laparoscopic surgery for colorectal cancers. **Methods:** From January 2013 to Dec 2015, 30 patients with primary rectal cancer underwent laparoscopic assisted surgery at our institution (kmio) Patients with rectal cancer recurrences, emergency cases , and rectal cancer treated by conventional methods, Fixed rectal cancer and metastatic rectal cancer were excluded from the study. **Results:** These preliminary data appear to suggest that rectal cancer resection can be performed by laparoscopy in accordance with established principles of cancer therapy. Operative time was 190 - 270 minutes , Reduced postoperative morbidity rate . The mean length of hospital stay was 10 days (post operative stay 3-5days)meaning Shorter post operative hospital stay and briefer use of parenteral narcotics and oral analgesics are also noted . In the laparoscopic surgery , average yield was 15 lymph nodes . There is slight increase in hospital costs. **Conclusion:** The laparoscopic approach is an acceptable alternative to open surgery for colon rectal cancer. It is also as safe and effective as laparotomy in the treatment of colorectal cancer, and was associated with increased operative time, shorter hospital stay ,less morbidity improved quality of life, and slightly increased hospital costs.

Predicting the Risk Factors for Regional Lymph Node Metastasis in Indian Patients with Penile Squamous Cell Carcinoma.

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Background: Our data represents the largest single institution experience in Indian patients with Penile Cancer. Penile Cancer is a common genitourinary malignancy in developing countries like India. The presence and the extent of lymph node metastasis is the most significant predictor of survival in patients with Penile invasive squamous cell Carcinoma. We performed the study to determine if histopathological factors of the primary penile tumour can predict the risk of development of inguinal node metastasis. **Materials and Methods:** This is a single institution prospective study of 117 indian patients with penile carcinoma between January 2012 to July 2015. All the patients who presented to us during the study period underwent treatment of the primary malignancy. Fifty two patients underwent inguinal block dissection (clinically / pathologically positive inguinal lymph nodes), no patients underwent a pelvic lymph node dissection. The parameters evaluated in the primary lesion included histopathological classification, histopathological grade, pathological stage, invasion depth, vascular invasion and the number and position of metastatic lymph nodes. Student t test and Chi-square test was used for statistical analysis. **Results:** No patients with verrucous carcinoma (n = 6) had lymph node metastasis. The rate of lymph node metastasis was 29%, 50% and 83.3% for stage pT1, pT2 and pT3 respectively ($p < 0.001$). The rate of lymph node metastasis increased with increasing grade of the primary the primary ($p = 0.002$). Among T1 tumours that constituted 85% of the study population (n = 99) , twelve patients had a positive node at presentation, that was treated. Of the remaining patients on a follow up (n = 87), 27 patients developed significant inguinal lymphadenopathy on follow up (mean follow up duration : 8.2 months) that needed to be addressed surgically. The mean depth of invasion was 9.085 mm among the patients with lymph node metastasis and 4.91mm among those with out lymph node metastasis ($p < 0.001$) **Conclusions:** Histopathological classification, stage , grade and depth of invasion of the primary disease on univariate analysis are significant predictive factors for regional lymph node metastasis in our patients with Penile Carcinoma. We propose a multi institutional randomised trial to prove this single institution study.

Keywords: Penile Carcinoma , Histopathology, Depth, Lymph node metastasis.

Short term results of laparoscopic Intersphincteric resection for lower rectal cancer

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Introduction: Radical surgical treatment for lower rectal cancer near the anus has generally been performed abdominoperineal resection. However, anal preservation is enabled by Intersphincteric resection (ISR) in selected patients with lower rectal cancer.Recently we have beenperforminglaparoscopic ISR by the merit of the effect of visibility and low invasiveness. **Objectives:** The present study aimed to evaluate the feasibility ofsafety,the oncologic outcomes, and anal function of laparoscopic ISR. **Patients and Methods:** 17 patientsunderwent laparoscopic ISRin our single institutionuntil March 2015. The basic adaptation of laparoscopic ISR in our hospital is for cT1,cT2 lower rectal tumorthat can secure DM and RM at less than 5cm from an anal verge.Wealso extended the adaptationof laparoscopic ISR for cT3/T4 lower rectal cancer after preoperative chemo radiotherapy(NACRT) recently. **Results:** There was one case that was converted to open surgery (5.9%). The operation time was 341 min (240-565 min). The blood loss was 80ml (10-1525ml). The median postoperative hospital stay was 11 days (8-25days).There was no perioperative mortality, 6 complications occurred in 6 patients, and the morbidity rate was 35.2% (6/17). Postoperative complications included ileus in 2 patients, anastomotic stenosisin 1 patient,SSI in 1 patient,urination disorder in 1 patient. However, there were no severe complications of grade ≥3b (Clavien-Dindo classification). Cancer recurrence was detected in 2 (5.6%) patients in 1 inguinal lymph node and 1 liver metastasis.Those metastatic lesions were extracted. Thus, all cases are relapse-free-survival at present. 13 cases performed the closure of the covering stoma. The anal function is good in all but one case. **Conclusions:** The present study showed laparoscopic Intersphincteric resection to have a safe postoperativecourse and to benefit oncologic outcomes.

Outcome of Patients with KRAS Exon 2 Wildtype (KRAS-wt) Metastatic Colorectal Carcinoma (mCRC) with Cetuximab-based first-line Treatment in the Noninterventional Study ERBITAG and Impact of Comorbidity and Age

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Background: Cetuximab in combination with irinotecan- or oxaliplatin-based chemotherapy has shown to increase ORR, PFS, OS of KRAS-wt mCRC patients (pts). ERBITAG aimed to evaluate safety and efficacy of cetuximab in combination with various first-line chemotherapy regimens in pts with unresectable KRAS-wt mCRC. **Methods:** KRAS-wt pts on a cetuximab-based first-line treatment with written informed consent could be enrolled in this prospective, non-interventional study. Primary endpoint was ORR, secondary endpoints were amongst others PFS, OS, TTF, and resection rate of liver metastasis. Comorbidities were documented and evaluated by the Charlson Comorbidity Index (CCI). **Results:** 817 eligible KRAS-wt mCRC pts were enrolled at 144 sites across Germany, documentations for 456 pts were finalised and evaluated. The median age was 65 [27-87] yrs, with 51.5% ≤65 yrs, 34.0% >65-75 yrs, and 14.5% >75 yrs. ECOG performance status was 0, 1, 2, or missing in 34.4%, 49.6%, 8.8%, and 7.2% of pts, respectively. CCI was 0 in 54.4%, and ≥1 in 45.6%. Resection of liver and/or lung metastases was done in 17.3% of pts, 13.4% were R0 resected. For pts with liver limited disease resection rate and R0-rate were 29.3% and 23.8%, respectively. Pts with CCI 0 had no different outcome regardless of age (table). Pts with CCI ≥1 and >75 yrs had a lower ORR and decreased TTF, pts >65-75 yrs had only a decreased TTF as compared to the ≤ 65 yrs age group (table). **Conclusions:** In this large observational trial outcomes (ORR and PFS) of KRAS-wt mCRC pts on a cetuximab-based firstline treatment were comparable to those reported in pivotal trials. Pts older than 75 yrs without comorbidities (CCI =0) showed no difference to younger pts in ORR, PFS, and TTF. Pts >75 yrs with CCI ≥ 1 had a significant lower ORR and decreased TTF.

Efficacy and Safety of First-line Cetuximab + FOLFIRI in Older and Younger Patients (pts) with RAS Wild-type (wt) Metastatic Colorectal Cancer (mCRC) in the CRYSTAL Study.

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Background: Pts with mCRC are often older, thus prompting interest in subgroup analyses based on age. Adding cetuximab to FOLFIRI in the first-line CRYSTAL trial improved progression-free survival (PFS), overall survival (OS), and objective response rate (ORR) in pts with *RAS* wt mCRC. This subgroup analysis evaluated the efficacy and safety of FOLFIRI ± cetuximab within age-defined subgroups from the *RAS*wt population of CRYSTAL. **Methods:** PFS, OS, ORR, and safety were evaluated in *RAS* wt pt subgroups in CRYSTAL, defined by age and treatment arm. Older pts were categorized as aged ≥65 y; younger pts were aged <65 y. Among pts ≥65 y, only 26 and 10 pts in the cetuximab + FOLFIRI arm and only 10 and 10 pts in the FOLFIRI arm were aged 70-75 y and ≥75 y, respectively; therefore, an analysis of an older-age cut off was not performed. **Results:** Among 367 pts with *RAS*wt tumors, 115 were older and 252 were younger. Baseline characteristics were similar between treatment arms in the younger subgroup; however, in the older subgroup, baseline ECOG status (ECOG=0; 45.9% vs 61.1%) and quality of life (>median; 36.1% vs 51.9%) favored the FOLFIRI arm This study was not designed to assess differences within and between age subgroups; therefore, interpretation is limited by baseline imbalances and the small number of older pts. Efficacy and safety data are summarized below. **Conclusions:** In *RAS* wt CRYSTAL pts, adding cetuximab to FOLFIRI improved ORR, PFS and, to a lesser extent, OS in both older and younger pts.

Impact of prophylactic treatments of cetuximab-based skin reactions in patients with metastatic colorectal carcinoma (mCRC): Interim analysis of the German noninterventional study ERBITAG.

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Background: Prophylactic treatments are widely used to ameliorate skin reactions induced by EGFR inhibition. Randomised studies have shown a positive impact of prophylactic antibiotics. **Methods:** Patients (Pts) with KRAS-wt and later RAS-wt mCRC treated with a first-line chemotherapy regimen plus cetuximab with written informed consent were eligible for this prospective, non-interventional study. Physicians were requested to complete a questionnaire and document any applied prophylactic and reactive skin toxicity treatment for every patient. Different prophylactic treatment regimens were categorized in 5 groups: systemic antibiotics (SA), skin care without antibiotics or corticosteroids (SC), other topical treatments (OT) (e.g. antibiotics or corticosteroids), any prophylaxis (P), and no prophylaxis (NP). **Results:** Data from 497 pts at 178 centers were finally collected and evaluable at data cut off. For all reported skin reactions the maximum NCI-CTCAE grade per patient and prophylactic treatment group was evaluated (table). Although none of the prophylactic regimens were significant different from NP, SA showed

			Younger (<65 y)		Older (≥65 y)	
			Cetuximab + FOLFIRI (n=117)	FOLFIRI (n=135)	Cetuximab + FOLFIRI (n=61)	FOLFIRI (n=54)
Efficacy	ORR	%	65.8	36.3	67.2	44.4
		Odds ratio (95% CI)	3.57 (2.09-6.08)		2.32 (1.07-5.02)	
	PFS	Median, mo	11.4	8.1	11.3	9.3
		HR (95% CI)	0.55 (0.38-0.81)		0.56 (0.31-1.03)	
	OS	Median, mo	28.8	19.3	26.3	24.2
		HR (95% CI)	0.61 (0.45-0.82)		0.91 (0.60-1.38)	
Safety	Any treatment related grade 3/4 AE	n (%)	78 (66.7)	56 (41.5)	47 (77.0)	31 (57.4)
	Grade 3/4 skin reaction	n (%)	24 (20.5)	1 (0.7)	15 (24.6)	1 (1.9)
	Grade 3/4 Infusion related reaction	n (%)	4 (3.4)	0	1 (1.6)	0

a numerically lower rate of all skin reactions by 8.1% (p=0.06) and of rash acneiforme by 5.3% (p=0.134) versus NP. 96.2% of reactive treatments of skin toxicities were done without consultation of a dermatologist and the medication was topical or systemic in 60.9% and 32.3%, respectively. Response to reactive treatment was complete remission or significant improvement of the skin reactions in 68.6% (topical) and 66.0% (systemic). **Conclusions:** Patients given prophylactic SA showed numerically fewer grade 3-4 skin reactions in comparison to NP (7.6% vs. 15.7%), but without significance. An important reason for failing significance may be the low number of pts receiving prophylactic SA (only in 18.5% of pts). Reactive treatment (systemic or topical) of skin toxicities led to an improvement in the majority of pts.

n = 497	All skin reactions grade 3/4 [%]	Rash acneiform grade 3/4 [%]
NP n = 198 (39.8%)	15.7	8.6
P n = 299 (60.2%)	11.4	6.4
SA n = 92 (18.5%)	7.6	3.3
SC n = 37 (7.5%)	18.9	13.5
OT n = 170 (34.2%)	11.8	6.5

Comparison of Two Definitive Chemoradiation Regimens Using Weekly Cisplatin and Capecitabine Versus Paclitaxel and Carboplatin Along with radiation Therapy in Locally Advanced Middle and Lower Carcinoma Oesophageal Cancer

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Introduction: Oesophageal cancer treatment is a multimodality appraoch with surgery, radiotherapy and chemotherapy.The standard of care for treatment of locally advanced oesophageal cancer is chemoradiation. This study was undertaken to compare regimes of cisplatinum and capecitabine versus paclitaxel and carboplatin in concurrent setting with radiation therapy in locally advanced cases of carcinoma oesophagus. **Objectives:** To compare the efficacy of two different chemotherapy regimens in a concurrent setting with radiotherapy in locally advanced oesophageal carcinoma. **Material and Methods**: A total of 50 patients who satisfied the inclusion criteria were enrolled in the study between April2014 to September2015 and randomised in two arms. Arm A patients received radiation dose of 50.4 Gy in 28 fractions along with concurrent paclitaxel 50mg/m2 and carboplatin AUC 2 i/v on day1 weekly for 5 weeks. Arm B patients received similar dose of radiotherapy along with weekly cisplatin 30mg/m2 on day1 of every week and capecitabine 800mg/m2 on day 1-5 every week. Follow up UGIE and CT scans were done for response at 4 weeks. Results were graded according to RECIST criteria. **Results:** In Arm A 52% patients showed CR as compared to 76% CR in Arm B. Toxicity profile of patients was better in Arm B as 92% of patients completed desired number of chemotherapy cycles as compared to only 80% in Arm A. **Conclusions:** In our study cisplatin and capecitabine arm emerged to be better in terms of superior response rate and favourable toxicity profile. Results although not statistically significant, but poured in favour of cisplatinum and capecitabine. It opens up broader horizon in management of carcinoma oesophagus and study needs to be evaluated on larger scale.

Role of ERK / p21 / p27 / p53 in fluoroquinolones induced cell cycle arrest and apoptosis in human Pancreatic Cancer cells

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Introduction: Pancreatic cancer is the fifth leading cause of cancer death worldwide. Poor diagnosis, single known chemotherapy & profound drug resistance have aggravated the situation. Fluoroquinolones being the broad spectrum antibiotics have the ability to cross the blood-pancreas barrier and are also comparably less toxic than current anticancer drugs. **Objectives:** Our study focuses around exploring the anticancer activity of Ciprofloxacin, Moxifloxacin & Gatifloxacin against pancreatic cancer cell lines(MIA PaCa-2 & Panc-1) and further elucidating underlying molecular mechanism respectively. **Material and Methods:** Cellular proliferation, viability & cell cycle distribution was assessed by MTT, Annexin assay, PI staining respectively in FACS. Underlying molecular mechanism was traced out using Real Time PCR & western blotting. **Results:** In our results we found out that all the 3 fluoroquinolones were able to suppress proliferation of both the cell lines in a time and dose dependent manner. Antiproliferative activity of fluoroquinolones in our study was mediated by cell cycle arrest followed by induction of apoptosis. Gatifloxacin shows its inhibitory effect only by arresting the cells in S & G2 phase of cell cycle via activation of p21/p27/p53. However, ciprofloxacin and moxifloxacin showed there anticancer effect by causing S-phase arrest & apoptosis via ERK activation. In terms of apoptosis we found ciprofloxacin to be the most effective followed by Moxifloxacin. **Conclusions:** For the first time we have convincingly observed the anticancer activity of three fluoroquinolones against pancreatic cancer. We found them to act synergistically with current chemotherapy & propose them to be as the possible neoadjuvant or adjuvant therapy for pancreatic cancer.

Recurrence pattern after radical prostatectomy: an initial experience at tertiary care centre

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Background: Prostate cancer is the fourth most common cancer in both sexes combined and the second commonest cancer in men worldwide. Data from national cancer registries show that incidence of prostate cancer is on rise in India. However, Indian data are silent on prostate cancer survival. Locally advanced prostate cancers (LAPC), i.e. those that extend beyond the prostate gland but are not metastatic, often carry a poor prognosis: between 10% and 40% of patients die within 5 years after diagnosis. The aim of this study is to see the pattern of recurrence and survival in patients with LAPC treated primarily with radical prostatectomy. **Material and Methods:** The medical records of a total of 211 cases, those had undergone surgery with procedure radical prostatectomy during July 2010 and August 2014at Rajiv Gandhi Cancer Institute and Research Centre, Delhi were reviewed.A number of 51 patients staged as LAPC after histopathological examinationpost surgery, were included in the study. The selection criteria were: cases with upfront surgery and LAPC, availability of information i.e. dietary, tobacco and alcohol intake habits, family history and complete treatment details with minimum 1 year follow-up post surgery. Biochemical recurrence along with its association with prognostic factors was assessed using. **Statistical Analyses:** The tumor grades and other prognostic parameters were evaluated to observe the association. Survival curves were drawn by the Kaplan-Meier method and differences assessed by the stratified log-rank test. **Results:** The mean and median ages at diagnosis were 65.7 (±5.6) and 65.0 (range 47-77) years respectively. The mean and median preoperative PSA levels were 27.3 (±26.8) and 20.7 (range 2.0-169.8) ng/ml. Family history was found to be positive in 31.4% of cases in this study group. On statistical analysis, biochemical recurrence was foundnot to be associated with any prognostic factor considered in the study. However, Gleason's score was observed to be in significant association with pathological stage (p=.008), lymph node involvement (p=.005) and lymph vascular invasion (p=.011). The biochemical recurrence-free survival at 36 months among patients PSA ≤20 and PSA >20 was found to be 63% and 36% respectively. However, the cancer-specific survival at 36 months among patients PSA ≤20 and PSA >20 was found to be 93% and 82% respectively. **Conclusion:** Radical prostatectomy led to favorable cancer control in more

than 80% of patients with LAPC after 3 years. Higher Gleason's score was related with higher stage of disease, presence of metastatic lymph node and lymph vascular invasion.

Role of Laparoscopy in Staging and Assessment of Resectability in Gastric Cancer

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Introduction: Peritoneal carcinomatosis or surface liver metastases which are identified during exploratory laparotomy precludes curative treatment in a significant number of gastric cancer patients. Such futile laparotomies may be avoided by doing a simple staging laparoscopy as computed tomography (CT) is neither sensitive nor specific in identifying the above. **Materials and Methods:** Out of the 106 consecutive patients,53gastric cancer patients with no obvious evidence of distant metastasis who were willing to give consent and had no contraindication for laparoscopywere included in the study.Staging laparoscopy using a standard technique was done as a part of the work-up for definitive surgery and if found operable, cases were subjected to exploratory laparotomy. CT findings and laparoscopy findings were correlated with the histopathology to draw final results. **Results:** Thirteen patients (24.53%) were found to be inoperable due to disseminated disease and 12 (22.64%)unresectable due to locally advanced disease in staging laparoscopy. 5 patients (9.4%) who had doubtful resectability on CT were found to have resectable disease on laparoscopy. Sensitivity, Specificity and diagnostic accuracy of metastatic disease with laparoscopy was 100%. Sensitivity, specificity and diagnostic accuracy for the same with CT were 75%, 94.74% & 85.32% respectively. **Conclusions:** Laparoscopy avoided laparotomy in 47.17% of patients by detecting disseminated or unresectable disease in gastric cancer patients. It also helped in deciding laparotomy in 9.4% of patients who had doubtful resectability on CT. Hence, staging laparoscopy does play a role in deciding the management plan of gastric cancer patients.

Transition of non-cancer stem cell (non CSC) into cancer stem cells (CSC) via oxidative stress

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Introduction: Colon cancer metastasis is a major constrain which increases mortality. The underlying reason for such metastasis is the induction of CSC. Earlier studies have indicated that membrane glycoproteins such as CD44 and pathophysiological conditions such as hypoxia are key players in tumor metastasis. However, it is not elucidated in colon cancers whether hypoxia can induce the transition of a wild type (WT) and non-CSC population into CSCs. Hence, we attempted to induce CSC from WT and non-CSC populations of HT-29 human colorectal adenocarcinoma cell line using two common reactive oxygen species (ROS) inducers namely hydrogen peroxide and cobalt chloride. **Objectives:** 1. Isolation of non-CSC population (CD44-) from the human colon cancer cell line HT-29 using fluorescence activated cell sorting 2. Induction of hypoxia to the WT and CD44- HT29 cells using various concentrations of hydrogen peroxide and cobalt chloride. 3. Assessment of hypoxia induction using qRT-PCR gene expression analysis for superoxide dismutase (SOD), hypoxia inducible factor 1 α (HIF-1 α) and oxygen transporter that protect against hypoxia such as cytoglobin (CYGB). 4. Assessment of transition of non-CSC and WT cells into CSC. **Material and Methods:** The human colon cancer cell line HT -29 was obtained from National Centre for Cell Science (Pune, India). The cells were cultured in Dulbecco's Modified Eagle Medium (high glucose) supplemented with 10% fetal bovine serum and 1% PenStrep in 5 % CO_2. The CD 44^+ and CD 44^- were sorted using fluorescence activated cell sorting (Biorad S3e sorter). Sorted (CD44-) and WT cells were seeded to 96 well plate and hypoxic conditions were induced by adding H_2O_2 and $CoCl_2$. SOD, Hif-1 α and CYGB gene expression pattern were studied using RNeasy mini kit and real time PCR. Transition of WT and non-CSCs into CSCs were assessed by analytical flow cytometry using CD44 as a CSC marker. **Results:** H_2O_2 and $CoCl_2$ exhibited a dose response transition of non-CSC and WT into CSC. **Conclusions:** Mechanisms of CSC induction using known oxidative stress inducers might help in CSC therapeutics.

Keywords: Colorectal Adenocarcinoma, Hypoxia, CD44

Testicular Neoplasm with Inguinal Lymphnode Metastasis - An Unusual presentation

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Introduction: Testicular neoplasm and infertility are two common complications of cryptorchidism. Early surgical treatment of undescended testis that means after the age of 3 to 6 months and before the age of 12 months old appears to lower the risk of complications. But if it is done later the risk of testicular cancer cannot be eliminated. Another important thing is that for diagnosing testicular neoplasm open biopsy or core biopsy is usually not done before operation. If it is required it is then to be done through inguinal route during surgery (Frozen section biopsy), never through scrotal route until and otherwise it has already invaded scrotal skin causing ulceration. In that case there may be chance of spreading malignancy into inguinal lymph node/nodes. **Material and Methods:** (Case report)Mr. ShamimHaider a 34 years gentle man presented with a painless swelling of left testis, which was gradually increasing in size. He had history of bilateral incompletely descended testis. He underwent surgery thrice in his boyhood. In first two episodes surgeons failed to bring both testis in position. In last episode he lost his right testis for unknown reason but left was successfully positioned into scrotum. He got married by the year 2008 and tried to take baby from 2011 but failed to conceive. Then the couple attended infertility clinic. Here he was diagnosed as a case of obstructed azoospermiaand consultant collected sperm from testis through scrotal route (TESE-- testicular sperm extraction) for in vitro fertilization. Before TESE he was prescribed with some drugs including Clomiphene Citrate for spermatogenesis. From then patient felt heaviness of left testis along with gradual increasing in size. As the patient was using drugs both consultant and patient thoughtthat it was due to inducing spermatogenesis. During consultation with me his left testis was found 7x7x5 cm in size, surface smooth, and spermatic cord could not be palpable, overlying skin not fixed. Right side of scrotum was empty and not developed. Along with these one of his left inguinal lymphnodes was also palpable, which isapproximately 2X2cm in size, mobile, non-tender, having smooth surface and firm in consistency . Para-aortic lymphnodes, liver, spleen and Virchow's gland were not palpable. CT scan revealed enlarged left testis with inhomogeneous enhancement, an enlarged lymph node in left inguinal region, no iliac or para-aortic lymphadenopathy, no liver metastasis, no mediastinal lymphadenopathy, no lung metastasis and pleural effusion. His β-hCG level was 6440.0mIU/mL (Normal- upto10mIU/mL), α-Fetoprotein 58.0 ng/mL (Normal- upto 13.6ng/mL) and LDH 233.00 U/L (Normal- <248 U/L). Left sided orchiectomy done through inguinal route with difficulties as spermatic cord was not in proper anatomical place. During orchiectomy palpable lymphnodewas also excised. Histopathology report from testis revealed malignant mixed germ cell tumor containing terateratoma and embryonal carcinoma (teratocarcinoma) with areas of haemorrhage and necrosis. Lymph node is almost completely replaced by mixed germ cell tumor containing embryonalcarcinoma and seminoma. **Conclusions:** As infertility and testicular neoplasm are two well known complications of a patient of cryptorchidism, during transscrotal retrieval of sperm for IVF careful evaluation is mandatory. Because there may be chance of dissemination of malignancy in inguinal lymphnodes if the testis had already developed malignant transformation.

Metformin induces modulation of differentiation markers in colorectal cancer in vitro

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Background: Metformin is an anti-diabetic drug that has anti-carcinogenic activity. Its anticancer activity may be attributable to its ability to induce differentiation in cancer stem cells (CSCs). CSCs areresistant to conventional chemotherapy. We wanted to investigate if inducing differentiation can help targetCSCs. **Materials and Methods:** HCT116, a colon cancer cell line was cultured *in vitro*. MTT assay helped establish maximum tolerable non-toxic dose for Metformin. The cellswere treated with selected doses of Metformin for 2-3 weeks. Metformin-induced apoptosis was evaluated using flowcytometry (Annexin V, PI). Cell cycle analysis was performed using PI. Induction of differentiation was analyzed by evaluatingexpression of CDX1 (transcription factor) by RT-PCRand appearance of Cytokeratin 20 (CK20), a positive marker of differentiation by flowcytometry. Percentage of CSCs were analysed using CSC markers- CD44 (alexafluor 647) and CD166 (PE) by flow cytometry. **Results:** On the basis of MTT results, three doses of metformin were selected – 0.5,1 and 2.5 mM.After metformin treatment for two weeks apoptosis assay revealed no significant apoptosis in cells. Cell cycle analysis revealed that with 2.5mM metformin, maximum no of cells were in G2M phase.Expression of CK20 and CDX1 was also found to be altered by flowcytometry and RT-PCR respectively. **Conclusion:** Our findings indicate that metformin may induce differentiation in the undifferentiated CSC present in colorectal cancer cell line HCT116, thereby indicating its potential therapeutic role in targeting resistant CSCs.

Key words: Cancer stem cells (CSCs), Metformin, differentiation.

Case Report a Rare Renal Tumor

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Introduction: Primary thyroid –like follicular carcinoma of the kidney is a rare but newly emerging histological variant of renal cell carcinoma RCC,with only nine cases reported in the literature to date. **Objective** : To add to the literature one more rare case of primary thyroid like follicular carcinoma of kidney. **Material and Methods**: A 57 year old woman presented to the surgeon with an incidentally diagnosed left renal mass.She had no hematuria,urinary tract infection,or lower urinary tract symptoms,no relevant past medical or family history .Physical examination of the thyroid and abdomen was normal,although in past hemithyroidectomy of the patient was done which revealed colloidgoitre ten years back.Patient is a known case of hypothyroidism ,hypertension and diabetes.Laboratorydata ,including thyroid function tests were within normal limits, and a PET CT scan revealed large well defined soft tissue density lesion arising from upper and midpolar regions of left kidney with no extension into left renal vein. There was evidence of bilateral hilar and mediastinallymphadenopathy.She subsequently underwent a left radical nephrectomy and retroperitoneal lymph node dissection and umbilical hernia repair. **Result** : Final histopathology revealed a primary thyroid like follicular variant of renal cell carcinoma with involved renal sinus and uninvolved retroperitoneal lymph nodes. **Conclusion:** Follicular variant of renal cell carcinoma is an uncommon presentation.

Keywords: Kidney,Follicular variant of renal cell carcinoma.

Rarepresentations of Seminoma Testis: Report of Two Cases

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B**ackground:** Seminoma is a malignant testicular germ cell neoplasm and is one of the most treatable and curable cancers, with a survival rate above 95% if diagnosed in early stages.Initial presentation of this tumoras an asymptomatic neck massor as intestinal tract obstruction is extremely rare and warrants discussion. **Material and Methods:** Formaline fixed surgical specimen were sectioned and paraffin embedded. Sections were stained with routine haematoxylin and eosin stain. Relevant immunohistochemical stains using avidin biotin complex technique and diaminobenzidineas chromagenwere performed for rendering definitive diagnosis. **Results: CASE 1 :** A 57 years old male presented with chief complaints of enlarging neck mass for past 4 months. On examination, a firm to hard, non tender and immobileright cervical mass of size 8x5 cm was noted. Excision of the mass was done and sent for histopathological examination. The cut surface was grey white and multinodular. Histological examination revealed the structure of lymph node completely effaced by nodules of metastatic tumor cells divided by intervening fibrous septa with a moderate lymphocytic infiltrate . Examination of these cells on higher power showed loosely cohesive large cells with vesicular nuclei, prominent eosinophilic nucleoli and clear cytoplasm. Immunohistochemical stains demonstrated the tumor cells positivity for Placental alkaline phosphatise (PLAP) and CD117, focally positivity for cytokeratin and negativity for human chorionic gonadotropin (HCG), alpha-fetoprotein (AFP), CD10, CD3, and CD20. We concluded that the metastasis from seminoma testis cannot be ruled out and patient should be investigated for the same. Testicular ultrasound did reveal a 2.0 cm heterogeneous mass of the left testicle. PET scan showed hypermetabolic activity in the cervical lymph node and two retroperitoneal lymph nodes, consistent with metastatic lymphadenopathy. Two cycles of chemotherapy has been given till now. **CASE 2:** A 40 years old male presented with chief complaints of abdominal pain and discomfort, vomiting and nausea for two months. A clinical diagnosis of intestinal obstruction was made. Exploratory laparotomy was done and a segment of duodenum measuring 12 cm in length was received in Department of pathology. On cutting open, a grey white mass of 3x3 cm was identified obliterating the lumen. Microsections examined from the growth revealed the serosalinfilteration by tumor cells arranged in nests separated by fibrous septainfilterated by lymphoid cells reaching upto the muscularispropria. Mucosa was unremarkable. Individual tumor cells were uniform in size, with abundant clear cytoplasm, clumped chromatin pattern and prominent nucleolus. Immunohistochemical examination revealed tumor cell positivity for CD 117 and PLAP. Diagnosis of metastatic deposits from seminoma was rendered and patient was advised to be investigated for testicular involvement which yielded positive results. **Conclusion:** Malignant genitourinary tumorscan and do spread to the neck and should always be considered in the differential diagnosis of a neck mass. They should also be listed as differential alongwith other cancers such as melanoma, kidney and stomach that much more commonly metastasize to the small bowel and present as intestinal obstruction or bleeding.

Exploring Distal Surgical Margin: A Hunt for Prognostic & Predictive Markers in Colorectal Cancer

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Introduction: Colorectal cancer (CRC) stands as the 3rd most commonly occurring cancer globally. Though treatment modalities has improved a lot for Colorectal cancer, still drug resistance and unavailability of prognostics or predictive markers stand as major obstacles in disease cure. Clinical studies have shown that surgical margins do have role in poor prognosis and disease recurrence in CRC. (Nash et al.2010). So we put forth our working hypothesis that exploring role of surgical margins for drug resistance cells and molecular markers could answer for the present challenges in colorectal disease treatment. **Objectives:** To dissect the cellular and molecular profile of surgical margins for developing prognostic markers that could be used for clinical intervention. **Material and Methods:** Side population study and CSCs cells enrichment by FACS, Real-time analysis, Immunohistochemistry and western blot analysis. **Results:** We analyzed the CSC population in

tumor as well as margins by side population analysis and found that distal surgical margins harbor a significant number of CSC along with tumor. To further confirm this population we immune-phenotyped cells on the basis of established CSC surface markers (EpCAM, CD44, CD133) in tumor as well as margins and found that the prior side population data represent an enriched CSC population in distal margin along with tumor. Then we screened distal surgical margin using real-time quantitative PCR for several drug resistance markers including MRP1, MDR1, ABCG2,,OCT4,SOX2 SNAIL (EMT as well as drug resistance) in CRC patients and found that these genes expression are enriched in distal surgical margins. We confirmed these findings in IHC/ IF imaging as well as immunoblotting. **Conclusions:** So our finding showed that though the distal surgical margins seems to be tumor free on simple histo-pathological analysis, but it harbors CSCs population which must be looked at for better prognosis of a CRC patient. Most importantly the post- operative treatment of a CRC patient could be decided on the basis of molecular signatures or CSCs population enrichment in distal margin.

Renal Synovial Sarcoma: Rare Case Series

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Synovial sarcomas are predominantly extremity tumors. Primary renal synovial sarcoma is a rare entity .Very few cases have been reported in literature. Clinical and radiological features are similar to renal cellcarcinoma with the diagnosis being established after surgery based on histopathology, IHC and chromosome studies. There are no established guidelines on the role of adjuvant treatment in the management of this disease. We herein present a series of 2 cases managed at our institution. In the current series, surgery was the mainstay of treatment. One patient received neoadjuvant chemotherapy after a preoperative biopsy which was done as she did not respond to chemotherapy for a presumptive diagnosis of Wilm's tumor. The other patient was diagnosed after the nephrectomy and did not receive chemotherapy. Both the patients had renal vein thrombus. Renal Synovial sarcoma is an aggressive disease with poor prognosis. Due to lack of treatment guidelines, treatment has to be individualized . Surgery plays an important role. Important to detect this subset as unlike renal cell carcinoma , Chemotherapy too has a role in management. Also we need to look into features that may help identify these pre operatively and weather this will have any impact on our treatment.

Keywords: Synovial sarcoma, renal tumors, renal sarcoma

A Clinicopathological Study of Metastatic Hepatic Lesions With Special Reference To Metastasis From Unusual Primary Site

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Background and Aim: Liver is a potential site for blood borne metastasis for many malignancies of human body, besides giving rise to primary tumor itself. Often, hepatic metastasis can be the only mode of presentation in certain tumors that prompt us to search for the primary sites. Our study aims at proving that apart from gastrointestinal malignancies, especially adenocarcinoma of pancreas, stomach, large gut, gall bladder etc, which are generally known to commonly metastasize to the liver, the liver can also be the site of metastasis from a spectrum of other unusual primary sites. **Materials and Methods:** Retrospective study of 321 cases of ultrasound guided biopsies and FNACs from liver SOL, which were correlated with previous known primary and Immunohistochemistry studies wherever possible. **Results:** Ultrasound guided biopsies and FNACs were done from liver SOL in 321 patients. 284 patients (88.5%) were primarily diagnosed as metastatic hepatic lesion, of which 80 (28.2%) cases have a spectrum of unusual primary sites like breast, lung, ovary, prostate, thyroid, kidney, urinary bladder, cervix, vulva, oral cavity and gastrointestinal sarcomas and lymphomas. While the other 96 cases (33.8%) were adenocarcinoma of gastrointestinal origin, confirmed by previous known primary and Immunohistochemistry studies. Remaining 108 out of 284 cases (38%) were diagnosed as metastatic adenocarcinoma in which primary could not be ascertained. 37 cases (11.5%) were diagnosed as primary Hepatocellular carcinoma. **Conclusion:** Metastasis to liver is much more common than primary HCC. Liver can be a site of metastasis for malignancies; from unusual sites like breast, lung, ovary, prostate, thyroid, kidney, urinary bladder, cervix, vulva etc.

Endobiliary-RF Ablation Technique for Re-establishing the Patency of Occluded Metallic Biliary Stents

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Background: Biliary drainage with the use of metallic biliary stents (MBS) is a well-accepted palliative therapy for patients with unresectable malignant hilarobstruction.These stents often lose their patency over a period of 6-9 months secondary to tumor ingrowth or overgrowth, epithelial hyperplasia. Occlusion caused by sludge deposition or clot or stone formation. Limited treatment options are available for such a condition. Endobiliary radiofrequency ablation (RFA) has been shown to be an effective modality in the treatment of malignant biliary obstruction Here we present our experience with endobiliary RFA technique for restoring the patency of occluded MBS. **Materials and Methods:** Patients were taken with previously placed MBS for malignant aetiology, presented with rising serum bilirubin and signs of cholangitis secondary to occlusion of MBS.Percutaneous trans-hepatic biliary drainage was achieved in all cases. After negotiating guide-wire across the stent, biliary drainage was established.After treating cholangitis, endobiliary-RFA was performed. Post-procedure cholangiogram was performed to ascertain the patency. Periodic clinical follow-up was scheduled for 6-months or till their survival. **Follow up and Results:** The patients were followed up clinically and with USG to a minimum of 6 months or till their survival. The presence of pneumobilia on USG along with normal LFT were considered as the signs of stent patency. All patients showed restoration of patency on cholangiography examination performed on the following day of RFA (restored diameter 6-8 mm). The mean duration of stent patency after the first session of RFA was 3.9 months (range 2-7 months) which was comparable to the primary patency of these stents (4.8 months). This extended period of stent patency ensured administration of additional cycles of chemotherapy in these patients coupled with objective improvement in the quality of life. **Summary:** Progressive tumor in growth through the openings between the struts of the stents can lead to stent block, thereby significantly reducing their primary patency. Till date little progress has been made in terms of improving the duration of stent patency for malignant strictures. Endobiliary RF ablation is a recently developed option in the management of such patients. Stent patency achieved after RFA is comparable to the primary patency of biliary stents. **Conclusion:** Our experience suggests that endobiliary-RFA with balloon-sweep maneuver can be a safe and useful technique for re-establishing the patency of occluded MBS. Reopened stent with good short term patency offers medical oncologist a chance of administering additional chemotherapy which may improve patient's survival

Lymph Node Micrometastasis in Gall Bladder Cancer

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Background: Prognosis of Gall Bladder Cancer (GBC) is grim even after curative surgery. Lymph node metastasis is the most important prognostic factor, but distant relapses occurring in their absence point towards

additional factor. Lymph node micrometastasis could be one. The present study aims to evaluate the incidence and clinical significance of lymph node micrometastasis. **Methods:** Prospective study of patients undergoing curative surgery for GBC from 1st March 2013 to 30th April 2015, at our institute. All lymph nodes were examined with Hematoxylin& Eosin (H&E) and Immunohistochemistry (IHC) against CK7. The incidence of lymph node and its relation to other clinicopathological parameters, recurrence and survival was evaluated. **Results:** Out of 589 lymph nodes retrieved from 40 patients, metastasis was seen in 13(2.20%) nodes from 8(20%) patients and micrometastasis in 4(0.68%) nodes from 3(7.5%) patients. Micrometastases were absent in pT1 tumours (0/10 in pT1 vs 3/30 in pT2-4) and more common in patients with nodal metastasis (13% vs 6%). Though, the presence of micrometastasis would have upstaged the disease, it did not statistically relate to clinicopathological parameters, recurrence and survival. **Conclusions:** Incidence of lymph node micrometastasis in GBC is low and does not relate with other clinicopathological parameters, recurrence and survival.

Keywords: Gall Bladder Cancer, Micrometastasis, Lymph Nodes

Title : Robotic Assisted Video Endoscopic Inguinal Lymphadenectomy – A Prospective Assesment of Feasibility And Morbidity

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Introduction: R-VEIL is a minimally invasive surgical technique of groin node dissection in cancer penis. We present our experience with Saphenous vein sparing (SVS) R-VEIL, to avoid complications highlighting the important surgical steps. **Methods:** From Aug 2012 to July 2014, we have performed 14 R-VEIL in 11 patients. Eight patients had unilateral, 3 patients had bilateral surgery and 5 had SVS to minimize the edema of leg. Ten had N0 groin and three had N1 groin. Technique of R-VEIL involves a 2-cm mid-thigh incision and developing a plane just deep to Camper's fascia by using finger dissection. Inguinal triangle was dissected to include both superficial and deep lymph nodes in the dissection template. The great saphenous vein was preserved after taking all its tributaries in four groins. **Results:** Mean age was 57 years (48- 66), mean console time 138 mts (110-210) for each groin, blood loss 70 ml (30-100ml). None of the patient had wound related complications like necrosis, infection. Average time for lymphorrheoa to stop was 14 days. Seven patients had edema of leg upto 3-4 weeks. Four groins with saphenous sparing surgery did not develop any edema. With mean follow up of 15 months none of the patient had local recurrence. One developed para-aortic lymph node metastasis and died of disease. **Conclusions:** SVS may reduce post operative venous edema as shown in open surgery literature and is safe and technically feasible. However longer follow up with more number of cases is required to assess the oncological safety.

Standardized Analysis of a Single-Surgeon Learning Curve for Extended Pelvic Lymph Node Dissection During Robot-Assisted Radical Cystectomy: Perioperative Outcomes And Complications

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Introduction: Extended pelvic lymph node dissection is an integral part of radical cystectomy for muscle invasive bladder cancer.We report our experience ofePLND during robot-assisted radical cystectomy (RARC) and evaluate impact of a single-surgeon learning curve (LC) for ePLND on perioperative outcomes and complications. **Materials & Methods:** We prospectively collected clinical and pathological data of 58 consecutive patients undergone RARC and ePLND by a single surgeon experienced in open surgery since June 2012. To evaluate the effect of LC on outcomes, we compared 2 subgroups(1: cases 1-20; 2: cases 21-58) with respect to lymph node yield, complications and operative time. Complications were documented and classified according to Clavien System. **Results:** Mean operative time for ePLNDin group-1 was 65mts (50-90), group-2 was 45 mts (40-70) [p=0.04]. In Group 1 two patients had intraoperative bleeding due to injury to external iliac vein treated with suturing and due to injury to internal iliac arterytreated with open conversion. One had bleeding due to injury to obturator vessels. There were no intra operative complications in Group-2. One patient in group had obturator nerve injury.Average lymph nodes dissected in the group 1 was 13 (9-18) and 19 (12-31) in group 2 (p=0.02). All patients received low molecular weight heparin and mechanical calf compression post operatively. One patient of group one and none in group 2 had deep vein thrombosis. Symptomatic lymphoceles were detected in two patient in Group-1 and three patients in Group-2 which required percutaneous drainage. **Conclusion:** A surgeon with open experience is expected to have a safe learning curve with regard to ePLND during RARC. Overall complications rates, operative time and lymph node yield improved after performing 20 cases. It looks appropriate that learning curve of 20cases is required to perform better ePLND.

Role of Laparoscopy in Predicting Surgical Outcomes in Patients Undergoing Interval Cytoreduction for Advanced Ovarian Carcinoma

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Background: Epithelial ovarian cancersusually present at anadvanced stage.Cytoreductive surgery attaining optimal cytoreduction(OCR) is the most important determinant of patient survival. Various imaging modalities including CT scan are being used to predict optimal resectabilitybefore surgery but the false negative rates are very high.Various models based on laparoscopy are found to be better in predicting operability. Faggoti et al have developed a laparoscopic predictive index to assess operability using seven parameters. The aim of this study is to assess the safety and efficacy of diagnostic laparoscopy indetecting inoperable disease in patients undergoing interval cytoreduction.Primary outcome measured was the performance of laparoscopy based score developed by Fagotti et al in our population. **Materials and Methods:** This study is a non-randomized, single arm prospective trial.Patients undergoing interval cytoreduction for advanced ovarian cancer in the department of surgical oncology, Regional cancer centre, Thiruvananthapuram , Keralawere included. Patients underwent preoperative evaluation as perinstitute protocol including complete physical examination, CT scan, chest X-ray and CA -125 levels.During diagnostic laparoscopy seven parameters including omental involvement, peritoneal carcinomatosis, diaphragmatic carcinomatosis,mesenteric retraction, bowel infiltration, stomach infiltration and liver metastasis were assessed. Optimal cytoreduction was defined as residual disease less than one cm. **Results:** Ofthe total 73 patients, 59(80.9%) patient achieved OCR and in 14(19.1%) patients OCR could not be achieved. Laparoscopy could successfully predict inoperability in 12(16.4%) patients and thus can avoid 85% of unsuccessful surgeriesat cut off of 8 Faggoti's score. Sensitivity, specificity, PPV and accuracy of laparoscopy was 85%, 100%, 100% and 97% respectively at cut off of 8. (Table 1). **Conclusions:** Laparoscopy is safe and effective in predicting inoperabilty inpatients undergoing interval cytoreduction. Type of presentation- Oral, CTRI registration no – REF/2014/05/006884 ,

Keywords: ovarian cancer, laparoscopy, interval cytoreduction

Table 1.

Laparoscopy based score	Total	OCR achieved	OCR not achieved
0	35	35	0
2	12	11	1
4	11	11	0
6	3	2	1
8	7	0	7
10	5	0	5
12	0	0	0
14	0	0	0

Outcome and morbidity after cytoreductive surgery for advanced ovarian cancer

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Introduction: Ovarian cancer presents with advanced stage disease in majority of patients and is the most common cause of death due to gynecologic cancer. Advanced ovarian cancer is managed by aggressive surgical cytoreduction followed by platinum based chemotherapy. Recent studies showed that interval cytoreduction following neoadjuvant chemotherapy had higher chance of getting optimal cytoreduction. Cytoreductive surgery including bowel resections and extensive upper abdominal surgery although essential in attaining optimal cytoreduction leads to increased post operative morbidity. **Objective:** The aim of our study was to assess the surgical outcome andpost operative morbidity in patients who underwent cytoreductive surgery for advanced ovarian cancer. **Methods:** This is a retrospective study of all patients who underwent surgical cytoreduction in our hospital from January 2013 to Decenber 2014. Demographic data, clinicopathologic characteristics, comorbidities, duration of surgery, structures resected, attainment of optmalcytoreduction (OCR), intra and post operative complications were documented. **Results**: A total of 127 patients were identified, 4 stage IVA and 94 stage IIIC disease. The mean age was 54 years (41-75 yrs). 119 patients had stage III disease and 8 patients had stage IV disease. 17 patients had primary cytoreduction and 107 had interval cytoreduction. Bowel resection was done in 21 patients, diaphramatic stripping in five and splenectomy in 3 patients. Mean duration of surgical procedure was 185 minutes (90 – 320 minutes). Optimal cytoreduction was attained in 104 (82.54%)patients . Complications were seen in 58 patients (46.4%). Age above 60 and presence of multiple co morbidities were significant predictors of post-operative morbidity. Primary cytoreduction, bowel surgery, attainment of OCR were not significantly associated with increased post operative complications. **Conclusion**: Overall post-operative complication rate is acceptable and justifies aggressive cytoreduction in advanced ovarian cancer. Elderly patients and those with multiple comorbidities should be properly assessed and preventive measures initiated before cytoreductive surgeries to prevent major complications.

Genitourinary Malignancies: Non - Prostate Cancer/ Basic Science (tumor immunology)

Cytokeratin-20 (CK-20) immunocytochemistry in urine sediment smears – A potential low-cost adjunct to cytology in urothelial carcinoma diagnosis

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Background: Urinary bladder cancer is the fifth common site of cancer in men in the capital. Urine cytology is indispensible in urothelial cancer diagnosis and surveillance. At initial diagnosis 70% patients have non-muscle invasive disease with incidence of recurrence being as high as 50-75% requiring follow-up with cystoscopy and urine cytology.The stringent surveillance protocols place extensivefinancial burden on the healthcare system.Urine cytology has a high specificity (90- 96%) but lacks sensitivity (overall 50-60%), especially for low grade tumors.Currently there are six FDA approved urine based tumor markers (sensitivity% /specificity %) namely: BTA stat®(68/74), BTA TRAK® (61/71), NMP22®(75/75), NMP22BladderChek® (55.7/85.7),ImmunoCyt™ (74/80)and UroVysion™ (77/98).Amongst these, only UroVysion™ and ImmunoCyt™ have a significantly higher sensitivity when compared to cytology alone. However since they use FISH and fluorescence IHC technology respectively, cost becomes a limiting factor.CK-20 is expressed in dysplastic as well as malignant urothelial cells but not in benign urothelium. The aim of the present study was to evaluate CK-20 immunostaining in detection of bladder carcinoma in urine sediment smears. **Material And Methods:** A retrospective study was done in 48 patients from Oct 2012 to April 2014. Papanicolau (PAP) stained smears of 150 freshly voided urine samples from 42 patients with histologically confirmed urothelial carcinoma and six non neoplastic lesions were evaluated. CK20 immunostaining was performed on PAP smears after morphological evaluation.Cells or cell clusters on each slide were marked, photographed and stored after labelling. Slides were then destained for immunostaining for CK20. Statistical analysis of data by chi-square test.

RESULTS:

Histopathology	Urine Cytology	CK 20 positive	CK 20 negative
42 urothelial carcinomas			
14 high grade lesions (HG)	14 HG	14	0
26 low grade lesions (LG)	2 HG	2	0
	3 LG	2	1
	14 inconclusive	12	2
	7 negative	1	6
2 PULMP	2 inconclusive	1	1
6 Benign lesions	Benign	0	6

Sensitivity and specificity of urine cytology in diagnosis of urothelial carcinoma was 45.2% and 97.6% respectively and that of CK20 immunostainingwas 78.6% and 96.4% respectively. The combination of cytology and CK20 was found to have an overall sensitivity of 61.9% and specificity of 97%. **Conclusions:** The sensitivity of CK20 immunostaining was found to be higher than that of cytology for detection of malignant cells on voided urine samples. CK 20 immunostaining is especially useful in low grade lesions where it helps in assigning a diagnostic category to inconclusive cases.Sensitivity of CK 20 appears to be similar to that of UroVysion™; the former being much cheaper can be a low-cost adjunct to cytology in developing nations.

Keywords: CK-20, urothelial carcinoma, sensitivity

Disclosure: Data from this work has been presented as a poster at Delhi chapter of Indian Association of Cytology.

A Retrospective Study of Video Endoscopic Inguinal Lymphadenectomy via Laterally Placed Ports versus Open Inguinal Block Dissection

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Background: Inguinal lymphadenectomy is required in the treatment of cancers draining into inguinal region. The procedure is known to have high wound related morbidity (40-60%). Video endoscopic inguinal lymphadenectomy was designed with the intention of reducing this morbidity. There are twoport positions described for this surgery: axially placed ports & hypogastric approach. We have described a new approach in which the ports are placed over the lateral aspect of the thigh andhave comparedthe results withopen inguinal block dissection (OIBD). **Materials and Methods:** We retrospectively compared our short termoutcomes of video endoscopic inguinal lymphadenectomyvia laterally placed ports (L-VEIL)with that of OIBDperformed between2011 to 2014. A total of 90 inguinal block dissectionswere performed in this period. Of which 65 were OIBD and 25 wereL-VEIL. The primary disease in these cases included penile cancer, vulvar cancer, melanoma of lower limb and anal canal melanomas. **Results:** Of the 90procedures, 45 were performed on female and rest on males. Of these 65 were OIBD and 25 were L-VEIL. Operative time was 70 to 120 min for L-VEIL and 60 to 90 min for OIBD. Blood loss was 10-20ml for L-VEIL and 30-40 ml for open surgery. None of the cases needed conversion. Mean hospital stay for L-VEIL was 3.5 days & for OIBD was 12.3 days ($p<0.0001$). Mean day of drain removal was 5.5 vs 8.4 for L-VEILvsOIBD ($p<0.001$). Mean nodal yield was 10.2 vs 11.3 for L-VEILvsOIBD ($p=0.632$). The major complications of OIBD were wound infection without necrosis (38%), flap necrosis (15%), lymphorrhea (15%) and lymphedema (10%). The major complications of L-VEIL were lymphocele (4%), minor flap necrosis (4%) and lymphedema (8%). **Conclusions:** Our results indicate that L-VEIL is safe and effective procedure for addressing inguinal region. The pathological outcomes are similar to that of OIBD with better complication rates and shorter hospital stay. We also find that the lateral port position has several advantages over the axial port placement. The lateral position is ergonomically better for the surgeon and involves less amount of flap elevation. Saphenous vein is better visualised. Like in open surgery lateral medial dissection of nodes can be performed with better visualisation of femoral vessels.

Study of Factors to Predict Recurrence in Early Stage Endometrial Cancer

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Introduction: Risk stratification of patients with early endometrial cancer for recurrence is inadequate. **Objectives:** To study factors that influence recurrence in uterus- confined, early stage endometrial cancer (UCD). **Material and Methods:** We studied140 consecutive patients with endometrial cancer, operated at Action Cancer Hospital, Delhi, from August 2010 to September 2015. All patients underwent staging laparotomy, TAH +BSO +B/l pelvic lymphadenectomy +para-aortic LN sampling, and omental biopsy. Adjuvant treatment was given as per the NCCN guidelines. They were followed up 3 monthly for 2 years, and 6 monthly thereafter. 121 patients (86.4%) had UCD (FIGO stages IA, IB, II). Excluding one post-operative mortality, and 4 who were lost to follow up, we included 116 patients in this study. **Results:** The median age of these patients was 60.5 years (range:35-81 years), with median BMI of 31.2 kg/m2 (range=19.8-57.5). Diabetes or hypertension was present in either or both of 76 (65.5%) patients. The median pelvic LN harvest was 17 (range: 4-42). Eight (6.9%) patients had non-endometroid histology, and 5 (4.3%) patients had LVSI. Grade 1, 2, and 3 tumor was found in 74 (63.8%), 30 (25.9%), and 12 (10.3%) patients, respectively.The median follow up was 28 months (range 5-61 months), and recurrence was seen in 13 (11.2%) patients. On univariate analysis we found that age, co-morbidities (DM and HT), LVSI, and non-endometroid histology were related to recurrence. The tumor grade and adjuvant treatment did not influence recurrence rates. On multivariate analysis, presence of comorbidities and non-endometroid histology were independently related to disease recurrence ($p=0.044$, and 0.011, respectively). **Conclusions:** Disease recurrence was seen in one in ten patients with UCD, despite stage-appropriate treatment. Presence of co-morbidities and non-endometroid histology were independently related to recurrence

Evaluation of Co-testing for Cervical Screening Tests in Detection of High Grade Cervical Intraepithelial Neoplasia

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Background: Isolated cervical screening tests having varying and sufficiently not adequate. Aim was to evaluate the co-testing of conventional cervical screening tests such as Papanicolou (Pap) and visual inspection cervix and acetic acid (VIA) with careHPV on cervical samples (CHPV) or on vaginal samples (VHPV) in the detection of high grade CIN. **Methods:** All ever married women of age 30 to 59 years surveyed in a study of cross-sectional type in a rural community setting targeted for screening by CHPV, VHPV ,Pap and VIA methods. Confirmation of screen positives was done by histology. Importance of co-testing of CareHPV, Pap and VIA screening tests was assessed by positive and negative likelihood ratio tests for detection of Cervical Intraepithelial Neoplasia (CIN) of high grades CIN II + and CINIII+. **Results:** Of the total eligible women, responded for screening were 64.8% (5032/7704) and further analysis was on 4658 after excluding those who did not complete all screenings. Co-testing of CHPV (OR=246) or VHPV (OR=278) with Pap had highest association. Positive likelihood ratios of CHPVand VHPV with Pap in CINII+ detection were 13.0 and 11.8 and in CINIII+ detection were 18.0 and 16.0 respectively. Higher sensitivities and specificities observed in co-testing for CINIII+ detection as against CINII+. **Conclusion:** Choice of co-testing in a pair of tests for detection of high grade CIN depends on whether screening targeted for developed or low resource country. Co-testing of CHPV or VHPV with Pap performed best and next choice could be of with CHPV with VIA or Pap with VIA.

Keywords: Care HPV screening, cervical cancer, rural community

Long Term Results of Post-operative Pelvic Image Guided Intensity Modulated Radiotherapy in Gynecological Malignancies

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Background: Conventional whole pelvic radiotherapy is commonly employed in the treatment of gynecological malignancies. Image guided intensity modulated radiotherapy (IG-IMRT) may be helpful in minimizing the dose to critical structures like bladder, bowel and rectum in post operative gynecological(cervix and endometrium) patients that may reduce long term complications. Here we are presenting our experience with this modern technique at median follow up of 22 months. **Methods and Materials:** In this prospective study patients having at least 6 months of follow up after completion of radiotherapy were evaluated. All patients underwent surgery followed by adjuvant radiotherapy (IG-IMRT followed by brachytherapy). Contouring and toxicity grading was done according to RTOG guidelines. Dose prescribed to clinical target volume (postop bed and nodal volume) was 50.4 Gy followed by intravaginal brachytherapy. Most of the patients received brachytherapy at the dose of 7Gy in 3 fractions. **Results:** 80 patients were evaluated who were treated between January 2009 to December 2014.Median age of our patients was 56(31-75) years. Out of eighty,forty four patients were of carcinoma endometrium and rest were of carcinoma cervix.80% patients underwent radical surgery and 20% had TAH&BSO. 77.5%patients had stage 1 or 2 disease and 22.5% had stage 3 disease.Median follow up was 22 months (6-80). 5% (four) patients had late grade1 and 1.25% (one) grade 2 bladder toxicity.Our seven patients (8.75%) experienced late gastrointestinal toxicities .Out of these five(6.25%)patients had grade 3 or 4 toxicity.2.5% patients developed local recurrence,6.25% patient

developed nodal with distant metastases and 7.5% only distant metastases. Two of our patients developed lung cancer as second primary during follow up.80% patients are alive with regular follow up. **Conclusions:** WithIG-IMRT, bladder and gastrointestinal toxicity are much reduced in comparison with conventional radiotherapy as reported in literature and survival is also comparable. Henceforth IG-IMRT can be recommended as standard option for treatment of gynecological malignancies.

Keywords: Image guided intensity modulated radiotherapy,Gynecological malignancy, Gastrointestinal toxicity

Evolution of Surgical Complexity in Ovarian Cancer Since Adoption of R0 Resection Strategy

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Background: Complete cytoreduction (R0) improves survival in advanced ovarian cancer compared to optimal cytoreduction (< 1cm residual disease). In our institution, we instituted a change in practice since January 2015. **Aim**:-To compare the trend change in SCS (Aletti score) since adopting R0 resection for primary (PDS) and interval debulkingsurgery(IDS). **Methods:** Retrospective observational study. SCS was calculated from operation records obtained through hospital electronic database and compared between PDS and IDS at 6 monthly treatment periods P1- P7(P1:Jan - Jun 2012,P7:Jan-June 2015). **Result:**169 cases were evaluated; 56 PDS and 113 IDS. There was an increasing trend for performing PDS:P1-3/56 (5.35%); P2- 8/56 (14.28%),P3 -3/56(5.35%) P4 8/56(14.28%),P5 4/56(7.14%)P6 10/56(17.85%), P7- 20/56 (35.71%). Major resection procedures for PDS & IDS were: Diaphragm (30.35% vs. 13.27%), Pelvic peritoneum (41% vs. 18 %), Abdominal Peritoneum (21 % vs.20 %) Rectosigmoidectomy anastomosis(19% vs.16.81 %),Splenectomy (14.28%vs.7.07%), Small bowel(8.92 % vs.3.5%), Total Colectomy(5.35 vs. 0),lesser sac tumour(14.28 vs.2.65),portahepatistumor(8.92 vs. 0), Distal pancreatectomy(5.35 % vs. 0 %).There was an increasing trend for SCS in PDS; Mean SCS for PDS vs IDS was as follows: P1 (4.0 vs5.05),P2 (3.5 vs 4.09)and P3 (4.0 vs 5.31), P4 (3.5 vs 4.6),P5(4 vs 6.88),P6(5.6vs6.13) and P7(9.85vs 7.86) which may reflect selection bias for PDS prior to 2015. Optimal cytoreduction rates (OCR <1cm residual disease) and Complete cytoreduction (CCR-R0) rates were as follows: P1: IDS-OCR n1, IDS-CCR n2, PDS-OCR n3, PDS-CCR n4 till P7. **Conclusion**. There is increase in surgical complexity with R0 resection and PDS. Detailedprospective recording with regular audit of practice and outcome should be mandatory.

Malignant Germ Cell Ovarian Tumours Managed in B.P. Koirala Memorial Cancer Hospital

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Background: Germ cell malignancies account for about 5% of all ovarian cancers. These tumours grow rapidly and often produce symptoms quicker than the slow growing epithelial tumour. Commonly seen in the first two decades of life germ cell malignancies are highly chemosensitive and are potentially curable with surgery and chemotherapy. This study is the first of its kind regarding the epidemiology, management and outcome of patients with malignant germ cell tumour in Nepal. **Objective:** To analyze the clinical presentation and management outcomes of malignant germ cell tumours managed in B.P. Koirala Memorial Cancer Hospital, Nepal. **Methodology:** Descriptive study conducted in B.P. Koirala Memorial Cancer Hospital, Nepal. Case records of malignant germ cell tumours attending the hospital from January 1999 to December 2009 were analyzed regarding their illness history, clinical examination, investigations, treatment, follow-up and outcomes measured. **Observations:** Total 65 cases of malignant germ cell tumours with age range from 2 to 58 years (mean 21.7 years) were received. 42% cases were Tibeto-Burmese; 30% were Indo-Aryans. There were 15 cases (23 %) of dysgeminoma, 21 endodermal sinus tumor (32 %), 16 Immature Cystic Teratoma (24.5 %), 9 (14 %) Mixed Germ Cell, 2 unclassified GCT (3.5%) and 2 malignant transformation in teratoma (3,5%). 33 (49.5%) patients had early stage disease, 37 (57%) underwent fertility preserving surgery. 4 cases (9%) due to disseminated disease, underwent neoadjuvant chemotherapy followed by debulking surgery. 51 cases (78.5%) received adjuvant chemotherapy (BEP or EP regimen). The overall survival was 70%. **Conclusion:** Early stage germ cell malignancies can be safely managed by fertility preserving surgery followed by, chemotherapy if indicated. For advanced diseases, neoadjuvant chemotherapy followed by surgery can be undertaken with curable intent.

Unsatisfactory Conventional Cervicovaginal Smears: Why Do They Occur? (Poster)

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Introduction: Unsatisfactory cervicovaginal smears pose a screening challenge as well as represent an unrealized or missed screening opportunity. Since longitudinal studies have demonstrated higher risk of subsequent detection of epithelial abnormalities in such women, it becomes prudent to analyze the clinic-morphologic parameters of unsatisfactory smears. **Objectives:** To investigate clinical and cytomorphological determinants of unsatisfactory conventional Papanicolaou (Pap) smears. **Material and Methods:** This was a retrospective study of 82,108 conventional cervicovaginal smears received over a ten-year period. Various clinical parameters including age and history of surgical or other therapies were evaluated in relation to unsatisfactory smear outcome. Morphologic reasons for unsatisfactory results, i.e. cellularity, obscuration by blood and/or inflammation and drying artefact were compared in the group with history of hysterectomy or other treatments and the group without such history. **Results:** The overall unsatisfactory rate on conventional cervicovaginal cytology was 4.9%. On classification, this rate was 12.5% in post-treatment group vs 4.6% in non-treatment group. Advanced age (≥45 years) and history of hysterectomy, radiotherapy or chemotherapy were all found to be significantly associated with unsatisfactory smear outcomes ($P<0.001$). Morphologic determinants of unsatisfactory smear were also more frequent in the post-treatment group compared to non-treatment group. **Conclusion:** Older age and prior history of hysterectomy, radiotherapy or chemotherapy have a significant bearing on unsatisfactory outcome of Pap smear. Such patients should be identified in the clinic and extra care taken during

Simultaneous ^{68}Ga PSMA PET/MRI in Evaluation of Prostate Cancer-Initial Results and Preliminary Experience

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Aim: At present, Positron emission tomography (PET) combined with computed tomography (CT) is considered as the most accurate method of oncologic staging of recurrent prostate cancer. However PET/CT is marred by the limited soft tissue contrast of CT which may be overcome using a fully integrated, whole body simultaneous PET/MRI system combining high-resolution simultaneous morphologic and functional data. The purpose of this study was to assess the feasibility and the utility of whole body simultaneous ^{68}Ga PSMA PET/MRI in restaging recurrent prostrate carcinoma. **Materials and methods:** 38 patients with biopsy/ histopathologyproven prostrate adenocarcinoma (9 staging; 29 restaging

evaluationpost-surgery, radiotherapy or hormonal therapy) with raised serum PSA or clinical suspicion of recurrence underwent simultaneous PET/MRI using ^{68}Ga-PSMA-HBED-CC tracer. Prostatic bed recurrent lesion, nodes and metastases were evaluated on PET, MRI and PET/MRI for lesion count and diagnostic confidence (DC). Histopathology, clinical/imaging follow-up served as the reference standard. **Results:** 4/9 patients with raised serum PSA, referred for staging evaluation, had incidentally diagnosed adenocarcinoma on TURP. On PSMA PET/MRI, 2 did not reveal any locoregional or distant metastatic disease, 5 showed local organ-confined residual/multifocal disease and 1 demonstrated extensive local disease with bladder infiltration. 1/9 patient demonstrated organ confined local residual disease with PSMA avid pelvic and extra-pelvic nodal disease (28) and osseous metastasis (2). Of remaining 29 patients referred for restaging post treatment, 8 did not reveal any locoregional or distant metastatic disease on follow up; 4demonstrated only local recurrence in prostatic bed, 13 had lymph nodal involvement with upto 128 distinct lymph nodal lesions (41 pelvic and 87 extrapelvic) and 12 had distant metastasis yielding more than 54 distinct bony, brain, hepatic and lung metastatic lesions. PET/MRI demonstrated highest diagnostic confidence score as compared to PET or MRI alone. MRI demonstrated additional suspicious brain, bony and hepatic lesions, most of which were small sized and revealed either increased size on follow up imaging or resolution post RT. Apart from distinctly detectable larger nodal and bone lesions, ^{68}Ga-PSMA PET/MRI identified smaller metastases and small sized lymph nodal involvement. **Conclusions:** Preliminaryresults indicate evolving utility of ^{68}Ga-PSMA PET/MRI for initial staging and restaging prostate cancer. Possible incremental benefit of ^{68}Ga-PSMA PET/MRI compared to MRI or PSMA PET alone may translate into improved management.

Cervical Cytological Abnormalities and Human Papilloma Virus Infection in Women Infected with Human Immunodeficiency Virus in Southern India

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Background: To examine the association between CD4 count, HPV infection and the risk of cervical intraepithelial neoplasia (CIN) among HIV-infected women. **Methods**: A cross-sectional study was conducted among 104 HIV-infected women attending an antiretroviral therapy clinic. They underwent Pap smear and cervical HPV DNA testing. **Results:** The overall prevalence of HPV infection was 57.7%. HPV 16 was the commonest genotype found (38.5%); both HPV 16 and 18 contributed to 73.3% of HPV infection; 27.5% of HIV-infected women had squamous cell abnormalities. CIN was less likely among women with CD4 count >500/mm^3 (12%) and in those without opportunistic infections (17.8%). The prevalence of high risk HPV infection was higher in women with HSIL or greater lesions (85.7%) as compared to women with normal cytology (52.1%). **Conclusion:** The high prevalence of HPV infection and cervical intraepithelial neoplasia in HIV infected women warrant the need for regular Pap smear screening in these women and routine HPV vaccination for adolescents to reduce the burden of cervical cancer in India.

Keywords: HPV, HIV, Pap smear, cervical intraepithelial neoplasia

Vulvar Cancer: Patterns of Recurrence and Clinicopathological Prognostic Factors Involved in Recurrent Cases

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Background: Vulvar cancer is a rare gynaecologic malignancy and surgery remains the mainstay of management, with radiation or chemoradiation reserved for locally advanced and unresectable disease.The prognosis is generally good when using this multimodality approach; however, treatments are associated with significant morbidity and up to 40%–50% patients eventually develop recurrence [1,2].Given the rarity of the tumour, the information regarding prognostic factors involved recurrent cases is limited and conflicting.The psychosexual impact that radical surgical procedures have on the general well being of a patient has been well known for many years. This has lead to changing paradigms in the surgical management from the radical enbloc procedures to triple incision techniques, radical local .To walk this fine balance of maintaining the oncological safety and yet preserving the basic psychosexual quality of life is debatable and contentious until today. **Materials and Methods:** For this retrospective analysis, we retrieved the case records of all the vulvar cancer patients who were treated at our centre between 2007 and 2014. Information regarding patient's demography, clinical findings, treatment given, complications and follow-up details was collected. **Inclusion Criteria:** All patients of vulvar cancer undergoing primary surgery from January 2007 to January 2014 were analysed. Endpoints for this study were presence recurrent disease (locoregional, groin or distant), death, or last follow-up. Statistical analysis done using SPSS software, log-rank test and Kaplan-Meier curves; p-value<0.05 was considered statistically. **Results:** Eighty seven patients with primary vulvar cancer underwent surgery at Rajiv Gandhi Cancer Institute between 2007 to 20014. Nine cases were lost to follow up immediately after surgery and were excluded from further analysis. Seventeen patients (21.7%) had recurrent disease after a mean interval of 15 months (median 16, range 6-19 months). Nodal status, tumour classification, depth of invasion, lympho-vascular space invasion and resection margin came as being statistically significant prognostic factors for disease free and overall survivors by univariate analysis. On multivariate analysis, only tumour size, nodal positivity and margin status appeared as being statistically significant. **Conclusion :**In analogy to other gynaecological malignancies, clinicopathological patterns could help to stratify patients for adjuvant radiotherapy of the vulva. Intensified vulvoscopic follow-up needed to prevent multiple local recurrences especially those with high-risk prognostic factors. Our study has also raised a point about giving local vulvar radiation in these high-risk groups of patients in order to prevent local recurrences.

Audit on the Role and Efficacy of PET/CT in Recurrent Ovarian Cancer Settings in a Tertiary Care Centre in India

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Ovarian cancers tend to recur in 15-70 % cases .CA-125 - is a tumor marker used for monitoring therapeutic response, and in surveillance, for recurrent disease. However, it has a limited role as a persistent high level can signify either recurrence or persistence of residual tumor. Metastases from ovarian cancer primarily involve the peritoneum rather than parenchymal sites; thus, the presence of small-volume recurrence or metastatic deposits on the visceral surfaces poses a challenge for interpretation of CT and MR images. PET/CT utilizes its property of higher accumulation in malignant cells to provide both anatomic and functional information for diagnosing malignant tumors. **Objectives:** The objectives of the study were to find the correlation between PET/CT findings and final histopathological diagnosis after a secondary cytoreductive surgery in suspected ovarian cancer recurrences. **Materials and Methods:** PET/CT was done in cases with rising or above normal CA-125 and no radiological findings .These patients with abnormal PET/CT findings were taken up for a secondary cytoreductive surgery and histopathological proven were taken as the standard against which PET/CT positive findings was compared. **Results:** The mean age in our group of patients with suspected recurrence was 53 years(Range 39-74 years). Of the 52 patients with suspected recurrence, 40 patietnts with a PET-CT scan with findings suggestive of an avid uptake underwent surgery.22 patients had serous histology, 12 mucinous and 8 had clear cell carcinoma. Stage-wise distribution at the time of primary surgery is as follows stage I-3, stage II-7 , stage III-26, stage IV-4.Of the 40 patients who underwent a second look surgery 32 had histopathologically confirmed recurrence. PET-CT

detected a total of 86 lesions in the 40 patients who underwent surgery. Of these, 38 were in the lymph nodes 28 in para-aortic and 10 in pelvic , 32 were peritoneal lesions and 14 were pelvic, 2 were metastatic in the parenchyma of liver. Detection of the lesion on PET-CT was size dependant, of the 9 lesions were missed on PET-CT , 7 were less than 0.5 cm. The mean diameter of the lesions detected was 2.2cm (range 0.3-6.2 cm). PET-CT accurately identified 62 of 70 histopathologically proven lesions.The overall lesion-based sensitivity of PET-CT is 88.6%, specificity 56.2%, Positive predictive value being 72.1%, negative predictive value of 69.2%. Accuracy of detecting lesions greater than 1cm is 78.6% (44 of 56 lesions). **Conclusions:** Corelation between PET/CT and histopathologicaldisease : k (cohen value)= 0.81 which suggests excellent correlation.For selected patients with ovarian cancer recurrence may benefit from a comprehensive radiographic imaging survey (PET-CT) at the time of even no or minimal CA-125 elevation in early detection and successful cytoreductive surgical resection and an increase in overall survival.

Outcome Analysis of Robotic Partial Nephrectomy Cases: A Dedicated Robotic Uro-Oncology Centre Experience

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Introduction: Nephron Sparing Surgery (NSS) has become gold standard treatment modality for small renal masses because of conclusive evidence of reduced incidence of Chronic Kidney Disease (CKD) and ultimately mortality related to Cardio Vascular Disease. Various series have noted equal Oncological outcomes, Renal Function recovery and margin positivity rates with Robotic and Open NSS procedures. **Objectives:** The present study on Robotic NSS was carried out in this dedicated tertiary care Uro-oncology centre with an objective to find out incidence of perioperative and long term complication rates, Margin positivity, Oncological outcomes and renal functional recovery of Robotic NSS cases with a minimum of two years follow up period. **Material and Methods:** A total of 31 Robotic Partial Nephrectomy cases were selected in the present study after obtaining Institutional Ethics Committee approval. All patients underwent Routine haematological evaluation. 29 out of 31 patients had CE CT Scan of Abdomen for radiological and anatomical confirmation before study. All patients had DTPA based estimated GFR assessment as part of study protocol. PADUA score was calculated for all patients in the initial work up. All the patients were operated by a single Robotic Surgeon in our centre. All cases were performed by da Vinci Si Robotic system. Perioperative data as well as clinical and pathologic outcomes data were retrospectively reviewed. Patients were followed up after hospital discharge with serial physical examination including measurement of Blood Pressure at each visit and local abdominal examination at 1 month and the 3 monthly for 2 years. Serum Creatinine assessments was done at each visit. DTPA based GFR assessment was done as part of study protocol end of third month and one year. Ultrasound Abdomen scan was performed at every visit starting from third month of surgery. Yearly CECT scan of abdomen was done only in cases where post operative Histopathology was T2b or higher or Lymph node positive cases. **Results:** In our series24 patients were male and 7 were female with median age of 54 years. Majority of Patients fell in ASA grade 2 due to associated co-morbidity. Mean operative time was 192 mins (range 98-353 mins) and mean blood loss was 140 ml (range 50-700 ml).Mean warm ischaemia time was 19 min (7-30 min) with mean hospital stay of 4.7 days (3-8 days).None of the patients required Intraoperative conversion to open procedure. There was only minor postop complication in 6 patients. Mean tumor size was 3.5 cm with clear cell histology predominance. Majority of case were in stage pT1a (64.5%) f/b pT2b (25.8%). At 2 year follow up 3 patients developed worsening of CKD with no local recurrence. 20 patients had hypertension. **Conclusions:** Robotic Nephron Sparing Surgery offers a feasible alternative to open and laparoscopic partial nephrectomy for the treatment of small renal masses. The perioperative and postoperative outcomes including blood loss, hospital stay, complications, warm ischemia time and renal functional recovery make Robotic NSS an attractive treatment option for the management of Small Renal Masses.

Over View of Clinical Presentation, Management and Outcome of Cervical Cancer- A Tertiary Cancer Centre Experience

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Objectives: To understand the profile of cervical cancer patients attending our hospital from January 2011 till January 2015.

- To audit the type of care given to the patients with respect to their stage at presentation
- To compare the outcomes of open v/s robotic radical hysterectomy done for cervical cancer.

Methods: We prospectively analyzed all cases of cervical cancer from January 2011 to January 2015 presenting at our institute. Data was retrieved from patient's records and institute's tumor registry. We compared all patients undergoing open v/s robotic RH. All the data were analysed using SPSS version 21. **Results:** A total of 562 patients were treated for cervical cancer during the time period between 2011-2015. Of these there were 316 (56%) cases taken up for surgery- 212 robotic RH, 104 open radical hysterectomy and rest 246 (44%) patients received definitive CCRT. Most common age group was 40-54 yrs. IB1 stage was most common presenting stage. SCC was most common histology (75%). Immediate post op complication and oncological safety in terms of local recurrence was same in both groups. However length of stay and post operative blood requirement was significantly lower in robotic RH group. 45% of all patients who underwent surgery did not require adjuvant therapy in post op period while 35% patient required post op RT and 20% CCRT. 2.2% patient had local recurrence and most of the patients were in stage IIA1 at presentation. **Conclusion:** Cervical cancer is the most common gynecological cancer in our hospital registry. Mostly women were in the age group of 40-54 years. Most common stage at presentation was 1B and the histology being SCC. Not many differences seen in open v/s robotic techniques of radical hysterectomy except for shorter hospital stay and less need of blood transfusion in the robotic group. Local recurrence rates are comparable in both open and robotic groups

Keywords: Robotic radical hysterectomy, Open radical hysterectomy, Cervical cancer

Spectrum of Neoplastic Lesions in Hysterectomy Specimens: Tertiary Care Experience Gynaecological cancer

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Background: To evaluate the relative frequency of various benign and malignant lesions on histopathological examination and their distribution in relation to the anatomical sites in the hysterectomy specimens. **Material and Methods:** A total of 915 consecutive hysterectomy specimens with and without salpingo-opherectomy received in a tertiary care centre were included in the study.The specimens were examined, fixed,processed and microscopic examination done, Histopathological findings noted and various lesions of cervix, uterus, fallopian tube, and ovary were classified as per the World Health Organisation system of classification of tumours of female genital organs. Data collected was analysed using Descriptive statistics and Chi-square test. **Results:** Neoplastic lesions were seen in 745/915(81.4%) cases. Uterine tumours constituted majority of the neoplasms as seen in 586(78.7%), followed

by cervical lesions in 92(12.4%) while ovarian tumours accounted 67(8.9%) cases. Of the tumours percentage of malignant tumours were most in ovary 39/92(42.3%), followed by cervix 34/92(36.9%), endometrium18/92(19.5%) and least in myometrium 1/92(1.0%) while benign tumours were seen most in myometrium 504/653(77.1%), followed by endometrium 63/653(9.6%), cervix 58/653(8.8%) and ovary in 28/653 (4.2%) cases. **Conclusions:** The present study on histopathological examination of hysterectomy specimens displayed a wide spectrum of neoplasms. Benign neoplasms were seen mostly in perimenopausal age whilemalignant neoplasms in postmenopausal age group.

Keywords: Histopathology, hysterectomy, neoplasm

Evaluation of Concurrent Chemoradiation with Neoadjuvant and Adjuvant Chemotherapy Versus Concurrent Chemoradiation Alone in Locally Advanced Carcinoma Cervix: An Update on 150 Patients

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Background: Concurrent chemoradiation is a standard treatment for locally advanced carcinoma cervix and has improved survival outcomes compared to radiation alone. Despite an improved survival rate with concurrent chemoradiation against radiation therapy alone, local and distant failures (17% and 18%, respectively) of locally advanced carcinoma cervix are encountered with overall survival rates ranging from 60 to 65%. One method of improving treatment outcomes among these patients is to give additional chemotherapy along with the main treatment of concurrent chemoradiation therapy. **Aim:** Aim of the study was to compare concurrent chemoradiation with neoadjuvant and adjuvant chemotherapy versus concurrent chemoradiation alone in locally advanced carcinoma cervix in terms of treatment response and toxicities. **Material & Methods:** A randomized control study was done on 150 patients of locally advanced carcinoma cervix (stage IIB to IIIB) registered in Department of Radiotherapy, King George's Medical University, Lucknow, Uttar Pradesh between January 2014 to May 2015. Patients were randomly divided to receive either one cycle of cisplatin / 5-FU neoadjuvant chemotherapy and two cycles of same adjuvant chemotherapy with concurrent chemoradiation (Arm A) or only concurrent chemoradiation (Arm B). All patients received three fractions of HDR intracavitary brachytherapy. **Results:** A higher proportion of patients of chemotherapy arm achieved complete local control as compared to the non-chemotherapy arm, and this was statistically significant. There was a trend toward more treatment related acute toxicity with chemotherapy. **Conclusion:** These results have corroborated the view that if neoadjuvant and adjuvant chemotherapy are added to concurrent chemoradiation, it could further the effects of concurrent chemoradiation for patients with locally advanced cancer of uterine cervix.

Prevalence of Abnormal Cervical Cytology in Indonesian Population

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Background: Cervical cancer is the most common gynecological cancer in Indonesia, however prevalence of precancerous cervical lesion on screening program is not available yet. In this study we investigated the prevalence of various abnormal cervical cytology and possible risk factors of abnormal cervical cytology on Indonesian population. **Methods:** This cross-sectional study was conducted by sampling cervical material in Cipatujah a rural- and Cirebon an urban- region on West Java, Indonesia. The Bethesda 2011 System (TBS) was used for cytological diagnosis of liquid-based Pap smear. For each region odds ratios (ORs) and 95% confidence intervals (CIs) were calculated using the Multiple Logistic Regression method to estimate the association between cytological abnormalities and demographic risk factors. **Results:** In total, there were 273 women with average age of 35.7 years (SD±7.34). Epithelial cells abnormalities were detected in 4% samples, atypical squamous cells of undetermined significance (ASCUS) in 0.2%, low grade squamous intraepithelial lesion (LSIL) in 3.4% and high grade squamous intraepithelial lesion (HSIL) 0.4%. The precancerous lesions was more frequent in rural compared to urban region but the differences was not significant. Among the demographic factors, number of marriages was most associated with abnormal cervical cytology findings (OR 1.81 95% CI 1.31–2.51). **Conclusion:** Precancerous cervical lesions and risk factors are not uncommon in our set up and can be diagnosed early by pap smears.

Imrt in Carcinoma Cervix – Maximizing the Gain And Nipping the Side Effects – Rgci Experience

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Objective: To present a single institutional experience with acute toxicity, patterns of failure and survival in carcinoma cervix treated using definitive radiotherapy with IMRT technique. **Methods:** It is a retrospective analysis of 64 patients with carcinoma cervix treated with definitive chemoradiation (IMRT) from April 2011 to Jan 2013. Patients with squamous or adenocarcinoma histology and no metastasis, treated with definitive radiotherapy (IMRT) with or without concurrent chemotherapy were included.Acute toxicities were presented as proportions and kaplainmeier computation was done to calculate 3 years disease free survival (DFS) and 3 years overall survival (OS). **Results:** Median follow up was _months for the entire cohort. Mean age was 55.9 years (SD 9.93). Majority of patients (92.8%) had locally advanced disease (FIGO II and III)and squamous cell carcinoma (96.9%). Mean dose to pelvis with IMRT was 49.75 Gy (SD 1.78) followed by ICRT, EBRT boost and implant in 79.7%, 17.2% and 3.1%respectively (as indicated). Response evaluation done at 3 months of treatment completion showed 83.6% complete response, 11.5% partial response and 4.9% progressive disease. During follow up 21.6 % developed recurrence - 44.4 % failed locally, 16.7 % at para-aortic nodal region and 38.9 % at distant sites. The 3 year DFS and OS was 70.8 % and 60.3 % respectively. Patients had tolerable acute toxicities. Incidences of grade ≥3 acute toxicity were 3.1% for anemia, 10.9 % for neutropenia, 25 % for thrombocytopenia, 1.5 % for nausea, 0% for vomiting, 12 % for GU and 12 % for GI toxicities. Incidence of grade I, II and III radiation dermatitis were 38.89%, 27.78 % and 22.2 % respectively. None developed grade IV radiation dermatitis. **Conclusion:** IMRT for carcinoma cervix seems to provide improved outcomes and toxicity profile, although it should be compared with conventional radiotherapy in a well randomized control setting so as to have true and meaningful comparison.

The Impact of Tumour Regression in Locally Advanced Carcinoma Cervix During External Beam Radiotherapy And The Need For Adaptive Planning

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Aim: To study the impact of tumour regression occurring during IMRT

for locally advanced Carcinoma cervix and study dose distribution to target volume and OARs and hence the need for any replanning. **Methods and Materials:** 40 patients undergoing IM-IGRT and weekly chemotherapy were included in the study. After 36Gy, a second planning CT-scan was done and target volume and OARs were recontoured. First plan (non-adaptive) was compared with second plan (adaptive plan) to evaluate whether it would still offer sufficient target coverage to the CTV and spare the OARs after having delivered 36Gy. Finally new plan was created based on CT-images to investigate whether creating a new treatment plan would optimize target coverage and critical organ sparing.To measure the response of the primary tumour and pathologic nodes to EBRT, the differences in the volumes of the primary GTV and nodal GTV between the pretreatment and intratreatment CT images was calculated. Second intratreatment IMRT plans was generated, using the delineations of the intratreatment CT images. The first IMRT plan (based on the first CT-scan or non adaptive plan) was compared with second IMRT plan (based on the second CT-scan or adaptive plan). **Results**: 35% patients had regression in GTV in the range of 4.1% to 5%, 20% in the range of 1.1%-2%, 15% in the range of 2.1%-3% and 20% in the range of 6%-15%. There was significant mean decrease in GTV of 4.63cc (p=0.000). There was a significant decrease in CTV on repeat CT done after 36Gy by 23.31cc (p=0.000) and in PTV by 23.31cc (p=0.000). There was a statistically significant increase in CTV D98, CTV D95, CTV D50 and CTV D2 in repeat planning CT done after 36Gy. There was no significant alteration in OARs doses. **Conclusion**: Despite tumour regression and increased target coverage in locally advanced carcinoma cervix after a delivery of 36Gy there was no sparing of OARs. Primary advantage of adaptive RT seems to be in greater target coverage with non-significant normal tissue sparing.

Estrogen, Progesterone and Androgen receptor profiling of endometrial stromal sarcoma

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Introduction: Endometrial stromal sarcoma (ESS) is a rare neoplasm comprising only 0.2-1% of all uterine malignancies and afflicts women mostly between 40 and 55 years of age. On ultrasound the echogenecity of ESS resembles normal endometrial stroma; consequently the diagnosis may be missed. ESS is a hormonally responsive tumor frequently expressing estrogen receptor (ER) and progesterone receptor (PR). However, published literature contains scant data on the expression of androgen receptor (AR) and its correlation with clinicopathologic features. **Objectives:** To characterize the expression of AR along with ER, PR and their correlation with clinicopathologic features. **Material and Methods:** The clinical details, slides and blocks of 12 tumors from 11 patients (June 2013 - January 2016) were retrieved.The histology was reviewed and immunohistochemistry performed for ER, PR and AR. **Results:** Age ranged from 18 to 48 with mean age of 31 years. Low grade ESS (LGESS) (mean age 34.7) and high grade ESS (HGESS) (mean age 24.5) were diagnosed in 7 and 4 patients respectively. An 18-year-old woman who initially had LGESS suffered pelvic recurrence within 6 months of hysterectomy. The recurrent tumor exhibited features of HGESS. All the patients presented with abnormal vaginal bleeding. Hysterectomy was performed in 4 patients with imaging diagnosis of fibroid; all had LGESS on histology. Six patients were preoperatively diagnosed to have uterine tumor on imaging. One woman gave history of developing an anterior abdominal wall swelling at the scar site, 7 months after child birth by caesarean section. Magnetic resonance imaging confirmed a soft tissue mass in the subcutaneous plane without any intrabdominal extension and uterine/adnexal growth. The resected specimen revealed a HGESS. Overall immunoreactivity for ER, PR and AR were observed in 6 (50%), 7 (58.3%) and 7 (58.3%) tumors respectively. Among the 4 HGESS patients, only one (25%) strongly expressed all three receptors, one (25%) showed positivity for PR only, while the remaining two (50%) had triple negative tumors. The woman with recurrent tumor showed very focal staining for AR only in the primary LGESS while the recurrent HGESS was negative for all three receptors. Among the remaining 6 LGESS patients, all except one strongly expressed all three receptors. **Conclusions:** Our patients, especially those with HGESS, were much younger compared to published worldwide data. Overall hormonal receptors were more frequently expressed in LGESS as compared to HGESS. While AR positivity was observed in 85.7% of LGESS while only 25% of HGESS expressed it. Whether AR, in addition to ER and PR receptor status, may help guide the clinician in determining adjuvant hormonal therapy, especially in young LGESS patients who wish to preserve the ovaries remains to be investigated.

Clinical Profile of Uterine Sarcomas and Carcinosarcomas : Our 7 Year Experience

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Background: Uterine sarcoma accounts for nearly 3% of all uterine malignancies. They have 4 major pathology includes endometrial stromal sarcoma high grade, ESS low grade, uterine leiomyosarcoma (uLMS) and undifferentiated uterine sarcoma (UUS).). This study provides an overview of experience at our center with patients diagnosed with uterine sarcoma and carcinosarcoma, in relation to the clinical management and outcome. **Materials and Method:** We analyzed medical records of 48 patients of uterine sarcoma and carcinosarcoma. All available clinical and pathological data were collected and analyzed. Putative prognostic factors were entered into a multivariate analysis using a Cox proportional hazards ratio model, and survival data were calculated. **Results:** Total 48patient treated for uterine sarcoma at our institute. The histological diagnosis LMS (15/48), ESS-L(12/48),Carcinosarcoma (9/48), UUS(9/48) and ESS-H(3/48). Stage distribution was stage I,(18/48) stage II, (23/48) stage III, (5/48) and stage IV, (3/48). Two patients underwent completion surgery for outside myomectomy. The adjuvant treatment was CT with RT in 21/48 patients, CT alone 9/48 patients , HT in 12/48 patients with three patients were put on close follow up. Median follow up is 34 month with 30 patients alive, 12 succumb and three patients lost to follow up. On univariate analysis age, stage and histology were significant factors to affect survival and disease free interval. **Conclusion:** Uterine sarcoma are uncommon disease with historically dismal prognosis. No definitive adjuvant treatment guidelines available owing to paucity of literature. Present series showing improved survival with multimodality therapeutic approach, however having limited number of patients, with short follow up.

Laparoscopic and Open Surgical Staging for Adenocarcinoma Of The Endometrium – An Analysis Gynecological Cancer

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Introduction: Endometrial adenocarcinoma ranks third among gynaecological malignancies after cervix and ovarian cancer in India. The foundation of management of endometrial carcinoma is surgical staging - traditionally accomplished by laparotomy but the advent of laparoscopy has made possible this minimally invasive option to be used for achieving the same. **Objectives:** To compare & Analyse the patient, surgical, pathological& treatment characteristics of open& laparoscopic surgical staging for adenocarcinoma of the endometrium. **Material and Methods:** A retrospective analysis of 145 patients who presented with adenocarcinoma of the endometrium and treated by open or laparoscopic surgical staging at the Cancer Institute (WIA) from the year 2006 to 2010 was done and patient, surgico-pathological & treatment characters were analysed. **Results:** Patient characteristics like age, BMI& co-morbid illnesses, Tumor characters like grade & Stage distribution & Treatment characters like nodal yield were not significantly different in the two groups. Laparoscopic surgery resulted in significant reduction in hospital stay& incidence of complications especially surgical site infections & paralytic

ileus. While laparoscopic staging had an increased operating time, the blood loss remained comparable. There was no significant difference in the overall survival and disease free survival between the two groups. **Conclusion:** Laparoscopic approach to surgical staging in carcinoma endometrium can be performed as safely as the conventional open approach without compromising on the operative, pathological and oncological outcomes in the Indian Scenario as already shown in the Western setting.

Keywords: Endometrial adenocarcinoma, laparoscopic staging, laparoscopic lymphadenectomy

Disclosure: No financial interest.

Oral Topotecan and Cyclophosphamide in Relapsed Ovarian Cancer

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Objective: Women with relapsed epithelial ovarian cancer (EOC) often have a limited life expectancy .This Phase II study was carried out to investigate the efficacy, safety and response rate of oral Topotecan in combination with oral cyclophosphamide in patients with relapsedovarian carcinoma and metastatic carcinoma. **Methods:** Patients with relapsedovarian carcinoma after having received one or two regimen containing platinum-based chemotherapy and or liposomal doxorubicin were eligible for this study. Also patients with metastatic disease not in ression after the standard of care were also enrolled in this study. Topotecan was administered at 1 mg/m(2)/day for five consecutive days, and oral cyclophosphamide 50 mg per day for 21 days each cycle repeated every 3 weeks. **Results:** 15 patients were enrolled in the study. The response rate was 80 %. Signs of myelosuppression, such as neutropenia (Grade 3, 15%; Grade 4, ,40%), thrombocytopenia (Grade 3, 20 %; Grade 4, 30 %) and decreased hemoglobin (Grade 3, 40 %; Grade 4, 10 %), were the most common hematological toxicities during the first 2-3 cycles with hospital administration and supportive care given . Grade 3 febrile neutropenia occurred in 5 patients. Dose reduction was done for all patients to only 1 mg per day . 2 patients defaulted for treatment .2 patients had progressive disease. Remaining 11 patients (73.3 %) are alive with stable disease at end of 18 months (PFS). Longest surviver is now on 36 months on the oral chemotherapy. **Conclusions:** Topotecan at reduced dose of 1 mg perday for 5 days with cyclophosphamide 50 mg for 21 days is an effective with response rate of 73 % and tolerable therapeutic , median PFS of 18 months . It is a option for patients with relapsedovarian carcinoma. This is an excellent outpatients therapeutic option for patients in limited resource country.

3DCRT Planning in Carcinoma Cervix Patients: A Comparative Study of Cobalt-60 Vs 6 MV Linac

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Introduction: Telecobalt units are playing an important role in providing radiotherapy to patients. Addition of several advanced features like asymmetric jaws, motorized wedge, Multileaf collimation etc has made conformal planning possible with telecobalt units. In this study we compared the 3DCRT plans generated for 20 Ca cervix patients for both telecobalt unit and 6MV Linac. Comparison was made in terms of dose coverage to target volumes (PTV, CTV) and avoidance of the organ at risk (OAR) namely ano-rectum, urinary bladder(UB), bowel bag, femur head. **Materials and Method:** For this study we randomly selected 20 ca cervix patients (FIGO Stage II and III). These patients had already received treatment (50 Gy in 25 fractions) with a 6MV Linac (6MV X-rays with MLCs) based setup. The contouring of treatment volumes and organ at risk were checked. The treatment plans were now obtained for our configured telecobalt unit Bhabhatron-II TAW (asymmetric collimation in the Y Jaw). The planning was done on Eclipse T.P.S version 8.9.10 using CT scans obtained from Wipro G.E.C.T scan machine. All the patients were planned by isocentric method with the isocentre placed at the centre of the PTV. Asymmetric jaws and Blocks were used in the TPS to shield the normal structures. Beams were planned for 0^{o}, 90^{o}, 180^{o} and 270^{o} angles which are used routinely for 3DCRT planning. Dose calculation was done using Pencil Beam Convolution algorithm. The dose to the target structures and OARs mentioned above were evaluated. The maximum, mean and minimum dose to these structures were evaluated. Dose volume histograms (DVH) were used to evaluate the treated and irradiated volumes of the patients. All these evaluated parameters were compared with those of the Linac Based plans. **Results:**A comparative data in form of maximum, minimum and mean dose was obtained for target volumes(PTV, CTV) and OARs- ano-rectum, UB, bowel bag, femur head. DVH were also studied and compared. The maximum and mean dose for PTV and OARs for our telecobalt unit and Linac were comparable. **Conclusion:** In the present scenario telecobalt units are being developed with advanced features such as asymmetric jaws, motorized wedge, MLCs etc. These features shall be utilized to deliver conformal treatment.

Following table shows comparison details of the two machines:

Management of Malignant Ovarian Germ Cell Tumours - A Single Institutional Study

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Objective : To maintain the reproductive function following fertility preserving treatment simultaneously not compromising on the overall management of germ cell tumours. **Methods**: The current study is a retrospective review of 25 patients in a period of three years with malignant ovarian germ cell tumour treated by conservative surgery retaining Uterus and contralateral ovary to preserve ovarian function with or without chemo therapy. **Results:** A total of 25 patients with malignant ovarian germ cell tumours who had undergone conservative management retaining uterus and contra-lateral ovary to preserve ovarian function with or without chemo therapy in the past 3 years were analysed retrospectively. The factors taken into consideration for survival recurrence and reproductive status were evaluated. The mean follow up time was 5 years. The mean age of the

	Mean Dose(Gy)		Maximum Dose(Gy)		Minimum Dose(Gy)	
	Linac	Co-60	Linac	Co-60	Linac	Co-60
PTV	50.41±0.50	49.77±1.00	53.78±0.75	58.41±1.99	35.32±14.88	32.13±13.96
CTV	51.39±3.02	49.74±0.89	53.40±0.72	56.53±2.57	47.47±1.37	43.92±1.69
Rectum	45.77±3.63	44.61±4.01	51.78±0.76	50.34±1.12	10.69±11.88	15.10±12.60
Bladder	49.38±0.88	50.20±1.49	52.03±0.92	54.24±2.28	32.80±7.25	45.67±1.91
Bowel bag	28.17±12.85	32.23±14.1	53.00±0.82	57.08±1.97	10.47±13.58	10.29±16.74
Femur	27.58±2.88	31.84±4.99	51.6±0.58	53.24±1.41	3.04±2.08	5.39±4.97

patients was 20.9 years (range: 10 to 35 years). The 5 year survival rate for malignant ovarian germ cell tumours is 100% for dysgerminomas and 98% for the other subtypes of germ cell tumours. Out of 25 patients, 20 patients have a successfuloutcome. **Conclusion:** Conservative treatment has shown good prognosis and showed successful outcome irrespective of recurrence.

A Study to Compare Weekly Paclitaxel versus Four Weekly Cisplatin & Biweekly 5-Flourouracil as an adjunct to Radiation therapy in locally advanced Carcinoma Cervix

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Guru Gobind

Introduction: Cervical cancer is second most common cancer among females in India, most of patients presented with locally advanced stage. Advanced stage carcinoma cervix associated with poor prognosis. Chemo-radiotherapy is the mainstay of treatment. Taxanes or platinum based treatments is the accepted standards. Recent Cochrane Collaboration meta-analysis showed significant benefit with non-platinum based regimens containing 5-FU or mitomycin C. The combination including Cisplatin and 5-Fluorouracil (5-FU) has not been exploited aggressively. **Objectives:** To compare the clinical efficacy and safety of concurrent chemo-radiotherapy using weekly Paclitaxel versus four weekly cisplatin with biweekly 5-Flourouracil in patients with carcinoma cervix stage IIB-IVA presenting in rural tertiary centre. **Material and Methods:** It was 18 months prospective study (from March 2014 to October 2015) conducted in department of Radiotherapy, Guru Gobind Singh Medical College and Hospital, Faridkot. A total of 60 patients were included for prospective analysis. They were divided into two Arms, Arm A and Arm B. Arm A had 29 patients receiving concurrent weekly paclitaxel (60 mg/) along with external beam radiation (EBRT) followed by brachytherapy. In Arm B total of 31 patients receiving Cisplatin (50 mg/) on day one and day 29 with 5-FU (500 mg/) biweekly following same schedule of radiotherapy. Total of 54 patients were statistically evaluated for the results. There was no statistical difference in the clinical and pathological characteristics between the two groups. **Results:** Patients were evaluated by pelvic examination and CT scan before the start of chemo-radiotherapy and at 6 months post treatment.Radiation toxicity was evaluated with RTOG Toxicity criteria for acute and late toxicity. The median cumulative dose to point A was 79.8 Gy and overall treatment time was 68 days in both the groups. The most frequent toxicity was acute hematologic toxicity grade 1 or 2 in Arm A (88%) than Arm B (80%) while GI toxicity with grade 2 or 3 is more frequent in Arm B (86%) than Arm A (64%). The response rate were 70% (19/27) in Arm A and 88.9% (24/27) in Arm B in which there was significant difference but statistically not significant (p-value= .075). Median progression free survival in Arm A was 10 months and in Arm B was 11 months. The corresponding figure for median overall survival was 11 months in both the groups. **Conclusions:** The overall response rate is better in Arm B which was not statistically significant while other parameters in both the Arms were similar. Large scale trial with large sample size is needed to decipher the significant results.

Radiation Proctitis in Carcinoma Cervix: Analysis of Prognostic Factors

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Background: Radiotherapy is an important treatment modality for Carcinoma cervix. Radiation proctitis is most challenging complication following radiation therapy to pelvis. In This study we analyzed the factors associated with Radiation proctitis after chemoradiotherapy in patients with Carcinoma Cervix. **Methods:** Retrospective analysis of 417 patients with carcinoma cervix treated by radical External Beam Radiotherapy and Brachytherapy from 2011 through 2015 was done. Clinical information including Tenasmus, urgency, rectal pain, pain bleeding per rectum, anorectal ulceration were recorded. Radiation Proctitis grading was done according to CTCAEv4. Evaluation of clinical and dosimetric profiles performed. **Results:** The median age was 47 years. Distribution as per FIGO stage was: IIB-24%, IIIA-40%, III B-36%%. All patients received External Beam Radiotherapy to 50 Gy in 25 fractions in 5 weeks along with concurrent weekly chemotherapy, Followed by ICA Brachytherapy. 150 cases (36%) were treated by IMRT while 267 cases (64%) were treated by 3DCRT technique or 4 Field Box technique after CT simulation. ICA Brachytherapy was given in 7Gy weekly to point A, total 3 fractions or 6 Gy weekly, total 4 fractions. Median follow-up was 1year (range 6 months to 60 months). Locoregional failure was seen in 86 cases (32%). Distant Failure was seen in 8% cases. 7.6% patients (32 out of 417 patients) developed grade 2 or more radiation proctitis. Analysis of these 32 cases was performed. 25 cases (78%) were of stage III B while 7 cases (22%) were of stage II B. 11 cases (34.3%) were treated by IMRT while 21 cases (65.6%) were treated by 3DCRT or 4 Field Box technique. Mean dose and V45 to Rectum-PTV was higher in 3DCRT or 4 Field Box technique arm. **Conclusions:** Rate of Grade 2 or severe Radiation proctitis was lower in stage II B and IMRT arm compared to stage III and 3DCRT or 4 Field Box technique arm.

The Growing Teratoma Syndrome; Regional Cancer Institute Experience

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Introduction: Growing teratoma syndrome (GTS) is a rare condition presents as enlarging retroperitoneal or other metastatic masses containing mature teratoma during chemotherapy or after the chemotherapy for germ cell tumours and normalised tumour markers. The patients generally have a history of germ cell tumor in the past and presents during follow up period with increasing size of metastatic lesions and but typically the tumor markers will be normal.The histology of these excised lesions reveals benign mature teratoma elements. The complete surgical excision of teratoma is currently the gold standard. **Materials and Methods**: We present three cases of GTS from Kidwai Memorial Institute of Oncology diagnosed and treated in the Department of Gynaecologic Oncology from August 2013 to Dec 2015. **Results:** The metastatic masses being in the retro peritoneum in one case, one case had both retro peritoneum and intra-abdominal and other patient with intra-abdominal masses. All these patients had normal tumor markers with increasing metastatic lesions. One patient presented after 20 years, one after 11 years and another after 2 ½ years of primary surgery and chemotherapy. Surgical excision was carried out in all three patients. One of the case revealed additional neuroendocrine elements in the metastatic deposits, which happens to be 3rdreported case in the world literature. The disease free survivals in these patients ranging from 12 to 24 months after surgery. **Conclusion:** GTS is rare clinical phenomenon. Good treatment outcomes are dependent on the awareness of this condition with vigilant imaging of patients on chemotherapy for Germ cell tumour / NSGCTs, and early diagnosis and, complete surgical resection of tumors.

Keywords: Enlarging metastatic mass, growing teratoma, germ cell tumors.

R – Veil In Carcinoma Vulva – Our Experiences and Intermediate Results

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Introduction: Vulvar cancer accounts for about 3-5% of gynaecologic malignancies. Prognosis is strongly dependent on presence of inguinofemoral lymph node metastases. Effective management of regional lymph nodes is the most important factor in the curative management of early vulvar cancer. Despite careful dissection and maintaining vascularity of skin, surgical morbidity is seen in 50% cases.Video – endoscopic inguinofemoral lymphadenectomy was developed by Bishoff in 2003 by dissecting two cadaveric models and in one patient with stage T3N1M0 penile carcinoma. VEIL is an alternative to reduce the morbidity without compromising the oncologic outcomes. VEIL has continued to evolve into single site and robotic variants. R-VEIL is a minimally invasive procedure duplicating the standard open procedure with less morbidity. **Objectives:** To describe the technique of R-VEIL in vulvar cancer and discuss the advantages and outcome. **Material and Methods:** 12 patients of squamous cell cancer of vulva underwent 22 R-VEIL surgeries from February 2011 to February 2015. Their preoperative, intra-operative and postoperative data was collected.

Results: No patient required conversion to open surgery. The mean operative time was 77.1 minutes. Number of lymph nodes retrieved ranged from 4 to 26. Two patients had positive lymph nodes on histopathology (18.2%) and received adjuvant radiation therapy. Amongst the lymph related complications, seroma developed in 4 groins (18.2%), Lymphocoele developed in 4 groins (18.2%), lymphedema in 6 groins (27.3%) while prolonged lymphorrhea developed in one groin (4.5%). Amongst the wound complications, cellulitis developed in one groin (4.5% each), while flap necrosis developed in 2 groins (9.1%). Over a follow-up period ranging from 2-66 months, one patient developed recurrence in the inguinal nodes and one patient developed recurrence at the site of vulvectomy unrelated to R – VEIL. **Conclusions:** This is the first study on R – VEIL in patients with vulvar cancer. Our preliminary results show that R – VEIL is an attractive minimally invasive technique to do inguinal block dissection in a single sitting in patients with vulvar carcinoma as the surgeon does not get tired as happens in VEIL technique. R-VEIL allows the removal of inguinal lymph nodes within the same limits as in open procedure and potentially reduces surgical morbidity. It is better accepted cosmetically and reduces hospital stay. Long term oncological results are not available. Randomized multi-institutional studies are required to prove its efficacy over open counterpart.

Paget's Disease of the Vulva in Postmenopausal Women: A Case Report

Eliza Shrestha, Shweta Giri, Rupinder Shekon, Sudhir Rawal

Vulvar Paget's disease is an extremely rare neoplasm that accounts for less than 1%of Vulvar Malignancies. We present a case of a 66 year old woman, who had an ulcerated lesion involving the labia majora bilaterally; lymph nodes were not palpable in the inguinal region bilaterally. A biopsy of the Vulva showed Paget's disease. She underwent wide local excision. The specimens resected were reviewed with respect to involvement of the margins with Paget cells and the margin was negative. The patient remained disease free at 2 years follow up.

Keywords: Vulvar, Paget's disease.

Video demonstration of development of vaginal cuff in cancer cervix robotic hysterectomy cases

Rupinder Sekhon

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Objective: In a case of carcinoma cervix ,it is imperative to take adequate parametrium and vaginal margin. This video demonstrates development of a vaginal cuff, an indegenous approach developed at our institute, for the purpose of taking adequate vaginal margin in cases of robotic hysterectomy. **Methods:** Video demonstration in a case a ca cervix stage IB undergoing robotic hysterectomy. Prior to docking of the robot, development of vaginal cuff is done by dissecting the cervix vaginally and using a gauze piece and attaching it to the cervix and the vaginal wall anteriorly, posteriorly and to the lateral walls. After this, robotic surgery is carried out in the usual manner. **Results:** This method aids in resection of adequate parametrium and development of a vaginal cuff while doing robotic hysterectomy. Strategic placement of the gauze piece aids in easy development of planes for doing vaginectomy via the abdominal route. **Conclusion:** Routine use of this method for the development of an adequate vaginal cuff helps the surgeon save time and achieve precision in otherwise tedious step of robotic radical hysterectomy.

Robotic Radical Hysterectomy : Ureteral, Vascular and Bowel Complications and Their Management (Video Presentation)

Rupinder Sekhon

Rajiv Ghandi Cancer Hospital

Objective: To show a surgical educational video in which an incidental ureteral ,vascular and bowel injury were recognised intraoperatively and repaired during robotic-assisted radical hysterectomy. **Methods:** Step-by-step demonstration of ureterolysis and repair of ureteral injury via a ureteroureterostomy technique, vascular repair via application of a clip and bowel repair via primarily using endosuturing,all in an educational video. **Results:** Ureteral injuries are estimated to occur with a frequency of approximately 0.02% to 0.4% during laparoscopic hysterectomy. The sequelae from ureteral injury are not insignificant, which can easily be prevented by intraoperative recognition and immediate repair. Minimally invasive surgery using the robotic system has led to a paradigm shift in the management of urinary tract injuries, which has been traditionally approached with open surgery. This video also describes robotic management of a major vascular injury during pelvic lymphadenectomy by use of haemoclip. Inadvertent bowel injury was also repaired primarily via endosuturing. **Conclusion:** Robotic repair of various injuries described during gynecologic surgery was associated with good outcomes, is safe and feasible.

Video Demonstration of Robotic Retroperitoneal Lymph Node Dissection

Rupinder Sekhon

Rajiv Ghandi Cancer Hospital

To demonstrate retroperitoneal lymph node dissection in gynaecologic malignancy. **Methods:** Systematic (complete) para-aortic lymphadenectomy is defined as the complete removal of all fat and nodal tissues surrounding the aorta, inferior vena cava (IVC) and renal vessels from the left renal vein cranially to the midpoint of the common iliac vessels caudally. **Results:** There are various specific indications of doing retroperitoneal lymph node dissection in gynaecologic malignancies depending upon risk stratification of the particular malignancy in question. Robotic retroperitoneal lymph node dissection is an effective and safe method in gynaecologic malignancies

Image Guided Interstitial Brachytherapy for Locally Advanced Disease After External Beam Radiotherapy in a Case of Carcinoma Cervix – Our Institutional Experience

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Purpose/Objective: Cervical cancer is the third most common cancer in women worldwide. Definitive chemoradiation is the accepted standard of care for patients especially for locally advanced cervical cancers. Intracavitary brachytherapy (ICBT) is an important part of definitive radiotherapy shown to improve overall survival. Interstitial brachytherapy (ISBT) is generally reserved for patients either withextensive pelvic and/ or vaginal residual disease after external beam radiotherapy (EBRT)or with anatomy not allowing ICBT with standard applicatorsin an attempt to improve local control. We have conducted an observational study for patients who underwent image guided HDR-ISBT at our institute. **Materials and Methods:** Seven patients; diagnosed as a case of carcinoma cervix; wereselected from the period of 2012 to 2015 who receivedEBRT by IMRT and for whom ICBT couldn't be done for various reasons. These patients were then taken up for Martinez Universal Perineal Interstitial Template (MUPIT) image basedISBT.A descriptive analysis was done for doses received by HRCTV, bladder, rectum and sigmoid colon. At the end of treatment, early response at 3 months along with overall survival (OS) and disease free survival (DFS) was also calculated. **Results:** All the patients recruited were locally advanced with 3 patients in IIB, 1 patient in IIIA and 3 patients belonging to IIIB. The mean dose received by 95% High Risk CTV (HRCTV) by IMRT was 49.75 Gy. Out of 7patients, 3 were taken up for ISBT due to anatomical restriction whereas remaining 4 patients were included because of lack of dose coverage by ICBT. The mean doses received by 90% of HRCTV, 2 cc bladder, 2 cc rectum and 2 cc sigmoid colon were 20.58 Gy, 2.73 Gy, 3.19 Gy and 2.82 Gy respectively. The early response at 3 months was 57.14%. The DFS at one year and OS at 3 year were 53.6% and 53.3% respectively. **Conclusions:** Our descriptive analysis of seven patients being treated by image based ISBT have revealed that locally advanced cervical cancer patients for whom ICBT is unsuitable can achieve equitable LRC and OS with a combination of EBRT by IMRT and image based HDR-ISBT.

Oral Topotecan and Cyclophosphamide in Relapsed Refractory Epithelial Ovarian carcinoma. A study from Indian subcontinent

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Introduction: Women with relapsed epithelial ovarian cancer (EOC) often have a limited life expectancy .This Phase II study was carried out to investigate the efficacy, safety and response rate of oral Topotecan in combination with oral cyclophosphamide in patients with relapsedovarian carcinoma and metastatic carcinoma. **Objectives:** The efficacy , safety , response rate and survival of metronomic combination. **Material and Methods**: Patients with relapsedovarian carcinoma after having received one or two regimen containing platinum-based chemotherapy and or liposomal doxorubicin were eligible for this study. Also patients with metastatic disease not in ression after the standard of care were also enrolled in this study. Topotecan was administered at 1 mg/m(2)/day for five consecutive days, and oral cyclophosphamide 50 mg per day for 21 days each cycle repeated every 3 weeks. **Results:** 15 patients were enrolled in the study. The response rate was 80 %. Signs of myelosuppression, such as neutropenia (Grade 3, 15%; Grade 4, ,40 %), thrombocytopenia (Grade 3, 20 %; Grade 4, 30 %) and decreased hemoglobin (Grade 3, 40 %; Grade 4, 10 %), were the most common hematological toxicities during the first 2-3 cycles with hospital administration and supportive care given . Grade 3 febrile neutropenia occurred in 5 patients. Dose reduction was done for all patients to only 1 mg per day . 2 patients defaulted for treatment .2 patients had progressive disease. Remaining 11 patients (73.3 %) are alive with stable disease at end of 18 months (PFS). Longest surviver is now on 36 months on the oral chemotherapy. **Conclusions:** Topotecan at reduced dose of 1 mg per day for 5 days with cyclophosphamide 50 mg for 21 days is an effective with response rate of 73 % and tolerable therapeutic , median PFS of 18 months . It is a option for patients with relapsedovarian carcinoma. This is an excellent outpatients therapeutic option for patients in limited resource country.

Improved Outcomes of Patients with Locally Advanced Cervical Cancer with Addition of Taxol to Cisplatin Based Chemotherapy along with Radiation. A study from Developing Country. India

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Introduction: Standard treatment of locally advanced cervical carcinoma (CC) is actually represented by concomitant chemoradiotherapy followed by brachytherapy. However, in spite of good local control rates after treatment, local and regional relapses still a major cause of failure treatment.). **Objectives:** We performed study to evaluate whether (Cisplatin) CDDP-based doublet therapy improves survival compared to weekly CDDP plus RT (Radiotherapy) in these patients. **Material and Methods:** From 1 January 2011 to 31 December 2014 we prospectively selected series of consecutive 40 patients with clinical stage II -III carcinoma Uterine Cervix . Primary and secondary objectives included the rate of response , safety, predictive factors of relapse , overall survival and progression free survival. Patients received 2 cycles of neoadjuvant Paclitaxel (175 mg/ m^2) and Cisplatin (75 mg/m^2) once 3 weekly. All patients underwent Radiotherapy external beam and bachytherapy . Then another 4 cycles of CDDP- doublet combination.. They were followed up till December 2015. **Results:** Progressions occurred in 2 patients (5 %) with an average of three months as they defaulted treatment. Recurrences occurred in 5 patients (12.5%) with an average of 15 months. The overall treatment failure rate was 17.5%. Thirty-two (82.5%) of treated patients were in good locoregional control with a median follow of 24 months. Longest follow up 60 months alive and free of disease. **Conclusions:** Relapses of cervical cancer have a poor prognosis and long-term survival remains very poor. The suitable treatment of the primary disease, respecting essentially therapeutic times, is one guarantee of a good prognosis. Paclitaxol when added to first-line chemotherapy, for locally advanced CC, concurrent RT and with CDDP-based doublet chemotherapy significantly has now been shown to improve overall survival among women ,it is safe and effective for more then 80 % patients with locally advanced disease

Sclerosing Stromal Tumour of Ovary: A Rare Entity

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Introduction: Sclerosing stromal tumor (SST) is an extremely rare benign subtype of ovarian stromal neoplasm. It has distinctive clinical and pathological features which differentiate it from other stromal tumors. The tumor occurs predominantly in the 2nd and 3rd decades of life. **Objectives:** Due to the rarity of this particular ovarian neoplasm, a possibility of sclerosing stromal tumor should be kept in mind in young patients with ovarian mass, as almost all the sclerosing stromal tumors of the ovary reported in the literature are benign and are treated successfully by enucleation or unilateral ovariotomy. **Material and Methods:** A 18 year old girl was admitted to the hospital for menstrual irregularity, metrorrhagia and pelvic pain since last four months. Physical examination revealed no palpable abdominal lump nor hepatosplenomegaly. On ultrasonographic examination, there were solid and cystic areas in left ovary of approximately 8X6X4 cm in size. On CT scan, there was bulky left ovary measuring 5X4.4X3.2 cm with multiple cystic areas, largest measuring 3.2X2.4 cm, suggestive of neoplastic etiology. MRI showed minimal ascites in para-colic spaces & pelvis, a left ovarian solid-cystic mass measuring 5.2 cm, suggestive of neoplastic etiology. **Result**: The ovarian mass showed benign pathology on frozen section analysis which was subsequently removed by laparoscopic salpingo-oophorectomy. On histopathological examination, the tumor showed ovoid to spindle cells, luteinized cells arranged in lobules separated by dense to moderate fibrocollagenous stroma. Intercellular edema was seen with intervening thin walled large blood vessels. Immunohistochemical analysis demonstrated positivity forSMA and negativity for vimentin, cytokeratin. Ki-67 index was 1 to 2%. Subsequently the diagnosis of sclerosing stromal

tumor of the ovary was made. **Conclusion:**The definite diagnosis of SST can be made only by pathologic evaluation but at least a diagnosis of benign ovarian tumor is possible intraoperatively via frozen section analysis by examining the background of pseudolobular pattern, heterogeneity of the cellular areas and densely hyalinized or markedly edematous stroma.

Diagnostic Accuracy Of Intraoperative Frozen Section in Ovarian Neoplasms: Experience in a Tertiary Oncology Centre

Aims and Objectives: This study is done to assess the accuracy of intraoperative frozen section in the diagnosis of various categories of ovarian neoplasm conducted in RGCI. **Materials and Methods:** Intraoperative frozen sections for suspected ovarian neoplasm that underwent surgery as primary line of therapy at this institution were analyzed retrospectively from Jan. 2014 - Dec. 2015. The results of frozen section were compared with the final histopathology diagnosis on paraffin sections and the overall accuracy, sensitivity, specificity, positive and negative predictive values were determined. **Results:**The study included 159 cases and the mean age of patients was 44.72±14.28 years (Range 19-75years).The mean size of tumor was 12.5±5.9cm.Sensitivity of frozen section for benign, borderline and malignant tumors was 98.53%, 73.33% and 94.74% respectively. And the related specificities were 95.60%, 96.53% and 100% respectively. There were 150 concordant cases and 9 discordant cases. Overall diagnostic accuracy of frozen section was 94.33%. **Conclusion:** Intraoperative frozen section diagnosis appears to be an accurate and comparable technique for the histopathology diagnosis of ovarian tumours.It is a valuable tool to guide the surgical management of these patients.

Keywords: Frozen section, ovarian neoplasm

A Profile Of Endometrioid Adenocarcinoma of Uterus in a Tertiary Centre

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Introduction: The incidence of endometrial carcinoma(EC) is around 4.2 to 4.3 per 10,000 in India. Management of EC almost worldwide is surgery. Current practice is to perform removal of enlarged pelvic lymphmodes. Complete PLND is done in patients with high risk features. Women with early stage disease has a favourable prognosis overall, hence adjuvant treatment recommendations are challenging. Women with advanced disease receive adjuvant radiotherapy with or without chemotherapy depending upon the stage and high risk features. **Objectives:** 1. Assessment of clinic-pathological variables .2. Correlation of pre and post-operatives tumor grades. 3. Lymphnode metastases with tumor grade and myometrial invasion (MI). **Material and Methods:** A retrospective analysis of 40 endometrioid cases were done. Primary line of treatment was surgery. Radiotherapy chemotherapy was administered as adjuvant treatment. Continuous variables were reported using mean +/- SD. Categorical variables were reported using number and percentages. Pre and Post Grades were compared using Wilcoxon Sign Rank Test. All the analysis were done using SPSS version 18.0. **Results:**The mean age was 58.65 years, 29were post menopausal and 28 patients presented with post menopausal bleeding. 28 patients had endometrioid variant, 8 were complex hyperplasia, 2 had endometrial intraepithelial neoplasia, 1 had atrophic endometrium. 28 had complete surgical staging. Five out of 10 who were preoperatively diagnosed as grade 1 tumors were upgraded to grade 2 tumors, 2 out of 11 who were grade 2 tumors were downgraded to grade 1 tumors and 2 out of 7 who were grade 3 tumors were downgraded to grade 2 tumors in post operative specimen.Out of 5 patients with LN metastases, 3 had <50% MI, 2 had >50% MI, 2 had grade 1 tumor, 2 had grade 2 tumor and 1 had grade 3 tumor. **Conclusions:** Complete surgical staging is the most precise way of determining stage and requirement of adjuvant treatment and it defines the prognosis and survival in a better way.

Granulosa Cell Tumour of Ovary: A Clinicopathological Evaluation

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Introduction: Granulosa cell tumours of the ovary are very rare malignancies, represent around 2-3% of all malignant ovarian tumours. **Objective:** To evaluate the clinical characteristics and management of granulosa cell tumour of ovary. **Material and Methods:** The medical records of nine women diagnosed with granulosa cell tumour of ovary from June 2005 to October 2015 in the Department of Gynecologic Oncology of our institution were retrospectively evaluated. **Results:** The mean age of the women was 41.56 years (range –18-78 years). They presented with various symptoms: menorrhagia (44.45%), post-menoausal bleeding (22.23%), abdominal distension (33.34%) and pain abdomen (44.45%). One patient presented with abdominal pain and distension with breathlessness (chest X-ray showed multiple lung lesion? metastasis) and received neoadjuvant chemotherapy. Eight patients underwent primary surgery with complete staging in seven patients. Out of all, two patients underwent emergency laparotomy in view of massive haemoperitoneum. Four patients had ascites ranging from 100-3000 ml. Mean ovarian tumour size was 14cms (range 4-30cms). Fertility sparing surgery was done in one patient. The number of patients in various stages were I -4(IA-3, IC2-1); IIA-1; IIIC-1; IV-1 and unknown -2 according to the International Federation of Gynecology and Obstetrics (FIGO) -2014 criteria. The follow up duration ranged from 0-5 years. Two patients (one stage IA and other stage IIIC) recurred after three years. **Conclusion:** Granulosa cell tumour of the ovary occur in all ages. Symptoms related to hypere-strogenism occur in all age groups. Because of the high vascularity, tumour rupture is commonly seen. The primary management of these tumours is through surgery. The role of adjuvant therapy in early stages is controversial.

YKL-40 and CA-125 as Predictive Prognostic Serum Biomarker for Ovarian Cancer

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Background: There is constant development of new treatments and therapies to improve the five-year survival rate of patients of ovarian cancer. However still it remains the deadliest cancer of the femalereproductive tract. Unfortunately, most cases are diagnosed in the late stages of the disease dueto lack of precise early warning signs. Present study has been done to identify the prognostic suitable serum markers for early detection of ovarian cancer. **Material and Methods:** Clinical information was obtained from 50 ovarian cancer patients and age matched controls. A specialized questionnaire has been developed to record detailed information especially regardinghistory of ovarian cancer , the number of affected first- and second-degree relatives and otherrisk factors. Five ml of blood sample was collected from each subject and after 1hr, centrifugedat 4°C for 5 min at 1500 rpm. The aliquot of serum was then subdivided into small volumes and stored at -80°C. YKL- 40 and CA-125 levels were determined from all serum samples using. YKL-40 ELISA test and its serum concentrations were determined by measurement of absorbance at 450 nm which was read against a standard curve. . The value of 35 U/ml as the threshold of CA125 &121.5ng/ml as a threshold of YKL 40 was taken for predicting the possible diagnosis of ovarian cancer. **Results:** The relation between menstrual factors, reproductive history and ovarian cancer was analysed .Moderately elevated risk of ovarian cancer was observed among women with early menarche & late menopause .Preoperative serum level of YKL-40 was elevated in 10 patients [91%] & preoperative serum levels of CA125 in 7 patients (64%) with advanced and recurrent ovarian cancer for stage III/IV respectively(Table 1). Considerable elevated level of YKL40 was noted in patients of stage I/II indicating its diagnostic importance

along with CA 125. **Conclusion:** The ultimate aim is to bring a reduction in mortality from ovarian cancer. As early detection continues to be vital in ovarian cancer patients, biomarkers may hold the key to plan effective screening strategies for the general population. Currently available single markers are not highly sensitive or specific, a combination of markers may be utilized as a profile for risk assessment. Key words: Serum biomarker, ovarian cancer, YKL-40 & CA-125

HPV Screening Test as a Primary Method of Population Based Cervical Cancer Screening, Among Rural Population of Villupuram,Tamilnadu - A Pilot Study

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Introduction: Cervical cancer ranks as the first most frequent cancer among women in India and first most frequent cancer among women between 15 and 44yrs of age. Current estimates indicate that every year 134420 women are diagnosed with cervical cancer and 72825 die from the disease. Chennai region is one of the high incident regions for cervical cancer in India (Swaminathan et al). HPV is the necessary cause of cervical cancer. HPV DNA testing at affordable cost has been recommended as the screening tool for developing countries like India(Sankaranarayanan R). **Objective:** To study the feasibility and challenges to carry out the HPV DNA test by trained health workers in the field set up, as the primary screening method, in a rural population of Villupuram, a district200kms south of Chennai. **Methodology:** 2000 exfoliated cervical swab samples were collected from unscreened married women aged 30-59 years. Cervical smears (Pap Test) were done along with visual tests(VIA/VILI) on all women in the same sitting. HPV testing was done by Hybrid Capture assay (care HPV test) by trained health workers in a simple clinic set up in the field while cervical smearsfor cytological study were transported to the Cancer Institute,Chennai. **Results:** All the three test results were available for1959 women. 17 women who were ASCUS+ on cervix smears were called for further evaluation. 12 women complied for colposcopy guided biopsy and 10 women were found to have CIN2+ changes in the cervix, ie true positives. HPV test results were positive, picking up all the 10 true positives(precancer cases) and was negative for the remaining two cases, which were true negatives and without disease. **Conclusions:** Low cost HPV testing combined along with HPV vaccines is the recommended cervical control measure in high incident regions. Innovative implementation methods like self sampling and utilising local trained personnel will reduce the costs and improve screening coverage. Use of Platysmal Muscle Flap for Reconstructing floor of mouth defects : A single centre study of 34 cases

Keywords: Platysmal muscle flaps, floor of mouth, tongue lesions

Introduction: The floor of the mouth for the purpose of surgical planning is defined as the space between the mucosal surface and the mylohyoid muscle sling. The mylohyoid muscle sling separates the floor of the mouth from the right and left submandibular spaces and midline submental space. The smaller,superior portion of the submandibular gland hooks around the posterior aspect of the mylohyoid muscle with a finger like projection from the submandibular space into the posterior aspect of the floor of the mouth. To repair a defect after intraoral cancer excision, several factors should be considered, such as the site and complexity of the defect, the expertise of the surgeon and the need for coverage of the great vessels . Although numerous options can be used for reconstruction of the head and neck, including primary closure, skin grafts, pedicle flaps, healing by secondary intentions, and free flaps, all of these techniques have their limitations. Platysma myocutaneous flap (PMF) is a satisfactory reconstructive option for small- and medium-sized defects in the oral cavity. This technique was first introduced in the literature for intraoral reconstruction in 1978 . Since then, PMF has been generally used for the reconstruction of congenital abnormalities, traumatic injuries, and most commonly malignancies of head and neck . Three types of PMF have been described - transverse flap, vertical flap that preserves the facial artery and vein, and vertical flap that sacrifices the facial artery and vein. Some authors have reported that vertical PMF without the preservation of the facial vessels is unreliable. In this article, we demonstrate an interesting result in 34 patients who underwent platysmal muscle flap for reconstruction of floor of mouth defects that sacrificed the facial artery and vein for intraoral reconstruction. **Materials and Methods:** We reviewed 34 patients from September 2012 to September 2015 who underwent platysmal muscle flap for reconstruction of intraoral defect after a primary tumor excision at our institute. Modified radical or selective neck dissection was also performed on the patients. All 34 cases were reconstructed with platysmal muscle flaps that sacrificed the facial artery and vein. Tumor excision and defect reconstruction were both performed by the same team. The age and sex of the patients, location and size of the lesions, surgical complications, and outcome were recorded. We obtained the histological diagnosis from the resected specimens. Informed consent was obtained from all of the patients involved in the study. **Surgical Technique:** This is a unique flap in its own way as it can be tailored according to the defect size. It can be used to close majority of floor of mouth defects due to tongue lesions going into floor of mouth which lead to a defect in the floor after excision of tongue lesion.The defect so created is closed using platysma muscle flap. We generally use a Mc Fee incision to address the neck in oral malignancies. The upper incision in the neck is made at least 2 finger breadths below the mandible. After addressing the neck and removal of the primary tumour ,the platysma muscle is separated from the overlying subcutaneous tissue and skin using a scalpel for a desired width maintaining its attachment at its base(mandible).The muscle is then interposed in the defect covering it like a plug and hitched to the surrounding muscular structures in the floor of mouth using absorbable sutures. Thus the integrity of floor of mouth is restored and the defect covered which is further confirmed by the leak test. After restoration with the platysmal flap the practical issue of mainitaining the neck drain suction negativity is also taken care of as the flap acts as a bridge separating the two cavities i.e. the oral cavity and the neck. We do not normally remove the neck drains of such patients until they are allowed to take liquid diet as a measure of precaution against leak from the floor. Wound healing at triple point in Schobinger's incision may be a concern if platysmal flap is used in them. In such cases , it is advisable to leave a part of platysma muscle with the skin at the site of triple point but the author lacks any experience in such cases. **Inclusion criteria:** In our series, we included the following patients:

Use of Platysmal Muscle Flap for Reconstructing floor of mouth defects : A single centre study of 34 cases

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Lesions in anterior and middle one third of tongue in which floor of mouth is disrupted during excision of the primary tongue tumor. Patients with no scars or previous surgeries or trauma to the neck. Patients with very small lesions in floor of mouth. **Exclusion criteria:** 1) Lesions in posterior tongue and base of tongue 2) Lesions involving tonsillo-lingual sulcus or mandible. 3) Previous radiotherapy to the neck or previous surgeries or trauma to the neck or burns in the neck. **Results:** In this series of 34 selected patients, 33 patients had carcinoma tongue as follows: 30 patients had lesionsin the anterior and middle one third of the tongue and 3 patients had lesions in the middle and posteriorone third of tongue and none of the patients had tongue lesion involving the base of tongue.all the tonguelesions were away from the mandible and Tonsillo-lingual sulcus and none of them required resection ofthe mandible. 15 patients amongst these had received neo-adjuvant chemotherapy and 10 patients hadtheir tongue lesion going into floor of mouth or just abutting floor of mouth but away from the mandible .All these patients underwent wide local excision of tongue lesion with approximately 1cm margin and inall these cases,the continuity of the floor of the mouth was disrupted . Amongst the 34 patients, 1 patienthad carcinoma in the floor of mouth, the size being 1*0.5cm and not requiring mandible resection. Noneof the 34 patients had received pre-operative radiotherapy.After the excision of the primary tumor ,the defect in the floor of the mouth was

repaired primarily in 20cases and platysma flap put in addition and secured to the adjoininig structures and in the rest 14 cases,only platysma muscle was used to reconstruct floor of mouth defects without primary closure.Among the 34 patients with platysma flap, all the patients were allowed liquid diet from seventh postoperative day and amongst them , 2 patients had leak from the floor of mouth. This in one patient wasevident from the immediate post operative period when the neck drain negativity could not be maintainedand in the other patient it was manifested by increased amount of fluid in the neck drain. Both thesepatients were managed conservatively and they were kept nil per oral for long periods(15 to 20 days) andonly ryles tube feeding was given for this period and followed up regularly.30 patients among these were subjected to post-operative radiotherapy and none of them had anymorbidities related to the flap site. **Conclusions:** Vertical platysma muscle flap that sacrificed the facial artery, with the specific advantages of being easyto prepare and having few limitations, may provide an efficient method for reconstructing the floor ofmouth defects. The one thing which should be kept in mind is that while raising the skin flaps for neck dissection in cases of oral carcinoma, care should be taken to handle the platysma gently which otherwise may lead to tears in platysma and thus, making it unsuitable for use as a flap. Also , this flap may not be reliable in cases of large defects in floor of the mouth or lesions requiring mandible resection as well in which other flaps should be considered.

Can Metastatic Lymph Node Ratio be Used as an Independent Prognostic Factor in Carcinoma Tongue?

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Background: Lymph node metastasis is an established prognostic factor in carcinoma of tongue. The association between lymph node ratio (LNR) [ratio of positive lymph nodes to the total number of dissected lymph nodes] and survival has been recently studied. But the available literature is mostly retrospective in nature and they take the broad group of oral squamous cell carcinoma as a whole and not as a single sub site , also it does not take in to consideration the importance of standardising the minimum number of lymph nodes to be dissected or a single head and neck pathologist examining the specimen to avoid wide variations in the ratio and to reduce the bias. Hence we sought to determine, using a prospective study ,whether the lymph node ratio , as an independent factor , impacts survival in node-positive squamous cell carcinoma of tongue and whether a cut off can be arrived at to risk stratify the patients. **Methods:** We prospectively studied 51 consecutive pathologically node positive patients with squamous cell carcinoma tongue who satisfied our selection criteria. A standard surgery for the primary was done under frozen control and a comprehensive neck dissection done , with the minimum number of lymph node harvest kept at 15.All the specimens were examined by a single head and neck pathologist. Further adjuvant treatment was given according to our institution protocol. They were followed up with a regular clinical examination for an average period of 24 months. The 2 Yr OS and DFS were calculated using the Kaplan meier method .LNR was subjected to univariate and multi variate analyses. **Results:** The 2 yr OS was 37.8 % for patients with LNR > 0.10 compared with 88.2 % for patients with LNR < 0.10 (p value 0.0187) Similarly, the DFS was 46.3% for patients with LNR > 0.10 compared with 83.6% for those with LND <0.10 (p value 0.0859). LNR was a significant prognostic factor in both univariate and multi variate analyses. **Conclusion:** In squamous cell carcinoma of tongue, an increased Lymph node ratio (LNR) is a strong predictor of decreased survival. A lymph node ratio (LNR) > 0.10 is associated with a worse outcome.

Larynx Preservation -Does it preserve function?

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Objective: Focus of management of laryngeal cancer has shifted from surgical intervention to conservation or larynx preservation strategies .Though issues related to survival are addressed, questions pertaining to preserving function still remain unanswered. This has brought to light various challenges necessitating studies to re-examine the indications of organ preservation in laryngopharyngeal cancers. **Methods:** Prospective analysis of patients with T3 carcinoma of larynx and hypopharynx undergoing nonsurgical definitive treatment as per our institution protocol (either RT or CTR) were followed up from 2013 to 2016 at our centre .Factors like age, pre treatment tracheostomy , feeding tubes, site and subsite, stage of disease with history of continued habits ,residual or recurrences and salvage treatment with laryngoesophageal dysfunction were analysed. **Results:** 57 patients were enrolled in the study. Majority were found to be hypopharyngeal T3 cancers. 15% were tracheostomised preoperatively of which only 2 could be decanulated after definitive treatment. 16 patients developed recurrence either at the primary site or at nodal level of which 6 had salvage surgery and 8 had palliative treatment. Around 50% of subjects had signs or symptoms of dysfunctional larynx like persistent aspiration, tracheostomy tube and/or Ryles tube dependence. **Conclusions:** In the case of early cancers of the larynx and hypopharynx (T1 – T3), it is imperative that rather than blindly following guidelines and subjecting a patient to organ preservation protocols, 'conservation laryngeal surgery' option be offered to the patient, especially if surgical expertise is available.

Simultaneous Integrated Boost to Treat Locally Advanced Squamous Cell Carcinoma of Head And Neck – A Strike Off Between Acute Toxicites And Earlyresponse ? What Do We Choose?

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Background: The treatment for head and neck cancer (HNC) has considerably changed from previous conventional fractionation to SIB (Simultaneous integrated boost) IMRT. But despite sincere efforts, these approaches have been associated with comorbidities &locoregional disease recurrence. It has always been necessary to find new and novel ways of treating HNC to gain maximum locoregionalcontrol & decrease morbid side-effects both in terms of cost & adverse reactions (acute & long term). SMART (simultaneous modulated accelerated radiotherapy) or HD-SIB is one such new accelerated fractionation schedule requiring attention. **Aim:** To compare early tumour response(3 months post chemoradiation) &acute toxicities between IMRT using conventional fractionation&IMRT using HD-SIB radiotherapy (SMART) in locally advanced HNC. **Materials and Methods:** Forty patients were recruited in the study, divided equally in two arms – standard control arm & study arm.In the conventional fractionation IMRT arm (Arm A), patients received doses 70 Gy/35 #, 63 Gy/35# and 56 Gy/35# to PTV 1, PTV2 and PTV3 respectively. In the SMART boost IMRT arm (Arm B), patients received 60Gy/25# and 50Gy/25# to PTV1 and PTV2 respectively. Weekly Cisplatin 40mg/m2 was given concurrently in both arms.The endpoints were early tumor response & acute toxicities. **Results:** Heterogeneity analysis showed that both the arms were comparable in their patient and disease characteristics. The Analysis performed with the data available from 40 patients showed that the complete response rate in ARM B was superior to ARM A (88.2% (ARM B) Vs 52.6% (ARM A);p=0.024). It was also seen that patient being treated under ARM A had higher statistically significant break in radiation in comparison to ARM B (Mean: 2.45 days (ARM A) Vs 0.35 days (ARM B); p = 0.029). There was no statistically significant difference seen in mucositis, dermatitis, dysphagia, weight loss, assisted feeding, fatigue, xerostomia, dysguesia, hoarseness, vomiting, anemia, neutropenia and thrombocytopenia between both arms. **Conclusions:** Compared to IMRT using conventional fractionation schedule, IMRT using HD-SIBtechnique provides superior early tumour response without increasing acute toxicities. The added

potential advantage with this schedule is overcoming tumour repopulation by early completion of RT & lesser breaks in treatment required. Hence, we concludeHD-SIB technique (SMART)may increase the early tumour control rate in shorter duration of time.

Production of L-Asparaginase Enzyme in Inhibiting Lymphoblastic Cancer From Bacillus Species

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Several researches are conducted about the use of L-asparaginase in cancer therapy. L-asparaginase acts as a chemotherapeutic agent against acute lymphoblastic leukemia, lymphosarcoma mostly used in the treatment of children. In leukemic cells, the asparaginessynthetase enzyme is absent which impart on intracellular pools of L-asparaginase for the functioning of cell. Theoretically, the leukemic cells can be selectively killed by the deamination of asparagines serum, except normal cells, because they are capable of synthesizing asparagine intracellularly. The activity of L-asparaginase was broadly reported in plants, animals and micro organisms, but on industrial scale L-asparaginase is mainly produced by E. coli. Although the mechanism of action and toxicities of both the drugs are identical, their pharmacokinetic properties are different and patients allergic to one drug are normally resistant to the other. In cancer therapy, the use of L-asparaginase in clinical utility is limited by three factors. First, are the side effects related to L-asparaginase administration, commonly includes immunosuppressant and pancreatitis. Second, after successfully treated 10% of patients suffer with the reappearance of tumor that are resistant to additional L-asparaginase therapy. Lastly, long termed treatment with L- asparaginase enhances the growth of resistant tumor and results in increase in its metastatic activity. Two possible mechanisms have been proposed for L-asparaginase resistance. The first, it can be done by increasing in asparagine synthase level,which has been present in the blasts cells of patients having acutelymphoblastic leukemia.Second, can be done by producing the anti-asparaginase.

Objectives:

1. Isolation of Microorganisms
2. Screening of Mircoorganisms
3. Biochemical Tests
4. Production of Enzyme
5. Characterization of Enzymes.

Minimal Invasive Parathyroidectomy - Feasibility, Pros and Cons

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Background: Minimally invasive parathyroidectomy (MIP) is making the smallest incision possible that still provides adequate exposure to perform a safe surgery, usually <3 cm. This study aim to identify the feasibility, complications and localisation studies required for the MIP. **Materials And Methods:** It is a retrospective analysis done between 2007 - 2015. Total 43 patients studied. Indications for MIP are Single parathyroid adenoma, localizaton studies positive for adenoma, normal thyroid. Most common in females(29/43), common age group is in 5th decade. Most common presentation is abdominal symptoms. Most common location of parathyroid adenoma is left lower gland. Most common localization methods used were USG neck and sestambi scan. Performed under local anesthesia in 18 patients. One patient developed recurrent laryngeal nerve injury and 12 patients developed postoperative hypocalcemia, two patients developed recurrence of hypercalcemia, in one patient failed. **Conclusion:** Miniparathyroidectomy is an effective and safe procedure. Failure and complications rates are low. Can be performed even in centres with out introperative localization procedures.

Metabolic Toxicities in Non-Hematological Cancer Patients: A Cross-Sectional Study From a Tertiary Cancer Care Center in India

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Introduction: Developing world shares majority of overall global burden of malignancy. With increasing burden more number of patients are now a days undergoing cancer directed therapy. This has led to a steep rise in toxicities of anti-cancer therapy in these nations. **Objectives:** To evaluate the prevalence of metabolic toxicities in patients with different non-hematological malignancies, while on treatment, admitted in oncology ward of a tertiary cancer care center. **Materials and Methods:** This cross-sectional study was carried out over a period of seven months (January-July 2013) for all adult patients with non-hematological malignancies who, while on treatment, got admitted to our in-patient ward with features of metabolic toxicity. The clinico-demographic and treatment details were collected. Grading of toxicity was done using National Cancer Institute CTCAE V 4.0. Impact of different variables on metabolic toxicities and death were analyzed. Chi-square and Fisher's exact test were used for univariate and multivariate analysis although multivariate analysis was skipped for factors related to death due to small number of deaths. P value <0.05 were considered to be significant. SPSS version 20.0 was used for statistical analyses. **Result:** A total of 31 patients got admitted and a total of 46 events of metabolic toxicities were noted over this period. The median age of the study cohort was 41 years (range: 19-68 years). The male: female ratio was 1:0.63. Majority of them had a poor PS (ECOG ≥2), history of addiction (n=21) or comorbidities (n=16). The common sites of primary malignancy were lung (n=9) followed by head and neck (n=8) breast (n=3) and extremity sarcoma (n=3). Most of them received curative treatment (n=20) and were treated with more than one modality. The most common of them was hyperglycemia (n=10; grade ≤2: 8; grade ≥3:2). The others were hypokalemia (n=9, grade ≤2: 6; grade ≥3: 3), hyponatremia (n=9, grade ≤2: 7; grade ≥3: 2), hypernatremia (n=5; grade ≤2:3; grade ≥3: 2), hyperkalemia (n=5; grade ≤2: 4; grade ≥3:1), tumor lysis syndrome (n=4), hypercalcemia (n=2, both grade ≤2) and grade ≤2 hypomagnesaemia (n=2). However death occurred in 5 patients. Treatment interruptions took place in 19 patients (median duration=8.8 days). Prolonged hospital admission (>14 days), intensive care and artificial ventilation support were required in 10, 7 and 2 patients respectively. Age ≤40 years, ECOG performance status ≥ 2, history of addiction, comorbidities were associated with increased risk of having metabolic toxicities on univariate analysis. While on multivariate analysis only age, performance status and history of addiction retained their statistical significance (**Table: 1**). Age ≤40 years (p=0.02), use of more than one modality of treatment (p=0.021) and hyperglycemia (p=0.042) was associated with higher risk of death. **Conclusion**:Metabolic toxicities are common phenomena among cancer patients especially those with young age, and poor PS and history of addiction. They can be fatal especially when more than one treatment modality has been used more so in young adults and in presence of hyperglycemia.

Factors Influencing Early Recurrence and Survival of Oral Squamous Cell Carcinoma. A Report of 171 Cases

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Introduction: Oral squamous cell carcinoma (OSCC) is a common malignant tumor of the head and neck, and recurrence is an important prognostic factor in patients with OSCC. We explored the factors associated with recurrence of OSCC and analyzed the survival of patients after recurrence. Clinicopathologic and follow-up data of 275 patients with OSCC treated by surgery in the Cancer Institute and Hospital of Tianjin Medical University between 2002 and 2006 were analyzed. Recurrence factors were analyzed with Chi-square or Fisher's exact test and multivariate analysis. The prognosis of patients after recurrence was analyzed with the Kaplan-Meier method and log-rank test. The recurrence rate was 32.7%. The recurrence time ranged from 2 to 96 months, with a median of 14 months. Univariate analysis showed that T stage, degree of differentiation, pN stage, flap application, resection margin, and lymphovascular invasion were factors of recurrence ($P < 0.05$). Multivariate analysis showed that T stage, degree of differentiation, and pN stage were independent factors of recurrence ($P < 0.001$). The differences in gender, age, tumor site, region of lymph node metastasis, and perineural invasion between the recurrence and non-recurrence groups were not significant ($P > 0.05$). Kaplan-Meier and log-rank tests showed that the 2- and 5-year survival rates were significantly lower in the recurrence group than in non-recurrence group (67.6% vs. 88.0%, 31.8% vs. 79.9%, $P < 0.001$). Therefore, to improve prognosis, we recommend extended local excision, flap, radical neck dissection, and adjuvant chemoradiotherapy for patients more likely to undergo recurrence.

Keywords: Oral tumors, squamous cell carcinoma, recurrence, survival

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Oral squamous cell carcinoma (OSCC) is the most common malignant tumor of the head and neck, and its incidence has increased in recent years. Postoperative tumor recurrence leads to a poor prognosis and a poor quality of life. Identifying factors that affect the recurrence of OSCC to reduce postoperative recurrence is an emerging issue.In this study, we collected clinicopathologic and follow-up data of patients with OSCC and analyzed recurrence factors and patient survival. **Materials and Methods**:171 diagnosed patients with OSCC who were admitted in the Department of Oral and Maxillofacial Surgery, Dhaka Dental College and Hospital between January 2014 and December 2014 were included in the study. After curative surgeryof 98 patients, they were referred for consideration of adjuvant therapy to the oncology Department. Detail preoperative, operative and post-operative follow-up data were collected in a data sheet. Time to recurrence was determined by the duration from the first surgery to clinico-pathologically confirmed recurrence. **Results**:Out of 171 OSCC patients 57 patients were referred for palliative management, 16 patients were discharge on risk bond and curative surgery was done for 98 patients. 69 patients were regularly followed-up.46.4% patients had recurrence. Recurrence time ranged from 3 to 23 months. Most of the patients had recurrence at the primary tumor site. A lower recurrence rate was related with T1-T2 stage, well differentiation pN0 stage, negative tumor resection margin. Multivariate analysis showed that T stage, degree of differentiation, pN stage, and adjuvqant therapy status were associated with recurrence.Nineteen patients (27.5%) died due to recurrence or tumor-related diseases. 53.6% patients had no sign of recurrence till November 2015 (12-23 months). **Conclusion:** To prevent early recurrence and improve prognosis, we recommend giving emphasis on early diagnosis and surgery, extended local excision, and adjuvant chemoradiotherapy for patients with oral squamous cell carcinoma.

A Prospective Study of Quality of Life in Patients With Carcinoma Oropharynx Treated With Radiotherapy

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Aim: To evaluate the quality of life (QOL) of patients with carcinoma oropharynx during and after treatment with radiotherapy. **Methods:** Sixty patients participated in this prospective, descriptive study .Health-related quality of life was assessed at baseline , immediately at the end and at 6 months post radiotherapy treatment by means of the European Organization for Research and Treatment of Cancer (EORTC) Core Quality of Life Questionnaire and the EORTC head and neck cancer-specific questionnaire. **Results:** All patients filled in questionnaires. The general trend was that health related QOL deteriorated significantly during treatment, followed by a slow recovery of some symptoms until 6-month follow-up . Social function decline at end of radiotherapy treatment; The personal role performance was lower in the end of treatment and the emotional function was assigned the lowest mean value among all the functions. Considering the scale of symptoms, the occurrence of insomnia was higher at treatment onset; however, nausea, vomiting, pain, loss of appetite and constipation were higher at the end of the treatment followed by recovery at 6 month post radiotherapy . The QLQ-H&N35 specific questionnaire shows a difference at end of radiotherapy treatment , highly significant for taste and smell ($p = 0.02$), deglutition ($p = 0.04$), and weight loss ($p = 0.02$). Pain and swallowing, dental problems, and the use of analgesics - were symptoms of higher impact during and end of radiotherapy treatment. At the end of treatment, the use of food supplements, difficulties to open one's mouth, greater changes in senses (olfaction and taste), speech disorders, social difficulties in feeding, loss in sex drive and a feeling of being sick, had the higher mean values in relation to the other two moments. **Conclusion:** Radiation-induced hyposalivation invariably persists and correlates with poor global QOL scores seen during and at end of Radiotherapy. Post radiotherapy, there is a trend for some symptoms reversal toward pre-irradiation levels suggesting a subsiding inflammation or a probable functional recovery. EORTC QLQ 30 and QLQ-H&N35 questionnaire with the oral assessment may provide useful outcome measures for assessment of oral care prevention and management strategies in these patient populations. The results show that the questionnaire is responsive to change throughout the course of radiation therapy for head and neck cancer.

Factors Influencing Recurrence In Patients After Neck Dissections For Head And Neck Squamous Cell Cancers - A Prospective Cohort Study

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Background: Overall 57.5% of all head and neck cancers occur in Asia. Metastasis to regional lymph nodes reduces the 5-year survival rate by 50%, hence the management of the neck nodes is an integral part of treatment of head and neck cancer. Neck dissection is performed for the surgical control of metastatic neck disease. Despite great progress in chemotherapy, radiotherapy, and targeted therapy in the last three decades, the prognosis of Squamous cell carcinoma is poor due to aggressive local invasion, advanced stage of presentation in Asia & India, and metastasis, leading to recurrence. Thus, Squamous cell carcinoma is still a challenging disease to treat in the field of head and neck cancer. Recurrence is an important prognostic factor in patients with this disease. Locoregional recurrences are seen in 15 to 50 percent of patients with squamous cell carcinoma of the head and neck, and this is a major factor contributing to deaths from head and neck cancer Postoperative tumor recurrence leads to poor quality of life. Identifying factors that affect the recurrence of OSCC to reduce postoperative recurrence is an emerging issue in clinic. With this issue in mind we conducted a prospective study as we are a high volume centre for head and neck malignancy. **Material& Methods:** In this prospective study one hundred and two (n=102) patients underwent neck dissection from 2010 to 2012 were included. Patients with histologically confirmed malignancy were preoperatively assessed clinically and radiologically. This allows a decision to be made regarding the feasibility of achieving a complete resection and type of neck dissection to be performed A minimum follow-up of three year was set up as a essential prerequisite. Data was collected for patient details, clinical presentation, site of primary tumor, status of neck nodes, preoperative investigations including radiological and pathological studies,

surgical management and type of neck dissection performed, postoperative histopathology, recurrence, adjuvant therapies given. Univariate analyses were performed to correlate the outcome with independent variables. Chi-square test was used for correlation between two variables. T-test was applied and probability values p values of 0.05 or less were considered significant. **Results:** Out of 102 patients, there were 19 patients who developed local recurrence in the follow up period. Therefore the local recurrence rate was 18.6 %. Factors correlating with development of local recurrence:- 1- Age : Eighteen out of 19 patients who developed local recurrence were above 40 years of age while only one patient was in the age group of 0- 40 years. Recurrence rate was 26.1% in >40 years age group as compared to 7.7% in 0-40 years age group. This showed that older patients seemed to have a greater chance of developing neck recurrence and,therefore, worse evolution. However, on statistical analysis using chi-square test, advanced age was not shown to be statistically significant factor for development of local recurrence (p=0.149). 2- Sex - Recurrence rate was 23.9% in males and 20% in females. Sex of the patient did not correlate with development of recurrence on statistical analysis (p=0.747). 3- Site - The presence of neck recurrence among various primary sites was different. 5 patients had primary located in oral cavity, 6 patients had oropharyngeal cancer, 3 patients had carcinoma hypopharynx and 3 patients had MUO and one patient had carcinoma larynx. It was shown statistically that patients with primary in the hypopharynx and oropharynx had a greater chance of developing neck recurrence as compared to oral cavity and larynx (p=0.017). 4- Stage - There was a statistically significant correlation between clinical AJCC stage of the patient and development of neck recurrence. 14 patients out of 19 who developed neck recurrence in the follow up period had stage III disease at initial presentation while only 2 patients had presented with stage II disease. This showed that advanced stage at presentation was a positive predictor for development of neck recurrence (p=0.029). 5- Nodal status - Among the 19 patients who developed local recurrence, 15 patients were clinically node positive at initial presentation and only 4 patients had clinically node negative neck. Probability of developing neck recurrence showed direct correlation with increasing nodal stage. Recurrence rate was 6.2% in patients with N1 nodes, 35.7% in patients with N2 nodes and 60% in patients with N3 nodes. It was observed that patients with clinically node positive and N2/N3 disease had a significantly higher chance of developing local recurrence (p value=0.029). 6 T stage - There was no statistically significant correlation between clinical T stage of primary tumor and the appearance of neck recurrence (p=0.276). 7- Type of neck dissection - This did not show any statistically significant correlation with development of neck recurrence. Out of these 19 patients 11 had undergone RND, 7 patients were treated with MRND and SND was performed in one patient (p=0.742). 8- Upfront surgery group versus neoadjuvant treatment - Recurrence rate was 11.1% in the upfront surgery group and 32.6% in the neoadjuvant treatment treatment group. This difference statistically significant (p=0.022).This showed that the likelihood of developing local recurrence was more in patients with prior history of chemotherapy or radiotherapy before undergoing surgery as compared to patients undergoing upfront surgery. Amongst these 19 patients. Recurrence rate was 36.4% in patients receiving only chemotherapy, 25% in patients receiving only radiotherapy and 33.3% in patients receiving both chemotherapy and radiotherapy prior to surgery compared to just 11.1% in patients undergoing upfront surgery, a difference which was statistically significant. Figure LIX shows distribution of patients with local recurrence according to prior therapy. 9. Effect of adjuvant therapy on recurrence rates - Recurrence rate was 28% in adjuvant therapy group and 20% in patients who did not receive adjuvant therapy and this was not statistically significant. (p=0.395). Clinical and pathological node positivity, stage III-IV disease, oropharyngeal and hypopharyngeal tumors and neck dissection after induction therapy were all associated with higher recurrence rates. (p<0.05). **Conclusion:** Recurrence is not affected by the type of neck dissection in N0. In patient with node positive neck additional features such as age, grade & primary site should be taken into account.Advanced clinical stage at presentation and clinical and pathological node positive disease were identified as important positive predictors for development of recurrence and increased mortality. In advanced stage disease if deemed operable surgery should be offered upfront. Patients with hypopharyngeal and orophayrngeal malignancy should be kept on strict vigil and follow up as they are at high risk of recurrence.

Effectiveness of "Instructional Strategy" On Knowledge, Practice And Quality of Life of Head And Neck Cancer Patients Receiving Radiotherapy In Selected Cancer Research Institute, Uttarakhand

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The cancer is a disease of cell in which the normal mechanism of the control of growth and proliferation has been altered.Annually, nearly 500,000 people die of cancer in India. The WHO said this number is expected to rise to 700,000 by 2015. **Purpose:** The Purpose was to educate the patients with head and neck cancer undergoing radiation therapy about management of side effects to improve their quality of life. **Method:** A Quantitative research approach with Quasi-experimental pre-test post-test design. The study was conducted in selected Cancer Research Institute, Dehradun, Uttarakhand. Consecutive sampling technique was used for data collection from 60 Head and Neck cancer patients by using Structured Knowledge interview schedule, Structured self-reported practice checklist and EORTC H&N35 QLQ. **Result:** The mean post-test knowledge score in experimental group was 18.70±3.06 which was significantly higher than the control group 11.50±5.00. The mean post-test practice score in experimental group was 16.40±1.86 which was significantly higher than the control group 10.00±3.01. There was significant improvement in the Quality of Life of the patients in experimental group in different phases of radiation therapy. In multiple item scales-Pain (0.014 on 8th day &<0.001 on 16th day), swallowing (<0.001 on 16th day), sense problems (0.019 on 8th day & 0.020 on 16th day), speech problem (0.058 on 8th day & 0.041 on 16th day), social contact (0.005). In single item scale teeth (0.019 on 8th day), opening mouth (<0.001 on 16th day), dry mouth (<0.001 on 16th day), sticky saliva (0.040 on 8th day &<0.001 on 16th day), felt ill (0.017 on 16th day). Moderately positive correlation was found between post-test knowledge & practice score. **Conclusion:** The instructional strategy was effective in increasing knowledge, practice of Head and Neck cancer patients and also improving their Quality of life.

Key words: Head and Neck cancer patients undergoing radiation therapy, instructional strategy, knowledge practice and quality of life

Serum biomarker for the diagnosis of head and neck squamous cell carcinoma

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Introduction: Head and neck squamous cell carcinoma (HNSCC) is the sixth most common cancer in the world. HNSCC involves the upper aero digestive tract and can destroy the structure and function of organs of this system as well as vital structures necessary for survival. Nuclear factor of kB (NF- kB) is a small menagerie of closely related protein (p50, p52, RelA, RelB and c-Rel) that bind common motif sequence known as kB site. Nuclear transcription factor p50- RelA regulates several genes that mediate tumorigenesis and metastasis. In normal cells, p50-RelA hetero-dimeric form exists in an inactivated state by IkBawhile in cancer cell this is activated by various carcinogenic compounds which induce the IKK kinase enzyme leads to degradation of IkBa inhibitory protein through the proteasomal/ubiquitination degradation pathway. After activation hetero-dimer is translocated to the nucleus, binds the kB site and activate genes which are responsible for the development of cancer.

Objectives:

- Collection of blood samples from control and HNSCC patients

- Quantification of the serum NFkB-p50and IkBaprotein by surface plasmon resonance and western blot analysis.
- Statistical Analysis of the data by Graph Pad.

Material and Methods: The case control study was performed with 125 HNSCC patients and 104 control cases. The blood samples were collected from Head and Neck Cancer Clinic, Dr. B.R.A. Institute Rotary cancer Hospital (IRCH), All India Institute of Medical Sciences (AIIMS), New Delhi, India. The study was approved by an ethics subcommittee of AIIMS Ref. No. IESC/T-60/01.02.2013The level of NFkB -p50 and IkBaproteins in serum were evaluated at pre and post therapy by label free real time surface plasmon resonance (SPR) and western blot analysis. **Results:** The serum NFkB-p50 concentration were significantly (P < 0.0001) higher at the time of diagnosis i.e. pre therapy (Mean ± SD 27.06 ± 4.88 ng/ml) as compared to controls (Mean ± SD 16.96 ± 4.04 ng/ml) while it decline at post therapy (Mean ± SD 21.01 ± 4.98 ng/ml). Similarly, the concentration of IkBa protein in serum were slightly higher at pre therapy (Mean ± SD 8.33 ± 1.85 ng/ml) as compared to controls (Mean ± SD 7.27 ± 1.84 ng/ml) and declined at post therapy (Mean ± SD 7.09 ± 1.24 ng/ml). **Conclusions:** 1) HNSCC patients showed almost 2 fold elevated level of NFkB-p50 during the time of diagnosis compare to normal group. The elevated NFkB-p50 protein in serum level of HNSCC patients as well as in the early onset of the disease and it was down regulated after the treatment. 2) IκBα is less expressed compare to NFκB-p50 protein in serum of HNSCC. On the other hand its expression level in serum of HNSCC patients was slightly higher compared to control group. However, the protein level showed significant correlation with tumor size, stage and node involvement before and after therapy. 3) The specificity and sensitivity of NFkB-p50 proteins obtained from ROC analysis revealed the potentiality to be a diagnostic protein marker for HNSCC for its accuracy in the study cohort.

Keywords: Head and Neck Squamous Cell Carcinoma, Serum, Surface Plasmon Resonance

Single Institution Experience Of Rai Therapy in 246 Cases of Well Differentiated Thyroid Cancer -A Retrospective Study

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Introduction: Thyroid carcinoma is the most common endocrine malignancy. Worldwide prevalence of thyroid carcinoma varies from 0.5 to 10 per population. Radioactive Iodine therapy has been used to ablate residual, recurrent, and metastatic thyroid tissue in well differentiated thyroid cancer. **Materials And Methods:** A Retrospective observational study was done in 246 cases of well differentiated thyroid cancer who underwent RAI therapy from January 2014 toDecember 2014 and were observed for one year till December 2015. 65 patients who had developed distant metastasis were treated with RAI therapy followed by suppressive therapy with Eltroxin.Those who had no metastasis were put on suppressive therapy and were followed up regularly.In the present study the demographic details , pathological characters and outcome of RAI therapy were studied. **Results:** In my study of 246 cases of well differentiated thyroid cancer who underwent RAI therapy after total thyroidectomy, 96 cases of Follicular carcinoma and 150 cases of Papillary carcinoma were identified.Male : female ratio is 98:148.The metastatic spread to bone, lungs, neck nodes were 40,20,5 cases respectively. Rest 181 patients did not have any metastasis. Solitary nodule versus multinodulargoitre was 49:24. Cases were referred to KMIO from different parts of the country with diagnosis confirmed by FNAC, with hemithyroidectomy and with total thyroidectomy with or without neck dissection. **Conclusion:** RAI Therapy improves survival rate of patients in Papillary and Follicular Thyroid Cancer. It increases the ease of following the tumor marker thyroglobulin and thus destroys microscopic metastasis. We were able to pick up bone metastasis,pulmonary metastasis and neck node metastasis. In my study it is observed that all 246 patients are still on follow up and alive.

Tumour Volumes: Strongly Predictors of Early Treatment Response In Locally Advanced Head and Neck Cancers Treated With Definitive Chemoradiation

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Introduction: Locally advanced head and neck cancers (LAHNC) are 3-dimentional lesions. The largest diameter of these tumours measured for T-classification may not necessarily reflect the true tumour dimensions. Tumour volume (TV) accurately reflects the tumour burden because it is a measurement of tumour burden in all three dimensions. The purpose of this research is to analyseand predict early response (3 months post definitive CCRT) utilising TV data in LAHNC. **Methods:** It is a single institutional prospective study including 108 patients with LAHNC treated with definitive CCRT. TV data noted were primary tumour volume (PTV), total nodal volume (TNV) and total tumour volume (TTV). Response evaluation was done at 3 months after the completion of definitive CCRT and based on response patients were categorized either having achieved complete response (CR) or residual disease. **Results:** A Spearman's rank-order correlation showed a strong positive correlation between T-stage and PTV, $r_s(99)=0.686$ ($p<0.001$), between N-stage and TNV, $r_s(83)=0.540$ ($p<0.001$) and clinical stage and TTV, $r_s(99)=0.540$ ($p<0.001$).There was significant variability of TV within same stages as shown by Kruskal-Wallis H test which showed median PTVs, TNVs and TTVs to be statistically significantly different between four groups of T-stages (T1-T4), $\chi^2(3)=46.563$($p=0.000$), five N-stages (N1,N2a,N2b,N2c,N3) $\chi^2(4)=29.60$ ($p=0.000$) and three clinical stages (III,IVa,IVb) $\chi^2(3)=27.18$ ($p=0.000$) respectively. Of 101 patients available for response evaluation 56 (55.4%) were found to have CR and 45 (44.6%) residual disease. Patients who did not achieveCR were found to have larger TV compared with those who achieved CR. There were significant inverse correlations between PTV and response at 3 months, and between TTV and response at 3 months (Table). Receiver operating characteristic (ROC) analysis identified an "optimal cut-off" value of 41cc for PTV and 42cc for TTV above and below which there was greatest magnitude of difference in early response. **Conclusions:**If response to CCRT is to be predicted it is simply not enough to measure a largest single dimension of the tumour. TV measurement seems to be a better and more accurate reflection of the true total tumour burden or extent of the disease. It is concluded and claimed in our study that TVs, particularly PTV and TTV are powerful predictors for 3 months post CCRT response. Table : Association between Tumour volumes and Response at 3 months

	Complete Response		Residual		P Value
	Median	IQR	Median	IQR	
PTV	-	6.82-35.25	45.2	24.65-74.31	0.001
TNV	8.01	2.55-16.40	12.78	1.70-41.40	0.229
TTV	36.14	20.86-45.97	66.06	46.45-86.31	<0.001

Keywords: Head and neck, Prognostic factors, Tumour volume

Neoadjuvant chemotherapy and surgical margin in technically unresectable buccal mucosa cancers

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Introduction: T4buccal mucosa cancers with peritumoral edema reaching up to or above the level of zygomatic arch are termed as technically unresectable cancer. The risk of margin positive resection is high in such tumors. Neoadjuvant chemotherapy (NACT) followed by surgery remains an option in this group. Whether the margin positive rates of this cohort

is similar to our upfront operated T4 technically resectable tumors is not known. This audit was done to address this issue. The null hypothesis was that margin positive rate in technically unresectable buccal mucosa cancers post NACT would not be different from upfront operated T4 buccal mucosa cancers.**Method:** This was a 1:1 match pair analysis of oral cancer patients treated at Tata Memorial Hospital between 2010-2013. We had matched 215 upfront operated T4 buccal mucosa cancer patients to 215 T4 buccal mucosa cancer patients operated after NACT. In the upfront operated group surgery was performed with a 1 cm gross margin around the tumor while in post NACT group surgery was performed with a wide margin around the post NACT tumor. Chi-square test was used for comparison of margin status. **Result:** The demographic profile of these patients were similar. Overall we had a young cohort of patients in both groups and predominant population was of male gender. The table 1 shows the distribution in margin status and other important pathological characteristics associated with the tumor. In both groups the margin positive status was low. The unfavourable margin status (either positive or close margin) was seen in 5.1% of upfront operated patients while it was 3.3% in patients operated after NACT. It was interesting to note that perineural invasion was seen in quite high proportion of our upfront operated patients (23.3%) while it was not the case in post NACT patients (7.4%) (p=0.000).

Table 1 : Distribution of important post surgery pathological tumor parameters between the 2 groups.-Comparison done by chi-square test. p value in bold signifies statistical significance.**

	Upfront Surgery (n=215)	NACT-> Surgery (n=215)	P value
Positive margin	3 (1.4%)	0 (0.0%)	0.212**
Positive + Close margin	11 (5.1%)	07 (3.3%)	0.335**
Lymphovascular invasion	3 (1.4%)	3 (1.4%)	0.995**
Perineural invasion	50 (23.3%)	19 (7.4%)	0.000**

Conclusion: The result of this match pair upholds the null hypothesis. It's heartening to know that post NACT operated patients though at a high risk for margin positive resection upfront undergo R0 resections and the margin status is similar to our upfront operated patients.

Neoadjuvant Chemotherapy In Technically Unresectable Oral Cancers : Does Hpv Make a Difference?

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Background: HPV positive oropharyngeal cancers have favourable prognosis, though the impact of HPV positivity is dependent on level of tobacco exposure and on the tumour stage. We wanted to study the impact of HPV in locally advanced and technically inoperable oral cancers treated with neoadjuvant chemotherapy (NACT). **Methods:** We performed an analysis on 124 randomly selected patients of oral cancer who underwent NACT. They received 2 cycles of NACT followed by definitive local treatment. HPV positivity was identified by p16 immunohistochemistry on the pretreatment biopsy. The response rate after NACT (RECIST v. 1.1) in the HPV positive and negative cohorts were compared by proportion test. Difference in the overall survival (OS) was assessed by log rank (Mantel-Cox) test. Multivariate Cox proportional hazard regression model was applied to identify factors affecting OS. **Results:** 16 patients were HPV positive (12.9%). In HPV positive cohort, 58.3 % patients had response while in HPV negative cohort 30.3% patients had response to NACT(p=0.51). The locoregional failure rate was 45.2 % at 2 years. It was 31.3% in HPV positive and 47.2 % in HPV negative patients(p=0.40). The median OS for HPV negative patients was 684 days (95% CI 431-NA days) while it was not reached for HPV positive patients. (p=0.0845). **Conclusion:** HPV positive technically unresectable oral cancers seem to have better os. Larger prospective study is required to confirm the impact of HPV on OS in advanced oral cancers.

Transactivation of HnRNPD/Auf-1 by NF-κB(P65/RelA) in oral cancer

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Introduction: Head and neck oral squamous cell carcinoma (HNOSCC) is a heterogeneous group of malignancies that arise in upper aero-digestive tract. Approximately 90% of HNOSCC are squamous cell in origin. Regulation of mRNA stability is an important post transcriptional regulatory mechanism of gene expression which has been implicated in tumorigenesis. Approximately 16% of mRNA contains AU rich regions (ARE), in their 3'UTRs. Heterogeneous ribonucleoprotein D/Auf-1 is an RNA binding protein (AUBP), that binds to 3'UTR ARE of many mRNA and modulate their decay rates by deploying mRNA degrading proteins. Previously our laboratory has demonstrated over expression of hnRNPD in HNOSCC and established its correlation with poor prognosis of the disease. However, till date no systematic study has been carried out to elucidate the molecular mechanism of its over-expression in oral cancer. Therefore present study was undertaken to elucidate the mechanism of transcriptional regulation of hnRNPD expression in oral cancer. **Objectives**: PCR amplification and cloning of hnRNPD promoter region in pGL3-Basic vector followed by demonstration of promoter activity in the cloned fragment and identify the functional transcription factor(s) binding motif(s) on hnRNPD promoter by promoter deletion analysis. **Material and Methods:** Upstream region of hnRNPD gene was PCR amplified and subjected to double stranded DNA sequencing and the nucleotide sequence thus obtained was aligned with nucleotide sequence of upstream region of hnRNPD gene. Fragment exhibiting 100% homology to the upstream region of hnRNPD gene was cloned upstream to the promoterless luciferase reporter gene into pGL3-Basic vector. The resulting vector was transfected in two different oral cancer cell lines SCC-4 and SCC-25 to assess promoter activity of the cloned fragment. Promoter deletion analysis and ChIp assays were performed to identify the promoter region and transcription factor(s) respectively involved in regulation of hnRNPD expression. **Results:** Promoter reporter assay demonstrated significantly higher hnRNPD promoter activity in SCC4 cells as compared to SCC25 cells. *In silico* analysis of cloned hnRNPD promoter region revealed many putative transcription factors binding sites including four NF-κB1 and one NF-κB (RelA/P65) binding motifs. Deletion of NF-κB (RelA/P65) binding motif located between -1150 and -1161 resulted in a significant decrease in hnRNPD promoter activity. ChIP assay revealed binding of transcription factor NF-κB to this motif. Furthermore, treatment of SCC4 cells with PDTC, a specific inhibitor for NF-κB specific abolished NF-kB binding to this motif with a concomitant decrease in the level of hnRNPD in oral cancer cells. **Conclusions:** Results of the present study for the first time establish the involvement of NF-κB in transcriptional up regulation of hnRNPD expression in oral cancer.

A Prospective Randomised Comparative Study of Weekly Cetuximab Versus Weekly Cisplatin With Concurrent Radiotherapy In The Treatment of Locoregionally Advanced Head And Neck Squamous Cell Carcinoma

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Background/Objective(s): To assess and compare the efficacy and safety of weekly cetuximab versus weekly cisplatin withconcurrent radiotherapy in the treatment of locoregionally advanced head and neck squamous

cell carcinoma(HNSCC). **Material & Method**: 50 patients of previously untreated locally advanced HNSCC were recruited in the study. 25 patients were treated with weekly cetuximab along with concurrent radiation constituting the study arm and 25 patients by weekly cisplatin and concurrent radiation constituting the control arm.During and after chemoradiation patients were evaluated for response to treatment and related toxicity.[usingRECIST Criteria version 1.1, RTOG criteria, and CTCAE criteria].Significance of difference in proportion in both the group was inferred by Chi-square test. **Results:** Overall response(OR) in study group(CET+RT) is 76%(CR-56%+PR-20%), whereas OR in the control arm(CIS+RT) is 80%%(CR-52%+PR-28%), but the difference is statistically not significant(p=1.00). Grade 3 & 4mucositis (60% & 16%),grade 3 & 4 dysphagia(16%&12%), grade3nausea&vomiting(4%), were more in the cisplatin arm.Incidence of grade 3 Leucopenia were more in thecisplatin arm i.e 8% (2 patients) Incidence of Grade 3 dermatitis was more in cetuximab arm and was seen in 13 patients (52%) & none had grade 4 dermatitis, wheras only 3 patients (12%) had grade 3 dermatitis in cisplatin arm. Infusion reactions were also more in cetuximab arm, 1 patient (4%) had grade 3 infusion reaction, 4 patients (1 had grade 1, 3 had grade 2 infusion reactions). **Conclusions:** The overall response achieved incetuximab+RT arm is 76% (CR-56%+PR-20%) , wheras OR in cisplatin+RT arm is 80%(CR-52%+PR-28%), which is slightly more than the CET+RT arm) , but the results are statistically not significant.(p=1.00). Acute toxicities like oral mucositis, dysphagia, nausea, vomiting, leucopenia observed with cetuximab were acceptable andless as compared to that ofcisplatin, and were manageable with simple symptomatic & supportive measures. So we can conclude thatweeklycetuximab is a well tolerated regimen with concurrent radiotherapy with similar efficacy as that of cisplatin.

Keywords: Locally advanced head and neck cancer,cetuximab, cisplatin, radiotherapy

To Determine the Incidence of Clinical and Subclinical Hypothyroidism Among Head And Neck Cancer Patients Receiving Imrt To The Neck By Performing Thyroid Function Tests And Analysing Dose Volume Histograms (Dvh)

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Background: Hypothyroidism is a well known late toxicity after radiation therapy for head and neck cancer.The incidence that have been reported range from 17-47.7%. The purpose of present study was to determine the incidence of clinical and subclinical hypothyroidism among head and neck cancer patients receiving IMRT to the neck by performing Thyroid Function Tests and analysing Dose Volume Histograms(DVH) **Material And Methods**: Data from a total of 48patients undergoing IMRT for head and neck cancers was retrospectively evaluated.Patients who received External Beam Radiation between January 2011 and July 2015 were evaluated.The median follow-up term was 22 months (range, 3–48 months). The thyroid function was evaluated by measuring thyroid-stimulating hormone (TSH) , free thyroxine (FT4) levels and free T3 levels. The mean thyroid dose for patients developing hypothyroidism was 42.6Gy. Free T3,T4,TSH estimations were done at baseline , at 6 months and 12 months following RT. **Results**: Of the 48 patients, 44(91.6 %) were males and 4 (8.3 %) were females.Fifteen patients underwent prior neck dissection. Seven patients (14.5%) were found to have clinical hypothyroidism. Three (6.2%) patients were found to have subclinical hypothyroidism, with a total 10 out of 48 (20.8%) patients developing radiation-induced hypothyroidism. Five out of seven patients with clinical hypothyroidism were in the age group of 51 to 60 years. **Conclusion**: Hypothyroidism (clinical or subclinical) is an under-recognized morbidity of external radiation to the neck. Recognizing hypothyroidism (clinical or subclinical) early and treating it prevents associated complications. Hence, Thyroid Function Tests should be made routine during follow-up.

Salivary Gland Regeneration after Radioiodine Damage by Curcumin Administration in a Murine Model

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Introduction: Radioiodine (RI) therapy is known to induce oxidative stress to cellular components of salivary gland (SG) and result in SG dysfunction. Protective effects of antioxidants in RI-induced SG damage have not been well described in the literature. **Objectives**: In this study, we investigated the morphometric and functional changes that occurred during the 4 months after curcumin and amifostine supplement preceding to RI therapy in a murine model. **Material and Methods**:Four-week-old female C57BL/6 mice were divided into four groups; (i) normal control, (ii) RI-treated (0.01 mCi/g mouse, p.o.), (iii) curcumin and RI-treated, (iv) amifostine and RI-treated group. Salivary functions and morphological examinations were evaluated and TUNEL assay was performed. The changes in salivary ^{99m}Tc pertechnetate uptake and excretion were observed by single-photon emission computed tomography. **Results**:Curcumin administration exhibited improved salivation capacity after RI exposure. Morphologies of SGs were also improved in curcumin group compared to control group. Less apoptotic cells were observed in curcumin treated mice. In addition, patterns of ^{99m} Tc pertechnetate excretion in curcumin treated mice were quite different from those observed in controls.Conclusions:Curcumin supplement before RI therapy can be potential therapeutic agents to restore the function of SG damaged by RI.

Safety and efficacy of weekly versus three weekly paclitaxel plus platinum neo-adjuvant chemotherapy in patients with locally advanced squamous cellhead and neck carcinoma (SCHNC) : A Pilot Study (FOR ORAL PRESENTATION)

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Introduction:SCHNC is the third most common malignancy seen in both the sexes across the globe but is the commonest malignancy encountered in Indian males. There is enough published literature suggesting that weekly compared to 3 weekly paclitaxle plus platinum is superiorin terms of safety and efficacy in breast, ovary and lung carcinoma.Studies comparing weekly versus three weekly paclitaxel in the setting of SCHNC are lacking. In this study we assessed, in a randomized fashion, the safety and efficacy of weekly versus three weekly paclitaxel plus platinum neo-adjuvant chemotherapy in patients with locally advanced SCHNC. **Objectives:**To compare in a randomized study, the efficacy (response rates) and safety (adverse effect profile) of weekly paclitaxel plus platinum versus standard 3 weekly dosing of these agents in patients with locally advanced Head and Neck malignancies in neo adjuvant setting. **Material and Methods:**This is a hospital based comparative study done over a period of 12 months recruiting 50 newly diagnosed patients of locally advanced head and neck malignancies randomized in two groups to receive either weekly (90 mg/s.m) or standard three weekly paclitaxel (175 mg/s.m). Response was assessed using the standard RECIST 1.1 criteria. **Results:**The mean age for cases in the three weekly chemotherapy arm was 54.08 ± 11.191 (range 26-75 yrs) and in the weekly arm was 53.88 ± 9.536 (range 32-70 yrs). Highest prevalence by site was of oral and oro-pharyngeal cancers. In the three weekly arm overall haematological toxicities were present in 48% , 64% , 40% patients vs 16% , 32% , 08% patients in the weekly arm at 2, 4 and 6 months respectively. In the three weekly arm overall non-haematological toxicities were present in 24% , 36% , 40% patients vs 0% , 08% , 16% patients in the weekly arm at 2, 4 and 6 months respectively. In our study the overall response rate in the three weekly arm was 36%(12%

CR and 24% PR) while in the weekly arm it was 52%(20% CR and 32% PR) at 2, 4 and 6 months.Overall non compliance for subsequent curative treatment was seen in 48% patients post neo adjuvant chemotherapy and was similar in both groups. **Conclusions:**Data from our small study suggests that weekly paclitaxel plus platinum neo-adjuvant chemotherapy is better than the standard every three weekly chemotherapy, both, in terms of safety (adverse effect profile) and also efficacy (response rates) in patients with locally advanced SCHNC. Larger multi-centric studies are needed for confirmation.

ROLE OF NEOADJUVANT CHEMOTHERAPY IN ADVANCED UNRESECTABLE ESTHESIONEUROBLASTOMA: A CASE SERIES

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Background: Role of neoadjuvant chemotherapy in esthesioneuroblastoma is not clear. **Methods And Material**: This is a retrospective study of four patients of unresectable esthesioneuroblastoma evaluating the impact of neoadjuvant chemotherapy. This retrospective study evaluates the impact of neoadjuvant chemotherapy in locally advanced unresectable esthesioneuroblastoma patients treated between January 2011 and November 2013, in a tertiary care cancer centre in India. Data from a prospectively filled database were analyzed for patient characteristics, chemotherapy received, toxicity, response to chemotherapy, treatment offered, and overall survival.**Statistical analysis used**: Nominal data presented as numbers (percentages) and continuous data as median (range). **Results**: Four patients of Modified Kadish Stage C esthesioneuroblastoma were treated with etoposide and cisplatin based NACT. Partial response was achieved in three patients. 3 patients underwent curative intent therapy: 2 underwent surgery (R0 resections) and 1 received radical concurrent chemoradiotherapy. 1 patient was noted to have a complete pathological response. Grade 3/ 4 toxicity was seen in one patient.**Conclusion**: Neoadjuvant chemotherapy with etoposide and cisplatin is effective in locally advanced unresectable esthesioneuroblastoma where upfront R0 resection is not possible.

Keywords: Neoadjuvant, Chemotherapy, esthesioneuroblastoma

Lycopene v/s Aloevera in the treatment of oral Submucous fibrosis

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Background and Aim: Oral submucous fibrosis (OSMF) is a high-risk premalignant condition mainly seen in the Indian subcontinent.Aetiological factors including capsaicin, betal nut alkaloids, deficiency of iron and vitamines, autoimmunity, genetic predisposition and malnutrition have been suggested by various authors. Various studies have proven the use of antioxidants in the treatment of OSMF. The aim of the present study was to compare the efficacy of two antioxidants, lycopene and aloe vera in the management of OSMF. **Material and Methods:** Ninty four clinicopathologicalley diagnosed OSMF patients, were studied. They were equally divided into, Group L (lycopene group) and Group A (aloe vera group). Group L was administered 8mg lycopene in two divided doses , 4mg each dose and Group A was given 5mg aloe vera gel to be applied topically thrice daily for 3 month and follow up was done for next two months in both Groups . **Results:** Clinical improvements in tongue protrusion and mouth opening were significant in Group L ($P < 0.001$). Subjective symptoms of pain ($P = 0.006$), burning sensation ($P = 0.007$), and difficulty in swallowing ($P = 0.004$) improved in both the groups, but were insignificant. Size of the lesions decrease in both groups. **Conclusion:** Although, there is no definitive treatment of OSMF; however, lycopene use leads to significant clinical improvements in the symptoms like mouth opening and tongue protrusion when compared to aloe vera. Both the drugs appear to be promising in the treatment of OSMF.

Keywords: Aloe vera, antioxidants, lycopene, oral submucous fibrosis

Salvage Surgery In Management of Recurrent Head and Neck Carcinoma : Our Experience at Tertiary Care Hospital

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Aim: To determine factors affecting results after surgical salvage in head and neck carcinoma **Methodology:** Retrospective analysis was carried out on patients with the diagnosis of squamous cell carcinoma of the head and neck region who underwent definitive or adjuvant Radiation therapy +/- Chemotherapy as treatment. The demographic, patient, disease and treatment factors affecting the results of salvage surgery were analysed. **Results:** Demographic data and different factors affecting results of salvage surgery were analysed and were compared statistically using SPSS software **Conclusion:** Certain positive as well as adverse factors which contribute to better results following salvage surgery in head and neck carcinoma have been discussed.Very limited data in Indian population in respect to salvage surgery.

Sinonasal Tumours: A Retrospective Survey Over Six Years

Priya Malik

Pt Bd Sharma Pgims, Rohtak

Introduction: Tumours of nose and sinuses areuncommon,with several histological subtypes. Tumors of the nasal cavities are often grouped with those of the paranasal sinuses into benign and malignant. Malignant tumours have a poor prognosis because of the nonspecific nature of the symptoms and late diagnosis, at an already advanced stage, but benign lesions like angiofibroma can also be fatal due to extension to nearby vital structures like eye, optic nerve, intracranially. Hence, most sinonasal malignancies are treated with surgery and postoperative radiotherapy. Understanding the incidence and prevalence of clinical symptoms, pathology, diagnosis, and subsequent prognosis of the disease is important for early diagnosis. **Materials and Methods:** Data with a confirmed diagnosis of sinonasal cancer was retrospectively collected in a tertiary referral center over a period of six years. **Results:** There were a total of 53 patients, 32 (58.4%) male and 21 (41.5%) female and age ranged from 13-62 years, with a combined mean age of 55.07± 17.04 years. Malignant lesions were 24(45%) and benign were 29 (55%). Among benign lesions mostcommon was inverted papilloma (16) followed by hemangioma (6), fibrous dysplasia (4), osteoma (2), andfibromyxoma (1) respectively. Among malignant lesion most common was squamous cell carcinoma(8), followed by malignant melanoma(5), adenocystic carcinoma(4), olfactory neuroblastoma (3),adenocarcinoma (2), lymphoma (1), and rhabdomyosarcoma (1) respectively. The most common presenting symptom was nasal blockage in almost all patients, followes by facial swelling and epistaxis. The most common treatment was surgery. **Conclusion:** Due to their nonspecific symptoms, patients are diagnosed late, at an advanced stage and poorprognosis. All patients with nonspecific symptoms, all ages, should be evaluated properly, to reduce morbidity and mortality.

Key Words: benign, Carcinoma, Nose.

Results of elective neck dissection in carcinoma tongue at our institute.

Dr Ravi , with the contribution of Dr Roja Kiran and Dr Uday Chavan, Post-graduates in Dept. of Surgical Oncology, Dr M.Srinivasulu , Prof and HOD of the Dept. of Surgical Oncology,MNJ Institute of Oncology and Regional Cancer Centre,Hyderabad-500004.

MNJ Institute Of Oncology and Regional Cancer Centre

Aims Of Study: Incidence of cervical metastases in clinically silent neck (N 0) in carcinoma oral tongue. Incidence of isolated metastases in non-primary echelon levels of cervical lymph nodes. **Material And Methods:** All patients from January 2011 to present at MNJ Institute of Oncology & Regional Cancer Centre, Redhills, Hyderabad with carcinoma oral tongue involving anterior two-thirds not crossing the midline with a clinically N0 neck were included in the study as determined by histopathological examination, ultrasonography and CT scan. Lesion in the posterior third of tongue or crossing the midline , Post RT/CT were excluded from the study. **Results:** Out of the 84 patients with clinical N0 pathological positive nodes were present in 14 patients 16.67%. 4 patients had skip metastasis. Three had in level III and one in level IV. **Conclusions:** The incidence of occult cervical lymph node is 16.67%.There were no significant complications associated with elective lymph node dissection except three case of SAN paresis.Skip metastasis was present in 4 patients and three had in nodes in level III and one in level IV.In view of pathologically positive nodes beyond the primary echelon nodes in all patients with positive nodes in the present series, a comprehensive elective neck dissection is recommended as it adds little to the morbidity.

Immunohistochemistry combined with classical Cytogeneticanalysis and spectral Karyotypingin Oral Submucous Fibrosis, Oral Leukoplakia and Oral Squamous Cell Carcinoma

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Background: Tobacco and Arecanut related oral cancer occurs due to accumulation of genetic alterations induced by the genotoxins present in these substances. The Potentially oral malignant lesions and oral neoplasm lead to multiple chromosomal aberration and cytoskeletal changes, which are easily observed and analyzed in peripheral blood smear and tissue specimen. **Objective:**To evaluate and correlate the cytogenetic damage in the peripheral blood and tissue specimen of patients having Oral Submucous Fibrosis (OSMF), Oral Leukoplakia (OL), Oral Squamous Cell Carcinoma(OSCC) and Control subjects by analyzing the structural aberrations (STA). **Methodology:**The frequency of STA was analyzed in total 90 histo-pathologically diagnosed cases of OSMF, OL and OSCC. 5ml of fresh heparinized venous blood was collected from ante cubetal vein, from patients and age & sex matched control subjects for Leukocyte culture following standard Hungerford Method so as to investigate structural chromosome aberrations. Written informed consent was obtained from each participant. Cytogenetic damage was scored from giemsa stained metaphases. The chromatid and chromosome type was scored for the total STA. The metaphase cells were digitally imaged with Karyotyping software and Applied Spectral Imaging. The significant p value was less then 0.05. **Results and observations:** The STA showed significant p value between all the lesions and control group through ANOVA. It was also observed that the p value was significant through t-test between the pairs of group. STA showed a significant p value in cases when compared with controls and also showed an increased chromosomal alteration in OSMF, OL and OSCC, and in consonance with the clinical stages of the disease. The prominent STA in the experimental group could be attributed to the fact that they belong to high risk population for oral neoplasm. The STA identified in the present study may be used in future for early diagnosis and management of the arecanut and tobacco related oral cancer patients. **Conclusion:** The present study showed that the STA increases with the severity of the lesion that is from oral precancer to cancer. The high frequency of STA indicates high risk for cancer. Structural aberrations on chromosomes are accurate diagnostic markerfor cancer.

Neoadjuvant radiochemotherapy in technically inoperable advanced oral cavity cancers: preliminary results from a tertiary care centre.

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Background: Locally advanced technically unresectable oral cavity cancers continues to be a major therapeutic challenge despite the implementation of novel multi-modal treatment approaches.It haspoor prognosis with median overall survival of 2-12 months when treated with non surgical therapy. To improve local and loco-regional control and to allow functional reconstruction after ablative surgery, neoadjuvant protocols have been developed during the last decade implementing radiochemotherapy prior to selective surgery.The theoretical advantages of preoperative chemoradiotherapy are downstaging of the primary tumor, an increased resectability rate, and the elimination of micrometastases. We aimed to assess whether neoadjuvantradiochemotherapyregimen improves overall outcomes and operability rates in such patients. **Materials And Methods:** 36 patients were enrolled in this trial in this trial during the period from May 2014 to Nov 2015 and receivedfour cycles weekly of Cisplatin (40 mg/m2) with conventional radiotherapy (40 Gy). Within 3-4 weeks after chemoradiotherapy resection of the primary tumor and the regional neck nodes was performed. **Results:** 34 patients were evaluable for toxicity and response. Clinical complete response was seen in 22 of 36 patients (CR- 61%), and partial response in 10 of 34 patients (PR-28%). In 20 of the 36 patients complete pathological response (pCR- 56%) was documented in the resected specimen. Resectability was achieved in 32 of the 34 patients Toxicity seen were of low grade and reversible. So far local failure has been seen in 4 patients and neck failure in 2. **Conclusion:** Neoadjuvantradiochemotherapywas very effective in converting locally advanced technically unrtesectable oral cavity cancers in almost 90% patients. It was also associated with acceptable side effects and excellent clinical and pathological response rates.

Tongue Flap reconstruction for defects after resection of oral cancer

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Introduction: Defects following resection of oral cancer needs tissue replacement which provides coverage. Distant tissue transfer is not necessary for small intra-oral defects. Tongue flap can be versatile and dependable. It can be feasible alternative to technically demanding gold standard of free flap. **Objectives:** To evaluate reliability of tongue flap for small and medium size defect after resection of oral cancer in terms of viability, complications and functional outcome. **Material and Methods:** This was a retrospective database review carried out at Department of Surgical Oncology, King George's Medical University Lucknow, UP from May 2011 to May 2014. **Results:** A total of 21 patients of oral cancer underwent tongue flap reconstruction. Median age was 45 years (35 to 80 years) with male: female ratio 4:3. Sixteen patients were of carcinoma buccal mucosa, four patients had carcinoma of lower alveolus and one patient had carcinoma

of retromolar trigone. 18 patients underwent mandibulectomy (marginal mandibulectomy = 9 and segmental mandibulectomy = 9) 2 patients underwent upper alveolectomy and 2 patients had no bony resection. Median size of the defect was 5 cm (largest dimension). Average time to elevate the flap was 25 minute. Post surgery complications were bleeding 1/21 (4.8%); total flap loss 0/21; tip necrosis 2/21 (9.5%); fistula 2/21 (9.5%). All the complications were managed conservatively. Patients had satisfactory mouth opening, good mobility of tongue, swallowing & speech following surgery. **Conclusion:** Tongue flap reconstruction is simple and a reliable local flap. They have very few morbidities and functional outcomes are satisfactory. It also obviates need of distant tissue transfer.

Current TNM Staging System in Oral Cancer is Faulty: Its Need Amendment

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Introduction: TNM staging system is the universally accepted system for cancer staging including oral cancer. The basic purpose of staging is to predict prognosis and help in planning the treatment. However, the current TNM system in oral cancer do not truly reflect the burden of disease and so the prognosis &treatment strategy. It over and under stage the T disease and do not give importance to number of involved lymph nodes as in breast or colon cancer. We have analyzed our data and presenting the potential deficit and problems of current TNM system. **Methods:**It is a retrospective analysis of prospective cancer database of our department from 1st August 2006 to 31stDecember 2010. **Results:** Total 523 patients underwent surgery in this period.The M:F was 2.2:1. The age range from 13 to 89 yrs with mean of 49.8 yrs. The most common siteswerebuccal, alveolo-buccal and tongue. More than 2/3rd cancer were locally advanced (stage III-IV) by current TNM staging system.With median follow up of 18 months, patients with 4 or more nodes involvement have >80% recurrence rate whereas 1-3 LNs involvement have 28% relapse rate. Patients with ENS showed 38% relapse rate. Involvement of both skin and bone (not staged in conjunction) associated with 37% recurrence rate in comparison to involvement of isolated bone or skin involvement (T4) is associated with around 20% relapse rate. Patients with T4 stage without nodal disease have very low relapse rate (10.7%). **Conclusion:** Involvement of 4 or more node, extra nodal spread and combined involvement of skin and bone are poor prognostic factors in oral cancer. They are not placed anywhere in oral cancer TNM staging system. There is need to revise the TNM by including these 3 important factors. There is also need to make some new guidelines for adjuvant treatment in presence of these adverse factors for better outcome in oral cancer patients.

Key words: Oral cancer, TNM staging

Induction chemotherapy for undifferentiated carcinoma of the nasopharyngeal type in Algerian children and teenagers

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Background: Undifferentiated Carcinoma of the nasopharyngeal type (UCNT) is an endemic disease in some regions in the world such South-Eastern Asia, around Mediterranean Sea and Alaska. At the opposite of adults, UNCT in children and teenagers remains unfamiliar especially the treatment of advanced disease. **Methods:** A retrospective study held in our center, studying patients aged less than 21 years diagnosed with UCNT, treated between 2000 and 2013. **Results:** In our center, nasopharyngeal carcinoma represents 10% of all cancer types and 41.1% of head and neck cancers, with sex ratio of 2.1 and average age of 44 years. Undifferentiated Carcinoma (UCNT) represents 88.9% and differentiated carcinoma (DC) 6.2%Patients treated for nasopharyngeal carcinoma and aged less than 21 years represent 13.2% with sex ratio of 1.5 and average age of 17 years. UCNT was found in 97% and DC in 3%. or UCNT patients, the average time for diagnosis was 6.9 months and patients presented with different symptoms: lymph nodes 75.7%, rhinologic symptoms 64.0%, otologic symptoms 55.3%, neurologic symptoms 54.3%, ophthalmologic symptoms 5.8%.At time of diagnosis, 70% of patients were stage IV, 11.6% stage III, 8.7% stage II, 0.9% stage I. Metastases were found in 12.6% (10.7% in bone and 0.9% in lung).Induction chemotherapy was indicated in 88.3 % of patients with the average of 3.6 courses. The treatment regimen was platinum based chemotherapy in 94% and the most used association was doxorubicin + CDDP in 71.8%. After chemotherapy, complete response was obtained in 23.3%, partial response in 43.3%, progression in 10.0% and 23.3% of patients died because of uncontrolled disease. 33.9% of patients received second line of chemotherapy because of their progressive disease (10%), recurrent disease (7.4%) or metastatic evolution (16.5%) .36.9% of patients obtained a complete remission after their sequential treatment (chemotherapy then radiotherapy) and are still alive. 20.8% had never returned back to our center for active surveillance, and overall survival could not be calculated. **Conclusion**: Undifferentiated Carcinoma of the nasopharyngeal type is an aggressive and endemic subtype of head and neck cancer in Algeria, It occurs in adults but it does not save children or teenagers. It is diagnosed lately because of its rapid onset but responds well to chemotherapy and radiotherapy, and despite its advanced stage at diagnosis, it has a good prognosis. Diagnosed earlier and well managed by chemo-radiotherapy, it can be completely cured.

MSH3 polymorphism and the risk of squamous cell carcinoma of head and neck in north Indian population

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Background: Genetic polymorphisms in DNA repair genes are associated with a number of malignant transformations including squamous cell carcinoma of head and neck (SCCHN). MutS homolog 3 (*MSH3*) is involved in DNA repair and was found to be associated with SCCHN. However, study on the effect of MSH3 polymorphisms on SCCHN in Indian population is lacking. **Aim:** In our study for the first time we aimed to investigate the effect of MSH3 polymorphism on SCCHN in north Indian population. **Material and method:** We have genotyped 148 SCCHN cases and 160 healthy controls for the MSH3 A1036T (A>G) polymorphism by PCR-RFLP method. **Results:** Frequency distribution for all the three genotypes AA, AG and GG for MSH3 A1036T (A>G) polymorphism were calculated which showed more or less similar distribution among the SCCHN cases and the controls. Odds ratio and CI for AA vs AG and AA vs GG genotypes were respectively 0.77; 0.64-1.29 and 0.56; 0.16-1.99. We did not find any association of MSH3 A1036T (A>G) polymorphism even when the population were stratified as smoker and non smoker. **Conclusion:** We did not find any association of MSH3 A1036T (A>G) polymorphism with SCCHN development.

Key Words: SCCHN, MSH3, polymorphism

Gnathic Osteosarcoma - a case report

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Introduction: Osteosarcoma (OS) is a rare malignant bone tumour. It accounts for 20% of all the sarcomas and about 4%-6% occur in the maxillofacial region. The OS of the jaws usually presents at a later age than the conventional OS at extremities, with a lower incidence of metastasis and a higher survival rate. However local recurrence is common and usuallybecomes unresectable due to anatomical constrains. The exact cause of Primary OS is unknown. It may be secondary to Paget's disease, fibrous dysplasia, enchondromatosis and hereditary multiple exostosis or previous radiation therapy to the jaw region. Swelling and paresthaesia of

the involved region is the commonest presenting complaint unlike pain as in OS of extremities.Widening of the periodontal ligament space or attenuation of the lamina dura around the OS are striking radiographically findings. Early diagnosis and radical surgery account for high survival rates though some advocate adjunct chemotherapy and radiotherapy in improving prognosis. **Case Report:** A 54 year old gentleman with no comorbidities was evaluated for gradually progressive painless left lower alveolus lesion of 6 months duration. Multiple biopsies were inconclusive. CT revealed expansile lytic lesion in left body of mandible with cortical destructions mimicking chondrosarcoma.Wide excision of the lesion amounting to Left hemimandibulectomy with Modified Radical neck dissection Pectoralis major myocutaneous flap reconstruction was done Histopathological examination revealed bone destroyed and replaced by a neoplasm composed of spindle cells with irregular pleomorphic nuclei secreting osteoid confirming to be Osteogenic sarcoma - osteoblastic type - low grade and no significant nodes.Post op he received adjunt chemoradiation and is doing well at his 9 month followup. **Conclusions:**Rarity with complex clinicoradiological presentation of craniofacial osteosarcoma is the reason for presenting this case report. Also, to stress that histopathology alone confirms the diagnosis.

A Study Of Neoplastic Lesions Of Head And Neck Region In A Tertiary Care Hospital Of South-West Punjab.

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Introduction: Head and neck cancer has been the seventh most common malignancy and a major cause of morbidity and mortality, worldwide. Squamous Cell Carcinoma (SCC) is the most common histologic subtype of cancers originating from the head and neck region1. **Aims/Objectives:** To study the incidence the of head and neck malignancies in a tertiary care centre in relation to gender and histopathological features. **Materials & Methods:** The study was conducted in AIMSR, Bathinda over a period of one year on the specimens were received in the department of Pathology. H&E stained sections were studied along with special stains wherever necessary. **Observation/ Results:** Of the 1648 cases received from Dept of Otorhinolaryngology, 56 cases(3.4%) were found to be neoplastic. Among these cases (M:F::1.6:1) majority were malignant(73.2%) with most common site being tongue(28.5%) followed by thyroid(17.8%), larynx(16%), oral cavity(10.7%) and salivary glands(10.7%).SCC was the most common histopathological type,constituting 80.5% of all malignant tumors. The degree of differentiation was described in 33 cases of SCC with well differentiated(12.1%), moderately differentiated(39.4%) and poorly differentiated(48.5%). **Conclusion:** The most common malignancy of head and neck region is SCC commonly seen in males with majority being poorly differentiated at the time of diagnosis. Therefore, public enlightenment, early diagnosis &follow-up are urgently needed to improve outcomes of these patients.

Reference

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Comparative study of response between sequential chemoradiation and concurrent chemoradiation in the treatment of locally advanced squamous cell carcinoma of head and neck.

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Introduction: Squamous cell carcinoma of the head and neck (SCCHN) has been considered the sixth most common cancer in the world. Presentation with distant metastases occurs in about 10% of newly diagnosed patients with SCCHN. In a similar way, more than 50% of newly diagnosed patients with SCCHN will relapse locally or at a distant site. Because of high incidence of advanced disease at presentation and loco regional recurrences, the management of these patients remains to be a great challenge. **Material and Methods:** This comparative study was done to assess and compare the response between sequential chemoradiation and concurrent chemoradiation in the treatment of locally advanced squamous cell carcinoma of head and neck. The study was conducted during period of 1st January'2010 to 31st December'2010 at kyamch Cancer Center of KhwajaYunus Ali Medical College and Hospital, Sirajgonj. A total number of 50 patients with histopathologically proved squamous cell carcinoma of locally advanced head and neck region were selected randomly from the OPD, who met the selection criteria of the study. Arm A (25 patients) was treated with sequentially chemotherapy followed by radiotherapy and those were compared with control group i.e. Arm B (25 patients) treated with concurrent chemoradiation. Sampling was done by simple random technique. Every odd number of patients were included in Arm-A and even number of patients were included in Arm-B. Selected patients were evaluated before treatment. General management was given and then specific treatment was started. Findings of observation collected in prescribed data collection form. **Results:** Majority of the patients between 50-59 years comprised about 50% of total study population. About 86% patients were male with a ratio of male and female as 3.5:1. Most of the patients (60%) came from average socioeconomic status and 42% were businessman. About 74% patients resided in rural areas. Among 50 patients, 42(84%) were found smokers. Larynx was the commonest site on topographical distribution comprising 40% patients. Second most common site was oral cavity comprising 26%. Majority of the patients (90%) had local neck node swelling. In Arm A 60% of the patients showed complete disappearance of node after induction chemotherapy and none developed progressive nodes. Complete response was found more in Arm A (68%) in comparison to Arm B (48%), but no statistical significance were found between the treatment and response pattern. Regarding toxicities grade III mucositis was more in Arm B (64%) in comparison to Arm A (16%). 64% patients developed grade II skin reaction in arm B. Nausea, vomiting and weight loss are also found more marked in Arm B. Haematological toxicities are more pronounced in arm A. **Conclusion :**Sequential chemoradiation should little bit better response than concurrent chemoradiation and importantly toxicities were higher in arm B. So, sequential chemoradiation for locoregional control of locally advanced squamous cell carcinoma of head and neck applied here demanding favorable consideration. However, long term follow up is recommended for further comment.

Exploring Locally Advanced Angiocentric T Cell Lymphoma

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Background: Angiocentric T-cell lymphoma is a rare clinico-pathological entity representing approximately 1.5% of all lymphomas. Involvement of the nasal cavity, hard palate and paranasal sinuses by these tumors is uncommon. The lesion typically causes local destruction of cartilage, bone and soft tissues. **Material & Methods:** We explored a locally advanced case of Angiocentric T Cell Lymphoma and probed into review of literature. **Case Summary and Results:** A 45-year female with no prior comorbid conditions presented with history of nasal obstruction for two and a half years, associated with severe nasal crustingand had insidious onset of ulceration of soft palate of 5-months duration. Ulceration gradually progressed to hard palate to form an oronasal fistula, associated with foul smelling discharge, halitosis, distortion of nasal bridge and swelling over right side of face.On local examination, an irregular lesion with foul smelling discharge and necrotic debris was present on hard palate with mild crusting seen inside the nasal cavity. CT-PNS revealed defect in hard palate with absence of antero-inferior nasal septum andformation of oronasal fistula. Histopathological and IHC studies confirmed

the diagnosis as locally advanced angiocentric T cell lymphoma. Accordingly, patient was treated with 6-cycles of CHOP,following which there was significant relief in local symptoms. She underwent whole body FDG PET-CTto determine the extent of residual disease, which revealed mucosal thickening in bilateral maxillary sinuses with complete obliteration of left maxillary sinus and dehiscent medial wall of right maxillary sinus, erosion of anterior hard palate and involvement of left infra-parotid and superficial cervical lymph nodes accompanied by increase uptake of FDG in bilateral thyroid lobes. Patient further received EBRT 35Gy/ 20#/ 4.0weeks to bilateral face and neck. On follow-up, patient had residual disease as midline hard palate defect and in view of this, she further received six cycles of oral lenalidomide 25mg chemotherapy. On six month follow-up, patient is doing fine with good clinical regression of disease. **Conclusion:** It is very aggressive, rapidly progressive disease with poor prognosis, which can be improved by early diagnosis and treatment. Due to non-specific nature of the early clinical signs and symptoms, histological and immunohistochemical evaluation of the lesion is crucial to diagnosis.The mainstay of therapy is a combination of locoregional radiotherapy and CHOP chemotherapy. Additionally, autologous hematopoietic stem cell transplantation and prosthetic treatment of oronasal fistulas/defects can be good future prospects.

Keywords: Hard Palate, Angiocentric T-cell Lymphoma, CHOP

Different Pathways that Alcohol may Increase the Risk of Head & Neck Cancer

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Background: Head and neck cancer (HNC) is the seventh most common cancer in the world. Alcohol consumption has negative impact on health and social consequences. From a public health perspective, the global burden related to alcohol consumption, both in terms of morbidity and mortality, is considerable in most parts of the world. **Material and Methods:** In this study literature is explored to find out different mechanism of action that alcohol causes HNC. **Results:** More than 70% of HNC are estimated to be avoidable by lifestyle changes, particularly by effective reduction of exposure to well-known risk factors such as tobacco smoking and alcohol drinking.

- Alcohol probably acts as a local irritant especially in the anterior floor of mouth. It may also induce oral cancer via a coexisting malnutrition which in turn may depress immunological response.
- Inside the body, alcohol is metabolized into a toxic chemical called acetaldehyde, which is a probable human carcinogen, which can cause cancer by damaging DNA and proteins and stopping our cells from repairing this damage.
- Generating reactive oxygen species, which can damage DNA, proteins, and lipids through a process called oxidation.
- Impairing the body's ability to break down and absorb a variety of nutrients that may be associated with cancer risk.
- Category III alcohol user can add extra calories to the diet, which can contribute to weight gain and increases the risks of many types of cancer.
- Alcoholic beverages may also contain a variety of carcinogenic contaminants such as nitrosamines, asbestos fibers, phenols, and hydrocarbons.

In a review, some possible mechanisms of alcohol as a carcinogen are 1) induction of CYP2E1, a member of the cytochrome P450 mixed-function oxidase system, which is an important enzyme for the conversion of ethanol to acetaldehyde; 2) nutritional deficiencies; 3) interactions with retinoids; 4) alcohol and methylation; 5) alcohol and immune surveillance 6) depletion of S-adenosylmethionine and, consequently, induction of global DNA hypomethylation; 7) induction of increased production of inhibitory guanine nucleotide regulatory proteins and components of extracellular signal-regulated kinase–mitogen-activated protein kinase signaling, etc. **Conclusion:** Alcohol carries connotations of pleasure and sociability in the minds of many, harmful consequences of its use are diverse and widespread and have an enormous toll on lives and communities of the developing nations. There is a need to raise awareness among the population about the negative implications of alcohol consumption and to minimize them.

Keywords Alcohol; risk factor; HNC

Re-Defining The Preoperative Diagnosis Of Carcinoma Thyroid.

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Background : Thyroid Cancer is the most common endocrine malignancy. Fine Needle Aspiration Cytology (FNAC) and thyroid ultrasound are the most commonly performed preoperative diagnostic tests. We performed this study to test the diagnostic accuracy of preoperative thyroid ultrasound by correlating it with the final histopathology report. **Materials And Methods :** This is a single institution prospective study of 313 patients with thyroid swelling between August 2012 to December 2014. All patients underwent a preoperative FNAC and ultrasound of the neck. The FNAC results were classified according to the Bethesda staging system. All the patients underwent appropriate surgical treatment. The various features of ultrasound (hypoechogenicity, irregular margins, micro calcifications, increased vascularity and lymph nodes) were assessed when the initial FNAC was not suggestive of malignancy by keeping the final histopathology report as gold standard. Descriptive analysis, cross tabulation and Mc-nemar Chi square tests were used for statistical analysis. **Results :** Papillary Carcinoma of the thyroid constituted 56% of the initial FNAC. Among these patients the sensitivity and specificity of increased vascularity and micro calcification was 75% ,60% and 75% , 82% respectively ($p < 0.001$). Among the remaining patients (Bethesda class I - V) who underwent surgery, 37.5%, 26%, 62%, 81% and 94.7% turned out to be malignant in the final report among the Bethesda Class I,II,III,IV and V. Among these patients 112 were classified as positive based on the ultrasound criteria, who underwent surgery 88 were malignant of final histopathology. The ultrasound diagnosis had a sensitivity, specificity, positive predictive value and negative predictive value of 95.45%, 51%, 75% and 88.2% respectively. The risk of malignancy increased with an increase in the ultrasound characteristics suggestive of malignancy. **Conclusion :** The presence of more than two features on ultrasound is highly suspicious of malignancy when the initial FNAC was not malignant. We propose from our study to consider doing a Total Thyroidectomy when suspicious features are present on a preoperative ultrasound when the initial FNAC was non malignant.

Key words : Fine Needle Aspiration Cytology (FNAC), Ultrasound, Histopathology.

Metastasis of Malignant lesion to Oro-facial region with a special emphasis on histopathologic & cytogenetic analysis.

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Introduction: Metastasis to the oro-facial region is uncommon and accounts for only 1% of all malignant oral neoplasm. Till date, the reported incidence is very low may be due to failure in identifying metastasis. These tumors are of great clinical significance as their appearance may be the first indication of an undiscovered malignancy at a distant primary site or the first evidence of dissemination of a known tumour from its primary site. Metastasis is a consequence of a complex biological cascade which begins with the detachment of tumour cells from the primary tumors spreading in to the tissues. **Objectives:** To determine the incidence of jaw bone metastasis and correlate with existing literature. To analyse the histopathologic and

cytogenetic correlation. **Material and Methods:** The data of oral cancer patients from year 2012- 2015, available in the archives of the department of Oral Medicine and Radiology, K. M. Shah Dental College and Hospital, Sumandeep Vidyapeeth University, Vadodara; and cases with complete information of the primary site, biopsy,Immuno-histochemistry (IHC), & clinico-radiological findings of jaw bone involvement were considered. The tissue blocks were subjected for Karyotyping. The data was tabulated, analyzed and compared with the available literature. **Results:**There were total 56 patients whose record showed that they were cases of metastatic tumors involving the jaw bones. The age ranged from 40- 90 years with median age of 65 years. There were 41 (73.22%) males and 17 (26.78%) females. The identified primary site in males were lungs, liver, colon, prostrate, kidney & penis; whereas in females the most common sites were thyroid, breast, lung and uterus. The most common site of metastasis in oral cavity was mandible (50%) followed by maxilla, tongue, buccal mucosa and commissural area. The most common presentation in the oral cavity was of ulcero-proliferative type (49%) followed by Proliferative type (44%). The common symptoms observed were mobility of teeth & pain. Bony changes were observed on the radiograph in 67.85% patient. The IHC in majority of the cases proved to be having malignant changes at the cellular level. The cytogenetic analysis in all the cases (100 %) showed aberrations in the structure of the chromosomes. Majority of the patients were rendered surgery plus chemotherapy treatment (41.07%) and only radiotherapy (40%). **Conclusions:**Metastasis to the jaw bone is rare. Age and sex can provide important clue to the possible location of the primary lesion. The IHC and cytogenetic analysis in such cases will be helpful in the prognosis. Globally, variation may be observed in the primary sites. The metastasis with the jaw bone is associated with poor prognosis.

Sokal score and EUTOS score as predictive markers of Cytogenetic and Molecular response in Chronic Myeloid Leukemia patients treated with Imatinib-Experience from a Tertiary cancer centre in Southern India.

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Background: Sokal index was developed in the pre-imatinib era to predict and prognosticate the outcome of Chronic myeloid leukemia (CML) patients. In the Imatinib era, a new scoring system called EUTOS scoring system has been validated as a predictive marker in CML. Comparison of the scores has shown variable correlation with complete cytogenetic response and major molecular response. **Aim**: To compare Sokal score and EUTOS score as a predictive marker for complete cytogenetic response (CCyR) and major molecular response (MMR) for newly diagnosed CML-CP patients treated with Imatinib. **Materials and Methods**: 410 patients with newly diagnosed CML in chronic phase were included in the study. They were treated with upfront imatinib. They were followed up for a minimum 3 years. Cytogenetic and Molecular response to the treatment were monitored regularly. **Results**: Out of 410 patients, 287 (69%) of patients were having low EUTOS score and 127 (31%) were having high EUTOS score. Patients with low, intermediate and high sokal scores were 345 (84.2%), 50 (12.2%) and 15 (3.6%) respectively. 224 patients with low EUTOS score achieved CCgr in 18 months compared to 48 patients with high EUTOS score ($p<0.000$). 208 patients with low EUTOS score achieved MMR within 18 months compared to 24 patients with high EUTOS score ($p<0.000$). 230, 31, 11 patients with low intermediate and high sokal score have achieved CCgr in 18 months.($p=0.68$). 201, 25, 6 patients with low, intermediate and high sokal score have achieved MMR in 18 months ($p=0.22$). **Conclusion**: EUTOS is better than Sokal score as a predictive marker for achievement of MMR and CCgR at 18 months in CML-CP patients on Imatinib.

Key Words: CML, Sokal score, EUTOS score.

Profile and Pattern of Lymphomas: A Retrospective Analysis from a Tertiary Centre in North West India

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Introduction: Lymphomas encompass a heterogeneous range of malignancies which are broadly divided into Hodgkin and Non Hodgkin Lymphoma. Epidemiological data have shown that there exist ethnic, geographical variations and differences in treatment outcomes in this mixed group. Despite such variability; advances in diagnosis and chemotherapy have led to improvement in their outcomes. However the universal applicability of such improvements is questionable. In a resource restricted setting and an ethnically diverse country like India it is important to analyse the regional epidemiological factors to allocate and optimise management strategies. **Objectives:** To investigate the pattern of lymphomas and profile of patients with lymphoma presenting to the Christian Medical College & Hospital, Ludhiana, Punjab . **Material and Methods:** Medical files from patients diagnosed with lymphoma from 1st January 2010 till September 2015 were reviewed. Secondary data on the patient was obtained from the institution tumour registry. Relevant information (age of diagnosis, Dates of follow up, gender, and lymphoma subtype) were additionally collected from the clinical histories of each patient. Data analysis was undertaken using SPSS for Windows 23.0 statistical software (SPSS Inc., Chicago, IL, USA), including frequency distribution and cross-tabulation. **Results:** A total of 197 patients were newly diagnosed with Lymphoma during this period. The median age at presentation was 57 years (6-90) with majority of them being males 122 (61.9%). Non Hodgkin Lymphoma was the commoner subtype with 162 (81.8%) patients . The median LDH values at presentation was 530 IU/L (125-3680)Further subgroup analysis revealed that DLBCL was the most common subtype in NHL (n=162) with 86 (53.1%) and T cell lymphoma was seen in only 15 (9.2%) patients. The survival estimate of the most prevalent subgroup (DLBCL) showed a median OS at 2 year of 71.0±10.8 %.

Conclusions: Our analysis reports on distribution of lymphoma subtypes and outcomes in North West India. There appears to exist regional differences. Earlier detection and treatment might further aid in improving the treatment outcomes. Prospective studies are required in further validating these findings.

Childhood Non-Hodgkin Lymphoma (NHL) With Intensive Chemotherapy In A Tertiary Care Hospital Of A Resource Limited Country.

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Background: NHL is the 3rd most common malignant tumor in children and adolescent. With the current treatments of intensive chemotherapy and incorporation of CNS directed therapy, more than 80% patients will survive at least 5 years. Despite the high cure rates in developed countries, the success is not mirrored in resource poor countries. High number of abandonment, poverty and unavailability of some active drugs, inadequate supportive cares are responsible for inferior survival rates in resource limited countries like Bangladesh. For this feasibility of giving intensive chemotherapy in childhood NHL was required to see in relation of outcome and toxicities. **Method**: A prospective observational study was conducted with 40 newly diagnosed patients of NHL referred in the period of 1 year, June 2012 to May 2013. Among them 34 patients continued treatment and observed for the time being. Details of patient's history, family condition, parental education, immunization record, anthropometric assessment, initial clinical presentation with physical examination, time interval from onset of symptoms to diagnosis and starting treatment were enrolled in a preformed questionnaire. Diagnostic and staging workups were done by

histopathology (FNAC or excision biopsy), serous fluids/CSF cytology (cytospin), bone marrow aspiration, biochemistry and radio-imaging (X-ray, USG, CT or MRI). Intensive chemotherapy has been started soon after diagnosis according to histological subtypes of NHL; Burkitt (BL) patients treated with FAB-LMB-96 and Lymphoblastic lymphoma (LL) with BFM 95. Patients without definitive histological subtypes were treated according to primary site of tumor, abdominal variety as BL (LMB 96), thoracic variety as LL (BFM 95). All patients had been followed up regularly after each cycle of therapy until events like death, relapse, and discontinuation of treatment. **Result**: Among the 34 patients who continued treatment; BL was the commonest 23 (68%), LL was 11(32%). Median age 7.6 years; M:F 2.1:1; (In BL 2.8:1 and in LL 1.2:1). Most of families (79%) have less financial ability with 250 USD/month. Delayed diagnosis (required > 30 days from onset of symptoms to diagnosis) found in 59% patients, 32% came within 4 wks, and only 9% came within < 2 wks. Seven patients were initially diagnosed TB. Primary site of origin was abdomen 65%, Thorax 32%, Head-neck 3%. BL patients were treated with FAB-LMB 96 protocol and LL patients with BFM 95 protocol. They (79%) achieved complete remission in early phase of treatment (induction phase of chemotherapy); with LMB 96 protocol 87% of BL patients [61% after COP, 17.4% after COPADM-1 and 8.6%after COPADM-2]; and with BFM 95 protocol 100% LL patients [82% within 7 days and 18% within 33 days]. With this one year long observational study, it found that after receiving histology directed chemotherapy, 27 (79%) patient achieved complete remission (CR) irrespective of stage; [74% of BL & 91% of LL] Of thepatients who achieved remission; 9% had relapsed & expired, 12% failed to continue treatment. At the end of observation OS was 59% (BL 48%, LL 82%) and death 41%. Early staged patients (75%) survival was higher than advanced staged (57%) regardless of histology. Survival was 50% with CNS and 25% with bone marrow involvement regardless of histology. According to histology about 48% of BL have survived and remain disease free for 6 months, and 82% of LL has survived up to end of study period. Toxicities were observed all most every phases of chemotherapy; most commonly in early phase & even prior start. Most common toxic effects observed tumor lysis, mediastinal syndrome, myelosuppression, febrile neutropenia, septicemia, mucositis, diarrhoea, bleeding, cellulitis, hepatotoxicity, toxic death. Every patient had alopecia and minimal to moderate nausea and vomiting. **Conclusions**: The treatments of NHL were efficacious, feasible, and well tolerated in spite of all socio economical limitations. A good number of patients (79%) achieved CR irrespective of stage but 40% of them failed to survive due to toxicities. Delayed diagnosis, misdiagnosis, treatment refusal/abandonment, and excess toxicity must be reduced if we are to increase NHL survival rates.

Eltrombopag a safe and cost-effective measure in post hematopoetic stem cell transplant (HSCT) refractory thrombocytopenia.

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Introduction: Refractory thrombocytopenia is a common occurrence in post HSCT patients, requiring prolonged platelet support.Platelet transfusionis used to bridge the gap in the pre engraftment period to avoid serious bleeding.Eltrombopag is a thrombopoietin agonist that stimulates the megakaryocytes growth and differentiation from its precussor cells in the bone marrow. Thrombocytopenia in HSCT patients is often due to maturation arrest. Eltrombopag thus, could be used to fasten the platelet recovery and overcome the risk of bleeding. **Objectives:**To evaluate safety and efficacy of Eltrombopag as an alternative to prolonged platelet support. Eltrombopag was used only to increase the platelet count to avoid bleeding and not to normalise the platelet count. To evaluate the cost effectiveness of drug as compared to prolonged single donor platelet infusion. **Material and Methods:** Retrospective analysis of patients receiving Eltrombopag post HSCT from January 2012 to December 2015. Inclusion criteria: HSCT patients with refractory thrombocytopenia with recovering leucocyte counts (post engrafment) requiring prolonged platelet support.Exclusion: thrombocytopenia secondary to infection (CMV), drugs or past history of thromboembolism in last 6 months. **Results:** Total18 patients were evaluated.Median age was28.5years. Two patients received Eltrombopag in the dose of 50 mg, while 16 received at the dose of 25mg. About 14 had undergone Auto HSCT and 4 had Allo transplant. Median time of starting and stopping of Eltrombopag was28 and 58 days respectively. The drug was started at the median platelet count of 8000/uL, (range 2000/uL-11000/uL).Median duration of therapy was27.5days. Median totaldose received was 787.5mg,with Median platelet increment of 57000/uL. The cost of Eltrombopag was INR 6,300 for 25 mg and 12,500 for 50mg /week. The cost of hospitalization and one SDP at our centre is INR 13000, about 39000/week .Thus; Eltrombopag was cost effective, reducing the cost of transfusion by 30%. Allpatients tolerated the drugs without any side effects. The drug compliance was 100%.All patients achieved transfusion independence and none of them had bleeding episode. **Conclusions:**Eltrombopag 25-50mg single daily dose is cost effective alternative and accelerates platelet recovery in post HSCT patients. It is well toleratedhelps achieve transfusion independence,currently appears to be a promising alternative to prolonged SDP transfusion and should be tested in further studies.

Management Of Elderly Lymphoma : A tertiary Cancer Center Experience.

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Objective: Review the epidemiology,disease characteristics, frontline treatment outcomes of elderly patients with Lymphoma. **Methodology:** Electronic Medical Records (EMR) of 1955 consecutive adult lymphoma patients [>17 years] from May2011 to Dec 2014 was reviewed.692 patients greater than 60years (35%) were evaluated for demography,clinical features,staging,associated co-morbidities and first-line treatment response.209 patients with no definite treatment or follow up prescribed at our center were considered as 2nd opinion seekers and were not included for management assessment. **Results:**The median age was 67 years, with 61% between 60 and 69 years, 31% between 70 and 79 years and 8% above 80 years. The gender ratio was 2.3 : 1. High Grade comprised 44%, Low grade 35% and Hodgkin Lymphoma 5%. The remaining 14 % was T cell and lymphomas not specified. Co- morbidities at presentation [45%] included Hypertension in the majority, followed by Diabetes, hypothyroidism, COPD and IHD. 5 patients had hepatitis markers and 2 in the cohort were HIV positive.Three hundred and fifty two patients (51%) were evaluated for their 1ST line treatment. The subtypes were Hodgkin Lymphoma [HL#20], chronic lymphatic leukemia/small lymphatic leukemia [CLL/SLL # 61], follicular lymphoma [FL # 30], marginal zone [MZL # 24], mantle cell lymphoma [MCL # 16] and diffuse large B cell [DLBCL # 188], and others [13]. The common treatment regimens included ABVD for HL, Bendamustine Rituximab [B R] for low grade NHLs and CHOP like regimens for High grade NHL. The Overall response rates were similar to younger patients treated at our center. However the complete response rates were lower. The median progression free survival for our elderly cohort is 20 months [range 3 to 52 months]. Detailed results will be presented at the meeting.Thirty six (5%) were treated for Relapsed/Refractory disease and 95 [14%] treated elsewhere are on follow up at our center. **Conclusions:** Adult lymphoma patients above 60years comprise 35% presenting to the clinic.More than half of these patients (55%) take treatment for their diseases.The common co-morbidities observed are Hypertension/IHD. The CR rates were lower

than that for younger patients. Treatment decisions and completion were dependent on social support available.

Efficacy Of a reduced dose Rasburicase: Single Institution Experience

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Introduction: Tumor lysis syndrome (TLS) is an oncological emergency associated with potentially life threatening metabolic abnormalities like hyperuricemia, hyperkalemia, hypocalcemia and hyperphosphatemia. Rasburicase being a recombinant urate oxidase is highly efficacious in TLS. US FDA recommends use of rasburicase at a dose of 0.15mg/kg/day for 5 days.There are various studies suggesting the effectiveness of a reduced dose of rasburicase (6mg single dose). In a developing country like India whereaffordabilityis one ofthe major limitation to medical care,use of rasburicase at the dose recommended by US FDA is not always possible. There is no convincing data suggesting the efficacy of even a lower dose of rasburicase(single dose of 1.5 mg) in the treatment of TLS. **Objectives:**To study the efficacy of a single dose of rasburicase (1.5 mg flat dose) in adult patients with TLS. **Material and Methods:**One year retrospective review from January, 2015 to December, 2015 was conducted in adult oncology patients who received rasburicase. We evaluated the efficacy of a single dose of Rasburicase, (i.e. 1.5 mg flat dose) in patients aged 18yrs-72yrs presenting with TLS to our institution.Fifteen patients (28%) of multiple Myeloma, 14 patients (25%) with CLL, 14 patients (25%) with ALL, 10 patients (18%) with GCT and 1 patient (4%) with Burkitt's Lymphoma received single dose 1.5 mg of Rasburicase on day 1. These patients were also started on chemotherapy on day 1. The median serum uric acid levels were 8.8mg/dl (6.4mg/dl-11.8mg/dl). **Results:**Fifty (93%) out of fifty four patients had normalization of uric acid levels within 24 hours of intravenous Rasburicase. The low serum uric acid levels were maintained even on the 4th day of Rasburicase. Only four patients required another 1.5mg of rasburicase for hyperuricemia. The median serum creatinine level was 3.8mg/dl (1.9mg/dl-5.4mg/dl). Forty one patients (76%) had >50% reduction in the serum creatinine levels. Rasburicase was well tolerated. **Conclusion:** A reduced dose of Rasburicase at 1.5mg single dose is very efficacious in TLS. Further studies are required to evaluate the efficacy of rasburicase at such a dose.

Allogeneic Stem Cell Transplantation in Lymphoma patients: a single center experience

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Background: A significant number of patients with lymphomas are at very high risk of relapse/progressive disease despite intensive chemotherapies/ autologous stem cell transplantation (ASCT) especially primary refractory ymphoma, post ASCT relapse, relapse aggressive T cell lymphomas and hepato-splenic T cell lymphoma. Allogeneic stem cell transplantation (alloSCT) can salvage a significant number of high risk lymphoma patients. **Material and methods:** Here, we report the profile and outcomes of the lymphoma patients who underwent alloSCT since 1stJanuary2012 till 30thSept2015. Out of a total 168 alloSCT performed in study period, 10 were for lymphoma patients. Patients were followed up till 31stDec2015 for outcome(Table-1). **Results:** Male:Female is 7:3, mean age 42.5 years(16-61years) and indications were hodgkins lymphoma (HL) n=3 (post ASCT relapse-2, primary refractory-1) and NHL n=7 (relapsed and refractory mantle cell lymphoma-2, primary refractory DLBCL- 3, refractory PTCL-1, hepato-splenic T cell lymphoma-1). Median numbers of therapy lines given prior to alloSCT were 2(1-4).Types of transplants were matched related donor (MRD), matched unrelated donor (MUD), and haplo-identical (Haplo) in 6, 1 and 3 patients respectively. Conditioining regime used was non myeloablative (NMA) in 3 (haplo-2, MUD-1), reduced intensity (RIC) in 3 (all MRD) and myeloablative (MA) in 4 patients (MRD-3, Haplo-1). Overall 2 patients developed acute GvHD and 4 patients developed chronic GvHD. Three patients died (regimen related toxicity {RRT}-2 patients on day +19 and +26, progressive disease {PD}-1 patient on day +713), one patient rejected the graft with autologous recovery. Seven patients are surviving in complete remission (including one who rejected the graft) at a median follow up of 438 days (range 149-989 days) (calculated after excluding two early deaths because of RRT). **Conclusion:** With 70% survival at approx 10 months median follow up, these results supportrole of alloSCT in high risk cases of lymphoma.

Clinical Profile, Treatment And Outcomes Of Patients With Mantle Cell Lymphoma Treated In A Tertiary Care Centre In South India

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Introduction: Mantle cell lymphoma is an indolent lymphoma with an aggressive course, with unfavourable outcomes due to advanced presentation and poor treatment responses. We here present the clinical profile, treatment and outcomes of patients treated with this lymphoma at our centre. **Material and Methods:**A retrospective

Table-1

Patients	Age/ sex	Dx	Prior Rx	Prior ASCT	Donor	Conditioning	F/u duration	Alive/ dead	Cause of death
P-1	50 M	MCL	2	N	MRD	MA	950	Alive	-
P-2	16 F	HL	3	Y	Haplo	NMA	989	Alive	-
P-3	29 M	HL	4	Y	Haplo	MA	713	Dead	PD
P-4	61 M	DLBCL	3	N	MRD	MA	19	Dead	RRT
P-5	57 M	HL	2	N	MRD	RIC	576	Alive	-
P-6	38 M	DLBCL	2	N	MRD	MA	26	Dead	RRT
P-7	48 F	DLBCL	2	N	MUD	NMA	286	Alive	-
P-8	47 F	PTCL	2	N	MRD	RIC	238	Alive	-
P-9	54 M	MCL	3	N	MRD	RIC	149	Alive	-
P-10	25 M	HSTCL	1	N	Haplo	NMA	300	Alive	-

MCL-mantle cell lymphoma, HL hodgkins lymphoma, HSTCL- hepato-splenic T cell lymphoma, PD progressive disease, RRT- regimen related toxicity.

analysis was undertaken at Kidwai Memorial Institute of Oncology, a tertiary care centre in South India. The patients diagnosed as cases of mantle cell lymphoma between the years 2009 and 2014 were analysed. The survival analysis was done by Kaplan- Meier analysis, using the log rank test. **Results:**The median age was 55 years (35-72) with a male preponderance, male to female ratio- 6 to 1. All except 19 cases (25%) had extranodal disease, with intestine being the most common site of involvement, followed by stomach, spine and the lungs. 27 patients presented with bone marrow involvement. The number of patients who presented in stages I, II, III and IV involvement were 3, 13, 28 and 33 respectively. The number of patients with low, low-intermediate, high-intermediate and high risk IPI scores were 6, 24, 22 and 25 respectively. The median overall survival in stages I, II, III & IV were 47, 24, 19 and 13 months respectively. The median OS with early (stages I & II)(n=16) and advanced disease (stages III & IV) (n=61) were 31 and 18 months respectively (p=0.02) . Similarly, the patients who received R-CHOP had significantly better survival than those with received CHOP chemotherapy, 30 and 16 months (p=0.0002). Those aged < 60 years had a trend to better overall survival than > 60 years (p=0.07). There was no significant difference in survival with respect to gender, extranodal involvement or bone marrow involvement. **Conclusions:**Mantle cell lymphoma has an aggressive course with poor survival. Although rituximab based chemotherapy has improved survival outcomes, more intensive chemotherapy with stem cell transplantation would be required to achieve better outcomes.

Characteristic	N (percentage)	Median OS (months)	P value
Age			
< 60 years	57 (74)	21	0.07
>60 years	20 (26)	18	
Sex			
male	66 (85)		0.58
female	11 (15)		
Early stage (I & II)	16 (20.7)	31	0.02
Advanced stage (III & IV)	61 (79.3)	18	
R-CHOP	25 (32.5)	30	0.0002
CHOP	52 (67.5)	16	

Fostering outcomes post SMARTE R CHOP chemotherapy in newly diagnosed Diffuse Large B Cell Lymphoma patients : a single centre experience

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Introduction: The combination of cyclophosphamide, doxorubicin , vincristine and prednisone (CHOP) with rituximab (R) is considered a standard regimen for the Diffuse Large B cell Lymphoma (DLBCL) patients. Pharmacokinetics based, extended application of Rituximabon days -4, 0, 10, 29, 57, 99, 155, and 239 to achieve stable area under curve (AUC) and to maximize the exposure days along with CHOP regime at fixed interval for 6 cycles (SMARTE R CHOP) has been found to enhance the treatment outcomes in DLBCL patients. We, aim to find out the treatment outcomes in Indian cohort with SMARTE RCHOP therapy in DLBCL patients. **Methods:**Total 37 DLBCL patients have been started on SMARTE R CHOP therapy since August 2014. Out of these, 26 patients are evaluable for outcome. Patients are followed up till 31st January 2016 for outcome. (Table 1) **Results:**The complete remission rate was 77% and partial remission rate 7.69% (ORR 84.61 %) of 26 evaluable patients with median age of 63 years (40-81). ORR was 100% for good prognosis patients (IPI score 0-1) , 88.8% for intermediate prognosis patients (IPI score 2-3), and 58.3% for poor prognosis patients (IPI score 4-5).Events were recorded in 5 patients (19.2%) with two patients(poor risk) expired at day 34 and day 10 because of progression of disease and cardiac co-morbidity respectively, two patients having stable disease after chemotherapy and one patient relapsing 343 days after start of chemotherapy.Relapse rate is found to be 3.8%. After a median follow up of 299 days(10-510 days), the OS and EFS was 92.3% (n=24) and 80.76%(n=21) **Conclusion:**An EFS and OS rate of 80.76% and 92.3 % respectively at approximately 10 months of median follow up encourages the application of SMARTE R CHOP therapyin DLBCL and need to study this regime in prospective randomized fashion in a larger cohort.

Keywords:Diffuse Large B cell Lymphoma, SMARTE R CHOP

Characteristics	Value
Median Age, yrs (Range)	63.5(40-81)
Male : Female Ratio	18:8
IPI Risk (n)	
Good	5
Intermediate	9
Poor	12
Responses , n (%)	
Complete Response	20(77%)
Partial Response	2(7.6%)
Stable Disease	2 (7.6%)
Death	2(7.6%)
Events , n	
Death	2
Stable Disease	2
Relapse	1
Event Free Survival, n(%)	21(80.76%)
Overall Survival, n(%)	24 (92.3%)

Demography And Early Treatment Outcomes Of Lymphomas: Prospective Emr Data.

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Background: This prospective data attempts to study the epidemiology and treatment outcomes of Lymphoma patients presenting to a single center in the Eastern region. **Patients and methods:** Electronic Medical Records (EMR) of all consecutive patients with confirmed diagnosis of Lymphoma registered from May 2011 to Dec 2013 were reviewed for information on demography, clinical features, staging, treatment regimen, response rates, toxicities and follow up. The R-Lymph software was used to collect and analyze the data. Two-year progression-free (PFS) and overall survival (OS) was calculated with Kaplan-Meier method for the frequently occurring lymphomas. **Result:** 1264 patients with a diagnosis of Lymphoma were seen in the Clinical Hematology Department. Patients seen in the OPD for 2nd opinion have been excluded from the analysis. 795 patients who received frontline management (622), salvage therapy (67) and 106 patients on follow up have been analyzed for disease outcome. The epidemiology of the treated group had 234 female and 561 male patients. 41% of the adult lymphomas presented after the age of 61 years. 162 (20%) presented with Hodgkin lymphoma (HL) and 633 (80%) with non Hodgkin lymphoma (NHL). The common HL (#162) subtypes were mixed cellularity in 56%, nodular sclerosis in 26%, and Nodular lymphocytic predominant HL in 7%. 60% of HL presented below the age of 40 years and 11% patients treated were above the age of 61 years. The male to female ratio was 2.3:1.

50% patients presented in early stage. 76% received frontline therapy and 24 % presented after first line therapy. First line treatment was ABVD like regimen.The overall response rate to first line treatment was 92%(CR in 78%). The 2 years progression free survival (PFS) for stages 1 & 2 was 100% and 88%. The PFS at 2 years for all stages was 77%. The common NHL (#633) subtypes were diffuse large B cell lymphoma (DLBCL) in 49%, chronic lymphatic leukemia (CLL)/ small lymphatic leukemia (SLL) in 15%, follicular lymphoma (FL) in 12%. The male to female ratio was 2.4:1. 47% patients presented above the age of 61 years.Early stage DLBCL(43%) and late stage DLBCL was noted in 56%.The response rates for the first line therapy were CR(58%),PR(14%) and PD(10%). The 2year PFS was 77% for patients with DLBCL. **Conclusions:** This study from Eastern India highlights some of the key features of similarity and differences in the presentation of adult Lymphomas as compared to previous studies from India.

Primary thyroid lymphoma: A series of a rare extranodal site of primary lymphoma from a tertiary care centre in Northern India

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Introduction: Primary thyroid lymphoma (PTL) accounts for only 5% of all thyroid neoplasms and 1-2% of extranodal lymphomas. Early diagnosis and correct sub-typing is imperative as its management is very different from other thyroid neoplasms. There is paucity of literature on PTL from India. **Objectives:**We report a series of PTL cases diagnosed on histology, to contribute to itsexisting knowledge in order that it may enhance patient diagnosis and management. **Material and Methods:**All cases diagnosed as PTL (January 2009–March 2015) were retrieved. Clinical details were noted. Hematoxylin-and-eosin stained slides were reviewed. Immunohistochemistry (IHC) was performed with the following antibodies: CD3, CD20, CD5, CD23, CD10, cyclinD1, bcl2, bcl6, MUM1, CD43, MIB-1and p53 to facilitate classification according to the WHO classification of hematolymphoid neoplasms (2008). **Results:**Eleven patients with PTL were identified(mean age of 64.6 years, 3 males and 8 females). All had presented with midline neck mass of 2 to 36 months duration and diagnosed with Non-Hodgkin lymphoma (NHL), B-cell type. Further sub-classification was possible in ten patients; extranodal marginal zone lymphoma (EMZL) was the final diagnosis in six, remaining four had diffuse large B-cell lymphoma (DLBCL). Three EMZL cases showed focal large cell transformation (LCT). MIB-1 labelling index and MUM1 positivity showed trend toward association with aggressive histological types (DLBCL and EMZL-LCT). Three patients underwentprior fine needle aspiration cytology (FNAC); two were mistaken for poorly differentiated and anaplastic carcinoma respectively while the third was suspected to have a lymphoma. Nine patents sought treatment; all received chemotherapy followed by involved-field radiation in five patients with early stage disease. The commonest chemotherapy regimen was CHOP (cyclophosphamide, adriamycin, vincristine, prednisolone) (44.4%), followed by R-CHOP (Rituximab with CHOP) (33.3%). At last follow-up (range 2-50 months), five patients (two DLBCL and three EMZL) had achieved complete remission, one (EMZL-LCT) had progressive disease, one with DLBCL expired, and remaining two were lost to follow up after seeking partial therapy.The patients with poor outcome had received CHOP and not R-CHOP. **Conclusions:**PTL is a rare neoplasm, where FNAC though often is the initial modality of investigation, it may not always be diagnostic and histological evaluation supplemented by IHC remains the gold standard that must be performedin clinico-radiologically suspected cases. Although considered indolent, EMZL requires aggressive treatment when LCT is identified. MIB-1 and MUM1 IHC may facilitate identifying LCT, especially in small biopsies. Although the sample size is small, addition of rituximab appears to confer a definite benefit to patients with aggressive histology.

Key Words: Primary thyroid lymphoma, DLBCL, EMZL

A clinico-hematological study on pancytopenia in special reference to Idiopathic pancytopenia in north- eastern part of India.

Aim: The study was carried to study the various causes of pancytopenia in North-eastern India with special reference to Idiopathic pancytopenia. **Material & Method**: It was a prospective study conducted over a period of one year(Jan 2014-February 2015) at Department of Pathology in Institute of Medical sciences, Banaras Hindu university. Bone marrow examination was done in all the cases (140 cases). The data obtained were analyzed using SPSS software 6th version. **Result**: Out of 140 cases of pancytopenia, Aplastic anemia was the most common cause (31.4%). The second common cause was the Megaloblastic anemia in 22.1% of cases. The third common cause was Myelodysplasticsyndrome(MDS) (12.9%) followed by Acute leukemia(11.4%). Other causes were hypersplenism(4.3%), kalaazar (2.1%), drug induced (2.1%),two cases each of HIV (1.4%), myelofibrosis (1.4%), lymphoma(1.4%) &multiple myeloma(1.4%). One case of ITP (0.7%),SLE(0.7%), Fanconi anemia(0.7%). The Idiopathic pancytopenia constituentsaround 5% of cases (7 cases). On follow up at 6 months, out of 7 cases, 03 cases were having persisting pancytopenia without any specific complaints and these cases were regarded as Idiopathic cytopenia of undetermined significance (ICUS) whereas 4 cases died, so better to regard these cases as Idiopathic fatal pancytopenia instead of ICUS. The mean age range was 33.15±19.33 years. M: F ratio was 1.37:1. The most common symptom was generalized body weakness (90%) and the most common sign was pallor (97.1%). MCV, RDW and MPV was significantly raised in cases of megaloblastic anemia in comparison to other causes of pancytopenia. LDH levels were elevated in megaloblastic anemia cases. **Conclusion:** Pancytopenia is a common haematological problem encountered in clinical practice and should be suspected on clinical grounds. The "Idiopathic fatal pancytopenia (IFP)" is an emerging new entity with a grave prognosis. We wish to sensitize the medical community & the scientists to this rapidly fatal condition of unknown etiology. Further research may elucidate the underlying pathology & potential drugs to halt the inevitable death.

Keywords- Idiopathic pancytopenia, Idiopathic cytopenia of undetermined significance(ICUS), Idiopathic fatal pancytopenia

Experience of a 6 color flow cytometry based MRD detection approach inIndian cohort of B-Lineage Acute Lymphoblastic Leukemia patients.

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Introduction: Minimal Residual Disease (MRD) monitoring has a potent impact in prognosis of acute lymphoblastic leukemia (ALL) patients. Most of the studies available so far, has been carried out on 3-4 color flow cytometer. Spectrum of different LAIPs at presentation and their post induction modulation has been found with great variability across different study groups. We are here presenting our MRD assessment data performed on 6 color flow cytometry by using two different tubes. **Objectives:** To identify the frequency of various Leukemia Associated Immunohenotpes (LAIPs) , to delineate the post induction modulation pattern of different LAIPs and to evaluate the applicability of three different 6 color tubes for MRD assessment in B-ALL patients are 3 major objectives of our study. **Material and Methods:**Two different tubes alongwith one optional third tube were processed for all 178 B-ALL patients (1-60Yr) at presentation and 104 day 29-CR patients. Tube-1 comprised of Syto16 (FITC), CD19 (APC-Cy7), CD10(PE-Cy7), CD34 (PerCP), CD58 (PE), CD20 (APC), Tube-2 comprised Syto16 (FITC), CD19(APC-Cy7), CD10(PE-Cy7), CD34 (PE), CD38(APC), CD45 (PerCP-Cy5.5) and optional Tube-3 comprised Syto16 (FITC), CD19(APC-Cy7), CD10(PE-Cy7), CD34 (PerCP), CD13 (PE), CD33(APC). Samples were acquired in BD-FACS Canto (6 color, 2

LASER) and analyzed in BD-FACS Diva software. Cut-off for positivity was ≥0.01% . **Results:**CD38 under expression was found most frequent LAIP at presentation (71.9%) followed by CD58 overexpression (67.4%) and CD45 under expression (65.1%). Overexpression of CD10, CD20, CD34,CD19 and underexpression of CD20 was detected in 52.8%, 12.9%, 51.6%, 9.5%, 32.58% respectively. Asynchronous CD10+CD20+, CD10+CD45+ and CD20+CD34+ was detected in 11.2%, 3.3% and 9.5% cases respectively. Cross-Lineage exp of CD13 and CD33 as LAIP was found in 28.65% and 24.15% cases. Tube-1, 2 & 3 had the 83.1%, 91.5% and 23.5% applicability to achieve ≥2 LAIP at presentation and 100% with both Tube-1 and Tube 2. Total 41 (39.42%) out of 104 day +29 CR patients were detected MRD positive. Tube-1 and Tube-2 independently detected 32/41(78%) and 38/41 (92.6%) positive MRD cases respectively. 22% positive MRD cases missed by Tube-1 and 7.3% by Tube-2 compensated each other, however 4/5 (80%) positive cases were missed by tube-3. CD10 (66.6%), CD58 (66.6%) and CD45 (55%) were the three most common markers undergoing post induction modulation. **Conclusion:**.Constructing such rigorous, objective and simplified 6 color two tube model permits optimization easily and may overcome the necessity of multiple tubes of multiantigen panel . This also may be an attractive MRD

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Incidence and prognostic relevance of FLT3-ITD mutations and Beta Catenin mutations in de novo acute myeloid leukemia (AML)

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Background: Acute myeloid leukemia (AML) is a type of genetically heterogeneous leukemia. Activating mutations in receptor tyrosine kinases like internal tandem duplications (*FLT3*-ITD) and many signaling pathway mutations like Wnt signaling gene mutations have been elucidated in AML. Several studies have shown that mutations in the FLT3 ITD gene mutations are common events in AML, occur in variable frequency and have been associated with an unfavorable outcome. Wnt signaling genes like beta catenin mutations are less studied in AML and no correlation has been done with FLT3-ITD mutations. The aim of the present study was to know the incidence of FLT3 ITD mutation and beta catenin mutations in AML patients presenting at our centre and to correlate with survival. **Material and Methods:** In this prospective study peripheral blood or bone marrow after the informed consent was obtained at baseline from the newly diagnosed AML patients. Genomic DNA was extracted and FLT3 ITD mutations were detected using PCR by running the product through 3 % agarose gel to detect mutation. B-Catenin mutations analysis was by done direct DNA Sanger sequencing. The patients were treated with the standardized protocol of 3+7 Daunorubicin and AraC (Cytrabine). **Results:** A total of 122 AML patients were screened for the FLT3-ITD and for beta catenin mutations. The median age in entire cohort (n=122) was 17 years (Range 1-60 years) with male:female ratio of (3:2). The most common subtype based on FAB classification was M2. FLT3 ITD was present in 11 (9.0%) patients and beta catenin in 3 % only. Out of 122 patients 89 % achieved remission. The median DFS and OS for FLT3 ITD +ve and beta catenin +ve was 8 mo (6-41) and 6 mo (2-12) respectively and 10 mo (7-43) and 10 mo (7-13) respectively. CR with ITD and without ITD was 81 % and 89% respectively (p=0.614) and with beta catenin and with no beta catenin mutation was 80 % and 88 % respectively (p= 0.46), and relapse rate with ITD and without ITD was 77% and 62 % respectively (p=1.00) and with beta catenin and with no beta catenin mutation was 100% and 77% (p=0.57) and OS with ITD and without ITD (p= 0.524) and the base line characteristics Hb and Platelets had no significant correlation. **Conclusion:** This study at our centre suggested that the incidence of FLT3 ITD mutation and beta catenin is low in AML patients when compared to Western and other Asian patients with AML. FLT3 ITD positive and beta catenin mutations in patients showed inferior CR rate and higher relapse rate with no significant difference. Base line charactreristics were not significantly associated with survival in overall cohort. Further followup studies with a larger number of samples are required to confirm our findings. Rapid identification and detection of FLT3-ITD and beta catenin mutations at diagnosis should be incorporated into routine assessment to decide the treatment strategies for AML.

Key words: Acute myeloid leukemia, mutations, *FLT3*-ITD, beta catenin.

Investigating expression-pattern of CD49d in myeloma cellsand its role in flow cytometric immunophenotyping of multiple myeloma.

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Introduction: Multiple myeloma (MM) is characterized by a clonal proliferation of plasma cells (PCs) and develops mainly in bone marrow (BM). BM micro-environment plays a key role in the stimulation of growth & survival of myeloma cells (MCs). Interaction between myeloma cells and neighbouring stromal cells mainly occurs through adhesion molecules expressed on the surface of MCs. Hence, the study of adhesion molecules can be useful in the prognostication and prediction of therapeutic response in MM. CD49d, a subunit of very late antigen-4 (VLA-4), was identified as a critical molecule for the induction of cell adhesion-mediated drug resistance.

Objectives: To study the pattern of CD49d expression in myeloma cells and normal plasma cells. **Material and Methods:**We analyzed expression-pattern of CD49d in MCs in BM from 84 MM cases and in normal-PCs from 20 control samples (uninvolved staging BM). Flow cytometric characterization was performed using a comprehensive antibody panel on Navios instrument and data was analyzed using Kaluza-v1.3-software. **Results:**We evaluated CD49d expression in MCs from 84 MM patients with median age 59 yrs (range, 23-76 yrs) and M:F ratio 60:24. Mean, median, standard deviation of mean fluorescent intensity of CD49d on normal PCs and MCs were 18, 15.6, 7.3 and 27.4, 26.6, 5.7 respectively. CD49d showed strong to intermediate homogenous expression in 70% and weak heterogeneous expression in 30% of MM. It was expressed in more than 90% plasma cells in 92% of MM samples and 100% of normal samples. Expression pattern of CD49d did not revealed any significant differential expression in identifying MCs against normal PCs. **Conclusions:** CD49d shows strong and homogenous expression in MCs. Hence, it is potentially useful in the development of targeted therapy. In addition, it can be reliably used as a new gating marker in flow-cytometric analysis in MM.

CyBorD for Newly diagnosed Myeloma :Experience from a tertiary care centre in South India

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Introduction: The introduction of novel agents has helped change MM from a lethal malignancy with an average overall survival of 3 years to a chronic disease, where majority of patients now have a prolonged survival. We studied a three drug combination with bortezomib, cyclophosphamide and dexamethasone (CyBorD) on a 28 day cycle in the treatment of newly diagnosed multiple myeloma patients to assess response. **Objectives:** To assess response to the bortezomib, cyclophosphamide and dexamethasone based regimen in Multiple myeloma when inducted as primary therapy. **Material and Methods:** Eligible patients had newly diagnosed, symptomatic MM,ECOG performance status of ≤ 2.Patients had to have measurable disease as defined by standard criteria. The primary endpoint of the study was confirmed response with a goal of at least 40% achieving ≥VGPR. Secondary endpoints were overall response, progression-free survival, overall survival and toxicity of the regimen. **Results:**Forty-five newly diagnosed, symptomatic patients received bortezomib 1.3 mg/m2 s/c, cyclophosphamide 300 mg/m2 IV and dexamethasone 40 mg PO with acyclovir/valcyclovir prophylaxis. This was given as a weekly schedule on a 28 day cycle for 4 cycles. Median age was 59yrs with 28 males and 17 females. Majority were IgGsubtype and FLC Kappa restriction in 26patients. ISS stage I,II,IIIwas seen in 10,15 and 15 patients. Responses were rapid with a mean 80% decline in the sentinel monoclonal protein at the end of 8 weeks. The overall intent to treat response rate (≥ partial response) was 91% with 80% ≥VGPR and 75% CR/nCR. 10 patients underwent successful autologous transplant. Meaningful survival data have not been made available due to the short follow up time. **Conclusions:**CyBorD regimen with treatment given on a 28 day cycle is a highly active regimen in newly diagnosed MM and produces rapid and profound responses irrespective of the stage. The regimen is tolerable with manageable toxicities although neuropathy was common.

Clinical Features And Prognostic Factors In Solitary Plasmacytomas

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Background :Solitary plasmacytomas (SP) are an uncommon type of plasma cell dyscrasias, characterised by local proliferation of neoplastic monoclonal plasma cells with no radiological evidence of additional skeletal lesions, and a bone marrow that is either morphologically normal or with very low plasma cell infiltration(<10%) .They account for <5% of all plasma cell disorders .The aim of this study was to analyse the clinical features, treatment strategies, outcome and relative prognostic factors of a series of patients with Solitary Bone Plasmacytomas (SBP) and ExtramedullaryPlasmacytomas(EMP) . **Method:** Electronic medical records of patients with SBP and EMP between 2003 and 2014 at Amrita Institute of Medical sciences, Kochi were reviewed. Demographic, clinicopathological, laboratory and treatment details were collected for a series of 63 patients with SBP and EMP treated over a period of 11 years at our Institution and the prognostic factors were evaluated using SPSS 20. **Results:** Median age at diagnosis was 63 yrs(33-88 years). 51patients(80.9%) had SBP and 12(19%) had EMP.Treatment details were available only for 53 patients of whom 26 had surgery followed by radiotherapy(RT),26 had only RT and 1 had chemotherapy.Progression to myeloma was recorded in 26 of 63 patients (41.2%) ,23 of 51(45.1%) with SBPs and 2 of 12(16.7%) EMP's.Median OS was 51 months for all Solitary Plasmacytomas,51 months for SBP's and 47 months for EMP's. Median PFS was 32 months for all ,21 months for SBP and 34 Months for EMP. **Conclusion:** Data from 63 patients with solitary plastmacytomas treated at Amrita Institute of Medical Sciences were analysed.SBP's were more common (80.9%) with vertebra being most common site.Progression to myeloma occured in 41.2 % of all SP's .In our centreextramedullary solitary plasmacytomahad a slightly worse overall survival than bone solitary plasmacytomas,though progression free survival was better in extramedullary solitary plasmacytoma .

Key words - solitary plasmacytomas,extramedullary,myeloma

CHARACTERISTICS	N	%
AGE		
> 60 YEARS	37	58.7
<60 YEARS	26	41.2
SEX		
MALE	44	69.8
FEMALE	19	30.1
TYPE		
BONE	51	80.9
EXTRAMEDULLARY	12	19.1
LOCATION		
SBP	51	50.9
VERTEBRA	26	23.5
SPINE	12	5.9
SKULL	3	5.9
EXTREMITIES	3	5.9
RIB	3	3.9
CLAVICLE	2	3.9
PELVIS	2	16.7
EMP	12	25
PARANASAL	2	16.7
UPPER AIRWAY	3	16.7
LUNG &MEDIASTINUM	2	25
NODE	2	
OTHERS	3	

Prognostic Value and Impact of Pro-inflammatory bio-markers on treatment response in patients of DLBCL– A Prospective study

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Background and Aim: The currently available prognostic model for Diffuse Large B Cell Lymphoma (DLBCL) is not sufficient to predict theoutcome of this heterogeneous group of DLBCL. There is a need to find better prognostic markers for optimal risk stratificationof DLBCL patients. This study aimed to evaluate the prognostic significance of pro-inflammatory bio-markers in pretreatment peripheral blood sample of patientsof DLBCL **Methods:** We measured levels of Th1 and Th2 cytokines (IL2, IL4, IL6, IL10, IFN gammaand TNF alpha) and CRP in the pretreatment serum of 46 newly diagnosed DLBCL patients along within 10healthy controls. CRP was measured by nephelometry and cytokines were measured usingBD flowcytometric bead assay. We compared the levels of these pro-inflammatory markersbetween cases and control groups. We evaluated the correlation of levels of thesepro-inflammatory markers with disease characteristics like B symptoms, Ann Arbor stage, IPIand with treatment response. **Results:** The median age of the cases was 55 years (range 13-80 years) while that of the controls was46 years. Among DLBCL patients 72% were males and 28% were females. According to theIPI scoring the low, intermediate and high risk groups comprised of 28%, 28%, and 44%patients respectively. Of the 41 patients who received treatment, 58% achieved CR, 12%achieved PR and 24% had progressive disease, respectively after frontline treatment withchemotherapy. In this study we found that the levels of CRP, IL4, IL6, IL10 and IFNgamma were significantly elevated in DLBCL patients as compared to the control group. Thepretreatment serum level of CRP in DLBCL patients was significantly elevated in those with B symptoms and high risk IPI group as compared to those without B symptoms and low risk IPI, respectively. It was also noted that IL2 showed a significant inverse correlation with stage and IPI of DLBCL patients. The median serum value of CRP was 30.5mg/L and 81mg/L in patients who achieved CR and those who did not achieve CR respectively after the frontline chemotherapy (p value - 0.007). Overall response was significantly lowerin those with elevated IL6. **Conclusion:** Pro inflammatory markerscan bc used to predict treatment outcome inDLBCL patients. CRP has shown asignificant correlation with adverse disease characteristics and treatment response. It can emerge as a readily available and cost effective prognostic marker to predict treatment response in DLBCLpatients. Our work concludes that there is alteration in cytokine profile of patients withDLBCL with inclination towards heightened Th2 response. It is important to emphasize that serum cytokines are highly sensitive molecules with complex interplay amongst their levels. Any trend of significance in their levels should be validated by larger study.

Dominate tumor in synchronous multiple primary adenocarcinomas

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Introduction: The prognostic role of the dominate tumor and tumor combination pattern in synchronous multiple primary adenocarcinoma (SMPADCs) remain unclear. **Material and Methods:**The predominant histology pattern of each tumor among SMPADCs was determined according to the new IASLC/ATS/ERS classification system. For recurrence analysis, each tumor was further divided into low, intermediate and high grade prognostic group. The dominate tumor (DT) was representative of the highest prognostic grade in each SMPADCs. **Results:**From 2004 to 2012, there were 108 consecutive nodal-negative patients who underwent surgery for SMPADCs in a tertiary referral center. The median follow-up time was 52.4 months. During follow-up, 38 (35.2%) patients developed recurrence. The pattern of recurrence included local recurrence only in 8 patients (21.1%), distal metastasis only in 11 (28.9%), and both local recurrence and distal metastasis in 19 (50.0%). In multivariate analysis, the percentage of recurrence was significantly higher in older age ($p=0.002$; odds ratio 6.324) and DT presented with radiologic solid-appearance (vs. pure- , Mixed-GGNs, $p=0.032$; odds ratio 7.041). In addition, there was no tumor recurrence identified in 17 DTs presented with radiologic pure GGN and 6 DTs in low grade prognostic group. The 5-year overall and disease-free survival of SMPADCs determined by DT in low, intermittent and high grade were 100%, 84.6%, 32.5% ($p<0.001$) and 100%, 73.9%, 23.3%, respectively ($p<0.001$). Compared to low/intermediate grade, DT in high grade had significantly worse overallsurvival ($p=0.007$; hazard ratio 4.313) and disease-free survival ($p=0.045$; hazard ratio 2.360) in multivariate analysis. For further combination analysis, high grade DT combined with high grade 2nd dominate tumor had significantly worse disease-free survival than that combined with intermediate and low grade 2nd dominate tumors. **Conclusions:** DT analyzed with prognostic grouping of the IASLC/ATS/RES histological classification was an independent risk factor regarding to overall and disease-free survivals in complete resected nodal-negative SMPADCs.

Lung cancer : Role of a Radiologist

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Lung cancer is the most common cause of cancer in men and women worldwide. It is the leading cause of cancer related mortality. Imaging with X-ray,CT and PET/CT are instrumental. Here I would like to highlight roles played by a radiologists utilizing various modalities in detection, diagnosis, performing diagnostic and theurapatic interventions, staging, treatment planning, monitoring response to therapy and screening of lung cancer. Discuss the advantages and limitations of the modalities.

Surgery after neoadjuvant chemotherapy in NSCLC: What determines the outcome?

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Background: Non-small cell lung cancer (NSCLC) requires a multimodality approach for optimal treatment. Neoadjuvant chemotherapy (NACT) has shown survival benefit over surgery alone in resectable and locally advanced NSCLC. In this study we have analysed our experience of surgery after neoadjuvant chemotherapy and the factors predicting the outcome. **Material and Methods:** We retrospectively analysed prospectively maintained thoracic surgery database. Among 160 patients with NSCLC operated, 38(25%) patients received NACT. Patients underwent an initial staging workup that included a physical examination, imaging studies (chest CT scan, brain CT scan, PET scan), fibrotic bronchoscopy. Chemotherapy regimens mostly consisted of Paclitaxel and Carboplatin for squamous cell carcinoma and pemetrexed based regimen for adenocarcinoma. The decision of NACT before surgery was taken in multidisciplinary clinic in view of either N2 disease or proximity of tumour to vessels or possibility of pneumonectomy. All patients underwent complete mediastinal LN dissection according to the AJCC LN map (nodal stations 2R, 4R, 7, 8 and 9 for a right-sided tumour; 4L, 5, 6, 7, 8 and 9 for a left-sided tumour) after resection of the main tumour. Histopathologic evaluation of gross residual tumour and every LN were done. The association between clinical, imaging and histopathologic factors with survival was assessed by Univariate and multivariate Cox proportional hazards model using Stata Software (Release 9.0, Stata Corp.). **Results**: Total 38 patients underwent surgery after NACT. The median age of this cohort was 57 years (40-78) and male to female ratio was 4:1. Squamous cell histology was present in 20 patients. Mediastinal

N2 disease was present in 24 (62.5%) patients and 7 patients had tumours close to major vessels necessitating NACT before surgery. After NACT 21 patients underwent lobectomy/bilobectomy and 11 patients still required pneumonectomy. Pathological complete response (pCR) was achieved in 9(23.6%) patients. The median follow-up period was 20 months (range 7–87 months). All the patients with pCR were disease free. The median disease free survival(DFS) is 27 months (95% CI 0.28-0.72). Median overall survival(OS) not reached. Two-year Survival was 75%. All deaths(n=6) were cancer related. There were 12 recurrences and all were distant metastasis. The two most frequent sites were the brain (6/12) and bone (5/12). Univariate and multivariate cox regression analysis for factors predicting DFS is shown in the table. This analysis revealed that performance score 2 and post-surgery pathologic nodal status (residual N2) were associated with poor disease free survival **Conclusion**: Neoadjuvant chemotherapy is a feasible option and may result in pathological complete response in a proportion of patients with locally advanced NSCLC. Poor performance status at baseline and residual N2 disease even after NACT is associated with worst outcome.

Conordance between setup errors and PTV margins using Cone-Beam CT for SBRT of Lung Metastasis

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Background: Setup errors can be a grave problem in the radiation treatment and can influence the size of safety margins and thereby size of irradiation field. It is introduced by various known and unknown variables which could be related to human or mechanical error; however these can be reduced by daily meticulous procedural checks. They are defined as the difference between the actual and intended treatment position with respect to radiation delivery. Aim of the present study is to assess setup error and its effect on PTV margins for stereotactic body radiotherapy on lung metastasis. **Method And Methodology:** A total of 20 patients with lung metastasis from different primaries, who underwent stereotactic body radiotherapy treatment, were enrolled in the present study. These patients underwent 3 to 6 fraction on linear accelerator with HD MLC at our hospital with thermoplastic cast for immobilization. Daily verification of setup was done using CBCT after initial setup. CBCT images were registered to the planning CT images, and setup errors on x, y, z axis were analyzed. Setup errors were calculated by evaluating the deviations from measured distance between the irradiation field margin and thoracic cage. **Results:** A total of 86 CBCT scans were performed on 20 patients. With respect to lateral, cranio-caudal and antero posterior axis, the observed setup error ranged from 0.39+0.25, 0.41+0.15 cm and 0.25+0.14 cm respectively. **Conclusion:** Measurement and correction of setup errors before each fraction using CBCT could help us to improve the accuracy of radiotherapy. Daily CBCT scan verification helps to minimize setup errors and meticulous verification can decrease PTV margins for SBRT in lung metastasis.

Key words: Setup errors; CBCT; PTV margins; SBRT; Lung metastasis

Serum high sensitivity C-reactive protein as a prognostic and therapeutic marker in advanced stage Non-small cell lung cancer.

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Introduction: CRP is shown to be elevated in many malignancies including lung cancer.In patients of NSCLC, elevated CRP levels prior to therapy are related with bad prognosis. Studies have shown that high CRP is also related to advanced stages. CRP level is much higher in malignancy cases than only inflammatory condition like COPD.In cancer,CRP is possibly increased by tissue inflammation and cytokines releasedby tumor cells indicating a higher tumor burden. **Objectives:** This study wasdesigned to evaluate serum mean hs-CRP levels in advanced stage NSCLC at diagnosis, after every 2 cycles of chemotherapy and to correlate this with treatment response. Baseline hs-CRP with correlated with tumor stage and T size and also compared with baseline levels in patients of COPD andhealthy controls. **Material and Methods:** This Hospital based observational study included20 newly diagnosed patients of NSCLC(stage IIIB and IV) in good PS,20 patients of stable COPD and 20 healthy controls. Baseline hs-CRPvalues were compared among three groups. NSCLC cases were assessed for baseline hs-CRP, tumor size, subtypes, staging and treatment response. After every 2 cycles of chemotherapy, parameters were reassessed and compared. Hs-CRP was tested by routine clinical lab test protocols using instrument Labmate and tumor response was assessed using the RECIST 1.1 criteria. **Results:** Baseline mean hs-CRP values of NSCLC, COPD, controls were 28.11±16.02 mg/L,8.59±3.53 mg/L,0.60±0.30 mg/L respectively ($p<0.001$). Squamous Cell Carcinoma (SCC) had significantly higher CRP as compared to adenocarcinoma, and NSCLC-NOS. No statistical significance was found between SCC and large cell ca. After treatment, 15% had CR, 35% had PR, 25% had SD and 25% had PD. Baseline mean hs-CRP values in patients with CR, PR, SD and PD groups were 8.13±.80 mg/L,19.27±2.99 mg/L,29.60±6.2 mg/L and 50.98±8.6 mg/L ($p<0.001$).This statistical significant difference was also notedpost 2nd, 4th& 6th cycle of chemotherapy. Significant difference was noted in baseline mean tumor size and mean baseline hs-CRP (cut off 7cm).Strong correlation was found inchange in mean tumor size and mean hs-CRP during treatment in all treatment response groups($r > 0.8$). **Conclusions:** Despite the small number of patients in our study, we conclude the following. A high CRP value could suggest an occult lung cancer in patients of COPD. Higher stages at diagnosis have high level of CRP.Patients with high baseline tumor size have high level of baseline CRP. During treatmentchange in hs-CRP and change in tumor size have strong correlation.Patients having high baseline hs-CRP level are less likely to respond to chemotherapy and have progressive disease.hs-CRP mightbe useful for monitoring treatment response in Ca lung.

Key words: Hs-CRP,NSCLC, therapeutic & prognostic benefit

Study of Epidemiology, molecular profile and pattern of metastasis of adenocarcinoma lung in Indian females

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Background: Lung cancer is leading cause of cancer death worldwide. Epidemiology of lung cancer is varied depending upon the geographical location and smoking pattern. The data on lung cancer in female population is scarce. **Aims:** To study the epidemiology, molecular profiling and pattern of metastasis of Adenocarcinoma lung in Indian females. **Materials and Methods:** We have included 131 females of biopsy proven Adenocarcinoma lung treated at a tertiary care center in north India from January 2012 to December 2015. Demographic data, smoking history, stage at presentation, ECOG performance status at presentation, EGFR mutations and ALK rearrangements status and treatment details were collected and analyzed in SPSS. **Results:** Out of 131 patients included, majority (41%) of patients presented in 5th decade of life with a median age of 56 years. 89% patients were non smoker while 49% patients came with ECOG performance status 2 at initial presentation. 94% patients has metastatic disease while 5 % and 1 % patient were diagnosed in stage 3 and stage 2 respectively. 36 % patients were EGFR mutant (Most common is exon 19 deletion in 23% of cases) while ALK rearrangement were seen in 11% patients. Pleura (53%) followed by bone (44%) were the most common site of metastasis followed by contralateral lung (39%), brain (20%), Non regional lymph nodes (19%) and adrenal gland (11%). Patients with symptomatic brain metastasis at presentation received whole brain radiotherapy while others with

metastatic disease received chemotherapy/targeted therapy depending upon their EGFR/ALK status. **Discussion:** Majority of the patients in our study are non smoker and diagnosed in metastatic stage, much higher than previously reported studies. All patients diagnosed in stage II/III were non smokers. All ALK positive patients were non smoker while 93% of EGFR mutant patients were non smoker which highlight the importance of molecular testing in non-smoker subset. Treatment outcomes in this subset were also excellent as compared to EGFR wild and ALK negative patients.

Key words: adenocarcinoma, EGFR, ALK, non smoker

Profile Of Anaplastic Lymphoma Kinase Fusion Oncogene Positivepatients With Non Small Cell Lung Cancer

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Background: Lung cancer is a commonly diagnosed malignancy and one of the leading causes of mortality around the world. The time trends of lung cancer show a significant rise in different regions in both the sexes in India related to their geographic region, ethnicity and pattern of smoking. Non small cell lung cancer (NSCLC) is a common type of lung cancer and numerous driver mutations have been identified.The present study was conducted with the aim to evaluate the profile of Anaplastic lymphoma kinase (ALK) fusion oncogene positivepatients with NSCLC. **Materials & Methods:** A total of 50 ALK positive patients diagnosed with NSCLC during the time period March 2012 to September 2015 were recruited in the study. Details related to their demographic profile, tumor profile, further treatment and follow up were recorded.Alk mutation was reported by immunohistochemistry. **Results:** Majority of the alk positive patients (68%) were in the age group of >40 years at the time of diagnosis. Also, 26 (52%) patients were females. A history of smoking was reported in 12 (24%) patients. Also, 47 (94%) patients had adenocarcinoma on histology while 46 (92%) patients had stage 4 disease.Pemetrexed based chemotherapy was administered in 34 (68%) patients. Poor response/ progressive disease was reported in 20 (40%) patients. Crizotinib was given in 24 (48%) patients while it was offered as first line treatment in 7 (14%) patients.A total of 10deaths were reported and the overall survival of the patients was 28% at 8 years (follow up range 1-98 months). **Conclusion:** In today's era of personalized medicine, the importance of molecular testing is greatly highlighted as based on the presence/ absence of mutations and fusions, new drugs like crizotinib to suit individual requirements are being given. Molecular testing may thus also help in decreasing the toxicity related to the standard chemotherapy drugs.

c-Myb in lower respiratory tract adenoid cystic carcinomas: Potential biomarker for targeted therapy?

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Introduction: Adenoid cystic carcinoma (AdCC) is a malignant epithelial neoplasm that occurs rarely in lower respiratory tract (LRT).It has been seen that AdCC of various sites are associated with novel fusion transcript *MYB-NFIB* along with overexpression of the Myb protein. Expression of Myb protein in AdCC of LRT has not been evaluated extensively. **Objectives:**To evaluate the expression of Myb protein in AdCC of LRT **Material and Methods:**AdCC of LRT were retrieved from Institutional archives. c-Myb expression was analysed by immunohistochemistry (IHC). Clinicopathologic correlation of c-Myb expression was studied. **Results:**Twenty two samples of AdCC originating from LRT were included in the study. Majority of samples were from bronchopulmonary tree (68%), compared to trachea (23%) and larynx (9%). Most of the patients presented with endobronchial mass. The age of patients ranged from 24 to 80 years with a mean age of 50.0 years. A male predominance was seen with a sex ratio of 1.57: 1. The most common histological pattern was cribriform and majority of cases were of grade 1. IHC for c-Myb showed positivity in 59% of cases. Western blot was used in selected cases to validate IHC results. c-Myb immunopositivity did not correlate with tumour grade or pattern. Follow-up was available in five cases, ranging from 2months to 10months (mean 6.8 months) and all the patients were alive at last follow up. **Conclusions:**AdCC of LRT is rare and hence poses diagnostic difficulty. The presence of c-Myb immunopositivity in 59% cases may possibly make Myb a diagnostic biomarker and a therapeutic target for personalized treatment of patients of AdCC of LRT.

Effect of *Biophytum Sensitivum* and its isolated compound amentoflavone on the inhibition of experimental metastasis and the possible mechanism of action

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Introduction: The major clinical challenge for cancer therapy remains the eradication (or prevention) of metastasis. Many plants and natural products have been screened, in past, against cancer cell lines or in animal tumor models and have provided significant results which nudges us to look for more natural products from the traditional system of medicine. **Hypothesis:** *Biophytum sensitivum* and Amentoflavone possess antimetastatic efficacy **Materials and Methods:** Metastasis was induced in C57BL/6 mice using B16F-10 melanoma cells and monitored for their life span and the lung tumour nodule formation in the presence and absence of *Biophytum sensitivum* or amentoflavone treatment. Lung collagen hydroxyl proline content as well as the expression of prolyl hydroxylase and lysyl oxidase were carried out. Lung hexosamine, uronic acid as well as serum sialic acid and γGT levels were also analyzed. MMP-2, MMP-9, TIMP-1 and TIMP-2 expression in metastatic lungs were assessed. Further the effect of *Biophytum sensitivum* or amentoflavone on the activation and nuclear translocation of transcription factors were also analyzed **Results and Discussion:** *Biophytum sensitivum* or Amentoflavone treatment significantly showed increased lifespan accompanied with significantly less ($p<0.001$) tumor nodules. Lung collagen hydroxyproline, hexosamine, uronic acid as well as serum sialic acid and γGT showed marked reduction after *Biophytum sensitivum* or amentoflavone treatment. Significant inhibition in prolyl hydroxylase, lysyl oxidase, MMP-2 and MMP-9 expression were also observed after *Biophytum sensitivum* or amentoflavone treatment. Expression of TIMP-1 and TIMP-2 were increased. *Biophytum sensitivum* or Amentoflavone treatment also inhibited the invasion of B16F-10 melanoma cells. The activation of transcription factors such as p65, p50, c-Rel, c-fos, CREB and ATF-2 were inhibited in B16F-10 cells by *Biophytum sensitivum* or amentoflavone treatment **Conclusion:** Inhibition of tumor cell proliferation and invasion by *Biophytum sensitivum* or amentoflavone contribute to its antimetastatic/ therapeutic efficacy.

EGFR Exon 20 Insertion Mutations in Lung Adenocarcinoma: Prevalence, Molecular heterogeneity, and Clinicopathologic Characteristics in our Lung cancer patients

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Background EGFR Exon20 mutations have been considered to be markers of acquired resistance to TKI. The association between Oral TKI response and Baseline Exon20 Mutations has not been addressed in many studies and remains to be evaluated. **Methods** We conducted a retrospective audit of our prospectively maintained Lung cancer audit database in our institute in the year 2014.We reviewed data related to EGFR mutation testing by RQ-PCR assay and by direct sequencing.We also reviewed data relating to baseline demographics,clinical profile, patient treatment and outcome measures in terms of response and survival. **Results** We reviewed 807 sequentially tested lung cancer patients, who underwent molecular testing using RQ-PCR and Direct sequencing. Overall mutation rate was 23. 4% and 19 (2%) had baseline EGFR EXON20mutation. Median age of patients was 56yrs [range: 29-81yrs], with 7 patients being females. 7patients had past history of smoking. The most common site of metastasis was pleural effusion in8, followed by Bone in 6, Brain in 5 and Liver metastasis in 2patients. Histology was Adenocarcinoma in majority[16patients].Among the types of EXON20 Mutations, 7 patients had S7681, 4 patients had insGGT, 5patients had insGCCAGCGTGand 4 patients had T790M mutation. All patients received chemotherapy as first line treatment. Documented a response assessment at 2months in 8 patients, with progressive disease in 5[63%], stable disease in 2 and partial response in 1 patient. Second line therapy with Oral TKI was given to 9 patients, in whom we have documented response assessment in 6, all of whom had progressed.The median OS of Exon-20 mutation positive patients were 5.5months. [Range of 3.8-7.2months], in comparison with other types of EGFR mutations which showed median OS of 16.3months[range: 12.7-19.4months]. **Conclusion** EXON-20 Mutations in general proclaimgrave prognosis, diversity in biologic behavior, predicting limited benefit of chemotherapy and marked TKI resistance.

Key words: NSCLC ,metastatic, EGFR Exon 20 mutations

To study the epidemiological profile and clinical outcome of NSCLC patients who harbor EML4-ALK rearrangement

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Background: Advances in molecular biology have unveiled various targetable driver mutations in lung cancers which has revolutionized the treatment of advanced stage non small cell lung cancer. The anaplastic lymphoma kinase fusion gene is a key oncogenic driver in a small but significant subset of patients with advanced NSCLC. **Aims**: To study the epidemiological profile and clinical outcome of NSCLC patients who harbor EML4-ALK rearrangement. **Materials and Methods**: We retrospectively identified 27 patientswith stage IV NSCLC, diagnosed with EML4-ALK rearrangement by Fluorescence in situ hybridization or Immunohistochemistry methods. We collected data on clinicopathologic characteristics, patients' outcomes and treatment. **Results:** We evaluated 240 patients of advanced stage NSCLC from January 2014 to October 2015. EML4-ALK rearrangement was identified in 27 (13%) patientswith a median age of 56 years (range, 35 to 84 years), a high proportion of women (16 women *v* 11 men; 59%), and never-smokers (n= 20; 74%). Seven (26%) patients were either ex-smoker or current smoker. 25 patients had adenocarcinoma or2 had adenosquamous histology. Bone (51.8%) and brain (44.4%) were the most common sites of metastasis at presentation, followed by contralateral lung 11(40.7%), pleura 11(40.7%), non regional lymph node 8(29.6%) and liver 7(25.9%). Out of 27 patients, 16 patients received crizotinib, 9 as first line and 7 in second line. Overall response rate (ORR) with crizotinib was 87.5%. Progression-free survival (PFS) for patients with crizotinib was 8.03 months (PFS in first line, 9.1 months and in second line, 7.2 months). **Conclusion**: We report a higher incidence of EML4-ALK rearrangement in our series as IHC was predominant method used for its testing.We found that clinical criteria were not the only guide for testing EML4-ALK rearrangement. ORR and significant PFS in both first and second line confirmed Crizotinib benefit in ALK positive patients.

A Clinicopathological Study Of Leiomyosarcomas: A Study Of Ten Cases

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Background: Leiomyosarcomas are rare aggressive soft tissue sarcomas derived from smooth muscle cells typically of uterine, gastrointestinal or soft tissue origin. Women are affected more than men (2:1), with the disease typically occurring in the 5th and 6th decades of life. Accurate diagnosis, classification, and multi-modality treatmentare utmost important. The rarity of these tumors makes definitive treatment protocols difficult to be set. The prognosis is poor, with survival rates among the lowest of all soft tissue sarcomas. **Material And Methods :**Ten cases of leiomyosarcomas presenting at various sites were retrospectively reviewed to find the clinical characteristics and outcome. **Results:** Out of ten cases, four were of uterine leiomyosarcomas, three were located in the extremities involving the thigh, gluteal and perianal region respectively and single case of retroperitoneal origin was found. Two rare cases of scrotal and colonic leiomyosarcoma were also reviewed. Age of the patients ranged from 40-68 years with male: female ratio of 3:7. Diagnosis was made on the basis of histopathology and immunohistochemical profileof the tumor cells for smooth muscle actin and desmin. Standard treatment including surgery with adjuvant chemotherapy and/or radiotherapy was given depending upon the location, stage of tumor, age and general condition of the patient Cases of uterine leiomyosarcomas presented with variable complaints like bleeding pervaginum and lower abdominal heaviness and pain. Out of four, one case presented with multifocal lesions in the myometrium. Disease free survival period ranged from 4 months- 2.8 years . Recurrence at local site and distant metastasis to lung and brain was noted in these cases. Extremity leiomyosarcomas were found to be associated with features like multifocality, larger size of upto 17.0 cm, early recurrence and had dismal prognosis. One out of three cases, hadparaaorticlymphnode involvement, liver and bilateral lung metastasis at the time of initial presentation. Scrotal leiomyosarcoma, clinically misdiagnosed as sebaceous cystpresented as a small nodule of 2.0 cm size, was treated with wide surgical excisionalongwithadjuvant radiotherapy and patient has been kept on follow up. **Conclusion:** Leiomyosarcomas are aggressive tumors of smooth muscle origin that are often difficult to treat. Extensive studies including large number of cases need to be performed for setting definitive treatment protocols.

Novel bio macromolecular based Docetaxel and Gemcitabine loaded nanoparticle: Combinatorial regimen for effective tumour therapy

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Introduction: Combination therapy with two or more drugs has emerged as a promising strategy to suppress cancer drug resistance, as different drug molecules can exercise their therapeutic effects at varying stages of the growth cycles, thereby leading to synergistic anticancer response a promising tool to overcome the deleterious side effects associated with high doses of single drugs by accessing context-specific multi-target mechanisms. **Objectives:**In the purview to resolve the problem associated with delivery of poor physiochemical properties. The objective is to develop drug polymer conjugate of two drugs of contrasting lyophilicity directly with albumin i.e. Anacardic acid (AA) and Gemcitabine (GEM) with amine terminal and carboxylic terminal of albumin, respectively. Further, modified albumin is utilized in the formulation developed and evaluation of Docetaxel (DTX) loaded modified albumin nanoparticles (AA and GEM modified albumin NPs). **Material:** GEM and DTX were obtained as gift sample from Fresenius Kabi Oncology Limited, Gurgaon. Albumin, 1, 1'-Carbonyldiimidazole was purchased from Sigma Aldrich, USA. 1-ethyl-3-(3-dimethylamino) propyl

carbodiimide (EDC) and N-hydroxysuccinimide (NHS) were purchased from Fluka. **Methods:**Modified albumin was synthesis is detailed in four steps. These steps included: (i) EDC and NHS mediated activation of linker carboxylic group of AA; (ii) Amine group of albumin conjugated to the activated ester of AA; (iii) Activation of carboxylic group of albumin via EDC and NHS; (iv) Amine group of GEM conjugated to activated ester of Albumin. Developed conjugates were then evaluated by using spectroscopic tools and further utilized in the formulation of DTX loaded nanoparticles. The developed nanoformulation extensively optimized, characterized and evaluated for its pharmacodynamic activity. **Results:**Modified albumin was found to be possess optimum characteristics. DTX loaded AA-GEM ALB NPs were exhaustive optimization wascarried out by "Box-Behnken Design (BBD)". Morphological evaluation via SEM revealed the formation of almost spherical particles, while, Mannitol (5% w/v) resulted in the formation of fluffy, easy to redisperse freeze dried cake ofnanoparticles.Cell culture experiments revealed a significantly higher cellular uptake ofDTX loaded AA-GEM ALB NPsin MCF-7 breast cancer cell line, as compared to their free drug counterparts. Further, intracellulartracking demonstrated preferential localization of NPs in the vicinity of nucleus. Moreover, the developed NPs exhibits significantly higher cytotoxicity demonstrated via MTT assay, the results were further corroborated by In vitro apoptosis assay. Furthermore, the developed formulations exhibits significantly lower In vivo toxicity profile. **Conclusions:**DTX loaded AA-GEM modified ALB NPs were developed and characterized and holds promise as an effective tool to synergize the therapeutic indices of potential drug candidates for the effective treatment of breast cancer.

Utility of Screening with serum protein electrophoresis and serum free light chain ratio for monoclonal gammopathies in chronic kidney disease

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Introduction: Chronic kidney disease (CKD) may be one of the first manifestation of Multiple myeloma (MM).Hence Serum protein electrophoresis(SPE) is commonly included in the diagnostic screening tests in these patients. Quantitative measurement of serum free light chains (sFLC) has now been adopted into screening algorithms for multiple myeloma. The assay indicates monoclonal free light chain production by presence of abnormal kappa or lambda free light chain ratio (reference range 0.26-1.65). **Objectives:** The aim of the study was to evaluate the utility of Screening with SPE and sFLC ratio for monoclonal gammopathies in CKD patients. **Patients and Methods:** Patients who visited nephrologydepartment of our tertiary care centre due to renal insufficiency for a diagnostic workup for proteinuria or CKD of an unknown origin(or both)were enrolled. sFLC and SPE were performed.Free light chain tests were performed using Binding site kits and SPE done on automated instrument. **Results:** Among 62 patients, MM was confirmed in 4 patients(6.45%),out of that 2 patients had a highly abnormal FLC ratio and M-protein on SPE. One patient with biclonalgammopathy showed normal FLC ratio whereas 1 patient of LCMM showed normal on SPE and had highly abnormal FLC ratio. Out of remaining 58 patients, 6(9.7%) cases turned out to be MGUS (monoclonal gammopathy of uncertain significance). All MGUS cases showed small peak in SPE but only 3 of these patients showed abnormal FLC ratio. After the exclusion of the subjects with MM and MGUS, the abnormal kappa/ lambda ratio was found in 19 patients (36.5%) if reference range of 0.26-1.65 is considered and if renal reference of 0.3-3.1 is taken all these subjects will be considered normal. **Conclusions:** Our data demonstrate that screening with SPE and sFLC in patients with CKD is useful screening tests to identify monoclonal gammopathies.

Anti- proliferative activity of synthetic peptides, the sequence present in buffalo prolactin (buPRL).

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Introduction: Prolactin a polypeptide hormoneis now known for over 300 separate biological activities.Out of the myriad number of activities the intact prolactin possesses, the fragments of prolactin obtained by Cathepsin D digestion from rat, buffalo and human have shown antiangiogenic activity also.The antiangiogenic activity of buffalo prolactin fragments has been reported to act by inhibiting nitric oxide production and hence nitric oxide mediated angiogenesis stimulated by vascular endothelial growth factor (VEGF) or bradykinin (BK), however the underlying mechanism is not well reported and remain elusive.Angiogenesis which is derailed in many cancers attracts these fragments as an anti-angiogenic as well as anti-proliferative molecules for future cancer research and hence therapeutic use. For our study we have the synthetic analogue of these fragments (peptides) with slight modification. **Objectives:** (i) To study the cytotoxic activity of these fragments against cancer cell lines (ii) To study the in-vivo effects of these fragments. **Material and Methods:**MCF-7 cell line (human breast adenocarcinoma cell line) was treated with these peptides (10nanogram to 1microgram) and cell viability/cytotoxicity was done by MTT and LDH assay. Immunoblotting was done to check the effect of these peptides on various proliferative markers. **Results:** MTT and LDH assays have shown reduced cell viability. Immunoblotting has shown down-regulation of known proliferative markers such as c-jun and Akt. **Conclusion:** according to our data, we have shown that these peptides have anti-proliferative property with down regulation of known proliferative markers.

Key words: Buffalo prolactin, anti-angiogenic,anti-proliferative, Akt.

Pattern Of Occurrence And Treatment Outcome In Second Primary Malignancies: Need Of Screening And Early Detection

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Introduction: The reported incidenceof second primary malignancies (SPM) ranges from 0.734-11.3%.The reported incidence ranges from 0.734-11.3%. Apart from increased survival rates, this increased incidence of SPC can be attributed to a number of other factors including etiologic influences (tobacco and excessive alcohol intake), environmental determinants, host factors, genetic predisposition, gene–environment interactions and late sequelae of cytotoxic treatment for previous malignancy including radiotherapy and chemotherapy. Warren and Gate's criteria has been used to designate a case as multiple primary tumor. In this study, we have done a retrospective compilation of the pattern of occurrence of second primary malignancies after an index primary. **Material & Methods:** This retrospective study analyzed data for patients either presenting with histologically proven synchronous or metachronous double primaries over a period of seven years from January 2009 to July 2015. The inclusion criteria of patients in the study were the presence of at least two malignant lesions, confirmed by histopathological examination. **Results:** Over a period of 7 years total 36 cases of multiple primary malignancies were observed. The median age was 60 years (range 26-83). The most common age group were between 51-60 and 61-70 years with 10 patients in each decade.Twowere synchronous malignancy and thirty four were metachronous. The most common site of primary tumor was head and neck.Second most common site was breast (5). Among the second primary malignancy most common site was again head and neck (22) followed by gynaecological cancers (4). The time to occurrence of second primary varied from 2 months to 17 years. 15 patients underwent Surgery. Reirradiation was done in 21 patients in head and neck malignancies.At the time of analysis 17 patients were disease free, 9 patients expired due to disease progression and 3 patients were undergoing chemotherapy. **Conclusion:** With the population of cancer survivors growing at a fast pace, the early detection of a second primary is essential to reduce the morbidity and mortality.A regular follow-up with a meticulous history and examination is necessary. In general, survivors should undergo appropriate guidelines for screening along with some additional procedures depending on the presence of any high risk features.The treatment of SMP is as per standard guidelines and is no different from the primary tumour.

Treatment of the primary tumour should be kept in mind, while planning the management of the second malignancy.

A Study Of Pattern Of 300 Lymph Node Aspirations, North Indian Population

Introduction: Fine needle aspiration cytology (FNAC) is most popular diagnostic aid in patients with lymphadenopathy. This study supports its highly sensitive nature. **Materials and Methods:** The present study was done retrospectively to study nonneoplastic and neoplastic lesions of enlarged lymph nodes by FNAC in 300 patients who presented with lymphadenopathy over a period of two years from January 2014 to December 2015. **Results:** Out of total 300 cases studied by fine needle aspiration cytology, 269 cases (89.67%) were diagnosed as benign lesions and 17 cases (5.67%) were diagnosed as malignant lesions. Among benign lesions the most significant lesions encounterd was granulomatous (tubercular) lymphadenitis, 136 cases (45.33%). The second most common benign lesion encounterd was reactive lymphadenitis, 57 cases (19%). Out of 14 malignant lesions, primaries (n= 14) were more commonly encounterd than secondaries (n=3). **Conclusion:**FNAC proved to be a safe, inexpensive, repeatable and rapid procedure in which no hospitalization or anaesthesia is required.

Keywords: FNAC, lymphadenopathy, North India

Cancer Pharmacogenetics: G1934A & C100T variants (alleles *4 & *10) of CYP2D6 gene and personalized medicine in cancer treatment

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Introduction: Cytochrome P4502D6 (CYP2D6) is of great pharmacogenetics interest due to its involvement in the metabolism of several classes of drugs including anti-cancer drugs. CYP2D6*4 (G1934A), located on intron 3 and exon 4 junction, and CYP2D6*10 allele (C100T at exon 1), results in decreased catalytic activity of the enzyme and may lead to inappropriate metabolism of drugs thus, leading to variation in treatment outcome. Therefore, pharmacogenetic studies will help in standardization of chemotherapeutic drugs and better treatment outcome in cancer patients (precision medicine) carrying variant genotypes of CYP2D6. **Objectives:**The present study was undertaken to investigate the association of variant genotypes of CYP2D6 with the treatment response (personalized medicine approach) in Head and Neck cancer cases receiving chemotherapy or combination of chemo- and radiotherapy. **Material and Methods:**350 patients suffering from Head & Neck cancer and equal number of age matched controls were included in the study. Genomic DNA was isolated from the blood samples and CYP2D6 genotypes were determined in genomic DNA by PCR based RFLP. Follow-up carried out to correlate the association (if any) in between variants and treatment outcome. **Results:**The frequency of variant alleles of CYP2D6 (CYP2D6*4 & *10) was found to be significantly higher in the cases when compared to the controls. A higher number of non-responders to chemo-radiotherapy were encountered during in patients carrying variant genotype during the follow up. **Conclusions:**This study further suggest that the presence of the inactive CYP2D6*4 & *10 causes a reduction in the metabolic activation of anticancer agents, thereby lowering the risk of toxicity but worsening the therapeutic response. Further research into CYP2D6 may provide more insights that will aid in the development of immunotherapy for oral cancer.

Keywords: Pharmacogenetics, Personalized medicine, Head & Neck Cancer, chemotherapy

Use Of Nanotechnology In The Diagnosis And Treatment Of Cancer

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Introduction: Nanotechnology refers to the interactions of cellular and molecular components and engineered materials—typically, clusters of atoms, molecules, and molecular fragments into incredibly small particles—between 1 and 100 nm. Nanometer-sized particles have novel optical, electronic, and structural properties that are not available either in individual molecules or bulk solids. **Objectives:** Use of Nanotechnology in the Diagnosis and Treatment of Cancer **Material and Method:** The concept of nanoscale devices has led to the development of biodegradable self-assembled nanoparticles, which are being engineered for the targeted delivery of anticancer drugs and imaging contrast agents. Nanotechnology, along with other field such as theranostics, genomics, or proteomics, has one of the most potential uses in prevention, diagnosis, and treatment of disease' formulation of different nanoparticles and modification of their surface in general, is required to lower side effects of drugs and to improve their response in human body. Nanotechnology can be used for better cancer diagnosis. One of the main usage fields of optical nanoparticles is to allow better cancer detection such as using Nano pores, Nanotube, and Quantum dot.Moreover, together with imaging contrast agents nanoparticles have great perspective in cancer diagnosis. The most commonly used materials for nanoparticles carriers are magnetic nanoparticle, polymer drug conjugates, dendrimers, liposomes,Nanoshells andNanorobot etc. **Result:** The use of nanoparticles as drug carrier may improve cancer therapy and reduce harmful side effects of chemotherapy and also radiotherapy. **Conclusion:** Finally, nanotechnology is still developing science and can be defined as next generation techniques for cancer disease, at the same time it comes with many advantages to treat cancer patients.

Establishing wonder oil, Solanesol, as a novel inhibitor for Focal Adhesive Kinase by in silico strategies

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Focal adhesion kinase (FAK) plays a primary role in regulating the activity of many signaling molecules. Increased FAK expression has been implicated in a series of cellular processes, including cell migration and survival. Inhibiting the activity of FAK for cancer therapy is currently under investigation. Hence, FAK and its inhibitors has been the subject of intensive research. To understand the structural factors affecting inhibitory potency, kinetic analysis, molecular docking and molecular dynamics simulation were studied in this project. Though, Solanesol was found have inhibitory activities towards FAK, no *in silico* tests were ever done on the same. Solanesol is a highly flexible ligand (26 rotatable bonds) and extremely difficult to dock using classical methods hence a novel modified blind docking method and contact based scoring function, is introduced by this paper. All the molecular docking studies of Solanesol to FAK were performed using Autodock 4.2. Autodock uses a semi-empirical free energy force field to evaluate binding conformations of ligand while docking. The MGLTools-1.5.6 was used for preparing protein and ligand parameters files. Molecular dynamics simulations for Solanesol bound FAK was performed using the GROMACS 4.6 software with GROMOS96 (53a6) force field. PRODRG server was used to generate topology files for the ligand molecule. Charges were kept full and no energy minimization was done using PRODRG. Root mean square deviation (RMSD) and root mean square fluctuations (RMSF) of FAK backbone were calculated. Total solvent accessible surface area (SASA) was checked by for analyzing the change in surface area with respect to time. All the results establish Solanesol as novel FAK inhibitors, *in silico*.

Key words: Fak, Solanesol, Blind Docking, Contact Scoring, Gromacs, Sasa

*The product is submitted for patent processing.

Carcinogenicity induced by Hexavalent Chromium through Multipathway Exposure: A Review

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Hexavalent chromium (Cr^{+6}) is very reactive, oxidizing, highly soluble, mobile and known inorganic pollutant found in the environment basically due to anthropogenic activities like tannery, electroplating, steel and alloy, dye and paint, chemical and mining industries. This form of chromium (Cr^{+6}) is the more toxic as it is easily penetrable in cell membrane by reason of its similarity with sulfate. CrO_4^{2-} replace sulfate $(SO^4)^{2-}$ from sulfate uptake pathways of cellular membrane and enter into the cell. Intracellular chromate reduction by cellular reductans (ascorbic acid, glutathione, cytochrome and riboflavin) induce oxidative stress which ultimately protein and DNA damage. Though, detoxifying enzymes and DNA repair system minimize the toxicity of chromate but ultimately it disrupts cell metabolic activities. In general it causes carcinogenic, genotoxic and mutagenic effect which induced cardiovascular, respiratory, reproductive and developmental health hazards. Cr^{+6} impart toxicity through inhalation, ingestion and dermal pathways. Inhaled Cr^{+6} absorbed through lungs into bloods and extracted through liver and kidney. Epidemiological studies suggested that Cr^{+6} is well known nasal, lung carcinogen, after that USEPA estimated a screening level of Cr^{+6} (8×10^{-5} μgL^{-1}) that an individual can expose lifetime. Orally ingested Cr^{+6} firstly reduced in gastrointestinal tract because of low pH and leading DNA damage by via formation of $Cr^{+5}$and Cr^{+4} unstable radicals, oxidative stress condition and resulting cancer that may be in form of tumor. Dermal exposure of Cr^{+6} adsorbed by skin surface through oxidation and induced dermatotoxicity which provoke skin irritation, lesions, ulceration and allergy. To reduce Cr^{+6} toxicity in human, better understanding of its toxicity, mechanism pathway and mode of exposure is required. This review provides a brief explanation on toxic effect, way of exposure and intercellular mechanism pathway, which can be effective for the scientist, doctors and researchers who is working in this field.

Keywords: Carcinogenicity; Hexavalent chromium; Multipathway exposure

Clinico-Histopathological Correlation Of Hansen's Disease

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Leprosy is a chronic granulomatous disease caused by mycobacterium leprae, principally affecting cooler parts of the body mainly skin and peripheral nerves. It also involves muscles, eyes, bones, testis and internal organs. It is one of the major health problem in developing countries. Mycobacterium leprae, the causative agent of leprosy was discovered by G.H Amiauer Hansen in 1873, making it the first bacterium to be identified as causing disease in humans. Hansen observed a number of non refractile small rods in unstained tissue sections and was able to stain them with Ziehl's method in 1879. Histopathological study of leprosy is very important in understanding the disease, its varied manifestations and complications as well as for the early accurate diagnosis and adequate treatment. Since exact typing of leprosy is sometimes not clinically possible, to prevent false negative diagnosis, histopathological examination should be done in all suspected cases. **Methods**: Skin biopsies for the study were received in department of histopathology in 10% formalin and biopsies were stained with haematoxlin - eosin method and Fite Faracco stain for detection of acid fast bacilli. **Results**: 50 skin biopsies were obtained from patients age range of 10-80 years, majority were in 3rd decade (28%) with male to female ratio 1:1. Borderline Tuberculoid Leprosy is the most common type of leprosy constituting(38%)of the biopsies followed by indeterminate leprosy (30%), borderline leprosy (10%) , Lepromatous leprosy (8%), Tuberculoid leprosy (1.5%) , histoid leprosy (6%) and borderline borderline (2%) biopsies. Most common feature is loss of sensation. Atrophic epidermis and grenz zone were more common in histoid and borderline lepromatous leprosy. Majority of them were paucibacillary type. **Conclusions**: For accurate diagnosis, correlation of clinical and histopathological features along with bacterial index appear to be more useful.

Cell signaling pathways- Physiological perspective.

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Background: Cell signaling pathways are amplification of primary signal and distribution of signals to appropriate targets within cell. It occurs due to enzymatic changes, protein-protein interactions and second messengers. G proteins link receptors to effector molecule in cell membrane and convert signals to biological action. These are coupled to cell surface receptors and catalyse formation of intracellular second messenger like cAMP, cGMP, Ca^{2+},IP_3, DAG. JAK STAT pathway is a cell signaling pathway having tyrosine kinase activity, consisting of receptor, janus kinase and STAT (Signal Transducer and activator of Transcription). **Material and method:** A review study. **Results:** Binding of ligand to G-protein coupled receptors leads to conformational change in receptor which activates heterotrimeric G-protein on inner side of cell membrane. Increased G protein response occurs in acromegaly and Mc Cune Albright syndrome. Decreased G protein response occurs in pseudo-hypoparathyroidism. Binding of hormone to receptor leads to activation of kinase function of JAK which auto-phosphorylates the receptor itself and activates STAT which is dimerized and enters the nucleus of cell to cause transcription and gene expression. Growth hormone and erythropoietin acts via this pathway. **Conclusion**: Cell signaling pathways lead to amplification of the effect. Second messengers exert physiological effects like increased synthesis of enzymes, increased release of stored enzymes, gene expression and increased enzymatic activity.

Keywords : Cell signaling, G-proteins, JAK-STAT.

Holystic Management Of A Child With Acute Lymhoblastic Leukemia:a Case Study From Ocean Road Cancer Institute, Dar-Es-Salaam-Tanzania

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Palliative care as an approach that improves the quality of life for people with lifethreatening illness and their families, through the prevention, assessment and treatment of pain and other physical, psychosocial and spiritual problems or rather challenges (WHO). It provides relief from pain and other distressing symptoms; affirms life and regards dying as a normal process; offers a support system to help patients live as actively as possible until death and it also uses a team approach to address the needs of patients and their families, including bereavement counselling, if indicated. This is a case study of the child TD 13 years old boy who was admitted at Ocean road Cancer Institute. Upon admission he presented with neck swelling, difficulty in breathing, awareness of heart beat, severe loss of weight, neck pain and fever which was on and off.Both parents reported to be peasant with poor financial income. Their child had stopped school due to illness. Multicsiplinary approach was considered in addressing the problem of the child. Three unit of blood were transfused, haematenics, antibiotics, nutritional support were given. Pain assessment and management according to World health organization analgesic ladder were also provided. Chemotherapy was provided and was referred to spiritual leader as the child developed the sense of losing

hope. After four weeks in care, the condition of the child had significant improvement with well controlled physical and psychological pain.The use of multidisciplinary approach whereby health care workers, parents and the child (Family centred care) were involved helped to improve the quality of life to the child.Palliative care plays a vital role in managing children with Acute Lymphoblastic Leukaemia. Acute Lymphoblastic Leukaemia, ORCI, Palliative care, Family centred care

Combretastatin A-4 inspired novel 2-aryl-3-arylamino-imidazo-pyridines/pyrazines as tubulin polymerization inhibitors, antimitotic and anticancer agents

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Based on the pharmacophoric features of the natural product combretastatin A-4 (CA-4) and its synthetic analogues that inhibit tubulin polymerization, a series of novel 2-aryl-3-arylamino-imidazo-pyridines/ pyrazines as potential antitubulin anticancer agents were designed. They were synthesized by a one-pot method involving preparation of isocyanides from the anilines via formylation and subsequent dehydration followed by their reactions with heterocyclic-2-amidines and aldehydes. Compounds 1, 2,14, and 15 were found to exhibit significant tubulin polymerization inhibition and disruption of tubulin–microtubule dynamics similar to that of CA-4. They showed potent anticancer activities in kidney, breast and cervical cancer cell lines, and relatively low toxicity to normal cells, compared to CA-4. The compounds induced DNA and chromosomal damage, and apoptosis via cell cycle arrest in the G2/M phase. The molecular docking and molecular dynamics (MD) simulation studies revealed that disruption of microtubule dynamics might occur by interaction of the compounds at the colchicine binding site at the a,b-tubulin heterodimer interface, similar to that of CA-4. Molecular modelling analysis showed that two of the three methoxy groups at ring A of all four potent compounds (1, 2, 14, and 15) were involved in bifurcated hydrogen bonding with Cysb241, an important molecular recognition interaction to show tubulin inhibitory activity. In comparison to CA-4, the bridging NH and the imidazo-pyridine/pyrazine moieties in the title compounds provide flexibility for attaining the required dihedral relationship of two aryls and additional pharmacophoric features required for the interaction with the key residues of the colchicine binding site.

Biography

Sarita Das has completed her Msc in Biotechnology from KIIT University,India and is currently pursuing Phd in cancer biology from KIIT University India.

Analysis of EGFR Exon19 Over expression in Glioma and Prognostic Significance

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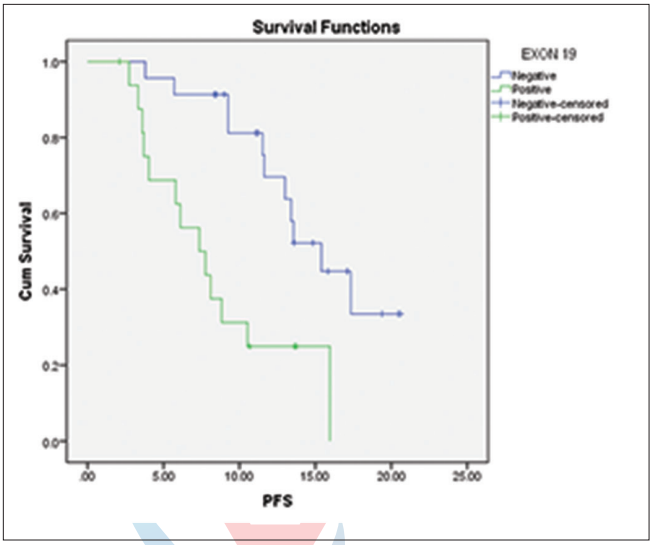
Introduction: Glioblastoma, despite multimodal therapies, including surgical resection, radiotherapy and chemotherapy has a median survival of one year. Amplification of the EGFR gene is a common genetic event in high-grade astrocytomas and occurs in about half of GBMs. **Objectives:** Theaim of this study was to study the EGFR expression in Glioma and its prognostic significance. **Materials and Methods:** A single centre, Non randomized, retrospective study with a prospective arm done on patients of GlioblastomaMultiforme. 40 samples were included into the study, EGFR sequencing was done using PCR for HRM analysis. Survival outcome analysis was done using the Kaplan Meier method. **Results:**The frequency of GBM with EGFR overexpression for Exon 19 was (42.5%). The Kaplan Meier analysis shows the overall median progression free survival (PFS) time among the whole cohort was 10.53 months with a std error of 1.32, the median progression free survival time in the EGFR exon 19 positive group was 7.36 months with a std error of 1.34 and the median progression free survival time of the EGFR exon 19 negative group was 13months with a std error of 1.49. The median survival time (OS) in the EGFR Exon 19 positive patients was 7.3 months with a std error of 1.66 as compared to patients who tested negative for EGFR exon 19 with median survival time of 15.4 months with a std error of 1.84. There was no statistical difference in age, extent of surgical resection, site and size of the tumour. **Conclusion:** In the present study, we found that a high percentage of GBM and exhibited EGFR overexpression and amplification. Our results represent a step forward for the identification of GBM patients in the Indian scenario who could respond to specific therapies targeting EGFR.



Role ofGlucoheponate Brain SPECT in the era of FDG PET for evaluation of brain lesions.

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Introduction: Glucoheptonate is glucose analog with strong affinity for neoplastic brain tissues and until recently was extensively used as a SPECT tracer to differentiate recurrent gliomas from radiation necrosis. However with the wider availability of PET scan facility it is now rarely used in favor of FDG-PET. Though limitation for FDG-PET is well documented in low grade brain tumors, it is considered as tracer of choice for high grade brain tumors. We report two cases where Tc99m-Glucoheptonate brain SPECT provided a definite clue to diagnosis when FDG PET study was inconclusive. **Material and method:** ***Patient 1:*** A 39 year old female patient who underwent resection of right temporal lobe anaplastic astrocytoma followed by radiotherapy 20 months back was referred to us for evaluation of suspected recurrence. She underwent a FDG-PET/CT scan and subsequently a Tc99m-Glucoheptonate SPECT of brain using the standard protocols. ***Patient 2:*** A63 year old male patient of renal cell carcinoma underwent a FDG PET/CT scan as he developed symptoms suspicious of brain involvement. The CT component revealed an ill-definedhypodense lesion in the deep white matter of frontal lobe on left side with minimal FDG uptake. As large numbers of RCC lesions are known to be FDG nonavid a Tc99m-Glucoheptonate SPECT of brain was performed for further lesion characterization. **Results:** ***Patient 1:*** Result of Both the FDG-PET and Tc99m-Glucoheptonate SPECT was reviewed by two nuclear medicine specialist independently and both concurred in their findings. The FDG-PET scan did not reveal any abnormal tracer uptake suggestive of tumor over the entire brain. Since clinical suspicion of tumor recurrence was very high

the patient underwent an additional Tc99m-Glucoheptonate brain SPECT. The study revealed increased tracer uptake in known tumor bed in right temporal lobe and a skip lesion on the contralateral posterior frontal lobe suggestive of viable recurrent tumor. ***Patient 2*:** Glucoheptonate SPECT did not reveal any abnormal tracer uptake in the suspicious area detected on PET/CT thereby excluding the possibility of tumor deposit. On subsequent detailed neurological evaluation includingmagnetic resonance study of brain, the lesion was diagnosed as a cerebral infract. **Conclusion:**Both the studies reveal the relevance of Tc99m-Glucoheptonate brain SPECT in the presentday Nuclear Medicine neuroimaging dominated by PET. The first case demonstrates that it is possible to have false negative FDG-PET/CT even in high grade brain tumors.The second case demonstrates the complementary roleof Tc99m-Glucoheptonate brain SPECT in a confounding clinical scenario.

Interleukin-1 Polymorphism and Expression in Hepatitis B Virus-Mediated Disease Outcome in India.

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Background: Hepatitis B Virus (HBV) infection is a primary factor of hepatocellular carcinoma (HCC), the fifth most frequent cancer, worldwide. Interleukin(IL)-1cytokine, is considered to be a key mediator in HBV linked disease progression. So, the aim of the presentstudy was to analyze the distribution of *IL-1B*(-511C>T) and *IL-1RN*(VNTR)polymorphism and haplotypes and their association with HBV-HCC risk. Also, to analyze the expression and levels of IL-1B in different categories of HBV patients. Material and methods: 406 subjects (153 healthy controls, 67 inactive HBV-carriers, 65 patients with chronic-active HBV, 62 HBV-cirrhotics, and 59 subjects with HBV-HCC) were enrolled in the study. Polymerase chain reaction (PCR)–restriction fragment length polymorphism was carried out to study the genotype frequencies. IL-1B expression was evaluated by real-time reverse transcriptase (RT)–PCR analysis by using sequence-specific primers. IL-1B levels in peripheral blood mononuclear cells (PBMCs) were estimated using an enzyme-linked immunosorbent assay (ELISA). **Results:** The study revealed no significant association of *IL-1B*(-511) CT and TT genotypes with HCC development. However, the IL-1 haplotypes 2 and 3 were found to be significant protective factors for hepatitis and subsequent HCC development, among controls while haplotype 4 shared a significant negative association with hepatitis only. A significant positive association of the *IL-1RN*(VNTR)1/2 genotype with HCC development was observed among controls and carriers. Besides, 2/2 genotypes acted as a potential risk factor for hepatitis and subsequent cirrhosis development, among the same groups. Moreover, proinflammatory IL-1B levels significantly and steadily elevated with the disease progression to HCC, as compared to controls. **Conclusion:** These preliminary findings indicate a key role of IL-1 in the HBV-mediated disease chronicity, in the Indian population.

Keywords: HBV, HCC, IL-1

Role of papaya leaf juice with or without steroid in the treatment of hemotherapy induced moderate thrombocytopenia : An observational study.

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Background: Thrombocytopenia following chemotherapy is a great challenge from the very beginning of cancer treatment. There are no effective methods to treat thrombocytopenia once it occurs. Transfusions, growth factor injections and steroids have their limitations. So there is increased need for research of drugs or alternatives that could prevent and treat thrombocytopenia. The objective of this study is to determine the effect of papaya leaf juice in the treatment of moderate thrombocytopenia and to prevent severe thrombocytopenia. **Methods:** A total of 40 patients included in this observational study, who have developed grade II-III thrombocytopenia (25,000-75,000 / mm^3) following chemotherapy. Out of them 20 patients were treated with papaya leaf juice and steroids (low dose prednisolone) and another 20 patients were treated with papaya leaf juice alone. Platelet count repeated on Day 5 and Day 7 of starting treatment and compared with the initial values. **Results:** Platelet count increased in most of the patients within 5-7 days of treatment by papaya leaf juice and no significant difference found with addition of steroid. Target achieved in all age group patients. Most of the platelet levels found on Day 7 were between 80000-120000 / mm^3. **Conclusion:** In case of moderate thrombocytopenia, we can consider papaya leaf juice for not only treatment but also to prevent severe thrombocytopenia from moderate. No significant role of steroids in such cases. Question is, should we use steroid unnecessarily in case of moderate thrombocytopenia?Long term study and follow-up needed for further comment.

Key words: Thrombocytopenia, Chemotherapy, Papaya leaf juice.

Multi-pathway cancer risk assessment of Chromium(VI) induced cytotoxicity in Sukinda Chromite Mine, Odisha, India: A case study

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Background: Contamination of heavy metals in water isprominent in mining sites. Elevatedheavy metals like As, Cr, Pd and Cd in drinking water have posed cancer threat on human.Sukinda chromite mine is one of the most polluted places of India due to higher chromium contamination in surface as well as ground water. Cr(VI) is very soluble, reactive and easily penetrable into cell wall thus higher concentration of Cr(VI) in drinking water leads togastrointestinal tract and kidney cancer. Numerous studies have been conducted on the carcinogenesis of Cr(VI) and researchers demonstrated that Cr(VI) enters in cell wall through sulfate transportation pathway, disrupt the enzymatic activities and cause DNA damage and mutagenesis.Elevated stomach cancer mortality among people who consumeCr(VI) contaminated water indicates that Cr(VI) causes gastrointestinal toxicity in people. The purpose of the study to identify cancer risk of Cr(VI) through oral and dermal exposure of drinking water of nearby Sukinda chromite mine.The cancer risk assessment of each location was carried out by mathematical models as per IRIS guidelines. **Material and Methods:** Sukinda Chromite mine area of Jajpur district, Odisha (India) was selected to estimate the Cr concentration in groundwater/drinking water and associated human health risk.Sampling was carried out in October 2013 from five different locations of the Sukinda Chromite Mine named S1, S2, S3, S4 and S5 in three replicates. Each groundwater sample were collected and stored in pretreated acid washed polypropylene bottles.Standard methods for preservation and analysis of TCr and Cr(VI) was followed as prescribed in APHA 22nd edition 2012.Atomic Absorption Spectrophotometer (Avanta, GBC, Australia) and UV Visible Spectrophotometer (Helios Aquamate, Thermo scientific, England) were used to analyze TCr and Cr(VI) respectively. The cancer risk assessment was carried out using empirical models as per IRIS guidelines for residing male and female population. **Resultsand Discussion:** The concentrations of Cr(VI) in the five locations (named S1, S2, S3, S4 and S5) of Sukindawere found in the range of 21.4-115.2 μgL^{-1}, that is 2.1-11.5 times higher as stated by drinking water guideline of California 2015.The total cumulative average cancer risk was calculated 2.04E-03 and 1.73E-03 for male and female population respectively, which is represents 204 and 173 deaths per 1000 populationin male and female respectively. IRIS standard guideline supported that this level of Cr(VI) causing 'very high' cancer risk in all the selected locations of the study area as per IRIS guideline. The cancer risk in male was found approximately 1.2 times higher than the female populations, because of

the higher water ingestion rate in male. The obtained cancer risk via dermal route was found 6 times lesser than the oral ingestion basically because of very less exposure time (0.58 h/d) during bathing. The study revealed that the minute elevation in Cr(VI) concentration in drinking and bathing water can cause drastic cancer risk on human beings. **Conclusion:** The TCr and Cr(VI) found in the range of 48.7-250.2 μg/l and 21.4-115.2 μgL^{-1} respectively and the proportion of Cr(VI) and Cr(III) were recorded 26.4-43.9% and 54.0-73.5% respectively. The obtained data revealed 'high' to 'very high' cancer risk in all the locations for both male and female populations. Location (S3) which is highly populated by socioeconomically marginalized people, found prone to 'very high'cancer risk. This paper revealed that the maximum cancer risk is due to oral exposure of Cr(VI), rather than dermal, due to the low exposure time of dermal pathway.

Keywords: Cancer risk assessment, Drinking water, Hexavalent chromium

Incremental life time cancer risk of polyaromatic hydrocarbons among kitchen workers

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Introduction: The exposure risk for environmental PAHs can be quantitatively evaluated by using the concept of incremental lifetime cancer risk (ILCR). In spite of some discrepancies over the cause of lung cancer incidences among kitchen workers in South East Asian countries, there has been no study focused on the human exposure risk assessment of PAHs in food production industry in India. The major objective of this study is to conduct the incremental lifetime cancer risk of PAHs in a commercial kitchen in North India. **Methods:** A cross sectional study was conducted among 94 male kitchen workers and their corresponding controls in commercial kitchen in North India. The PAHs concentration in indoor air sample of kitchen was measured using ultra high performance liquid chromatography. The ICLRs was calculated using the standard equation method. Urinary PAHs metabolites were measured using GC-MS/MS.. **Results:** PAHs concentration in indoor air samples of kitchen comprises of NAP (3100 ± 100), FLOUR (810 ± 100), ACEN (17,710 ± 2330), PHEN (210 ± 100), PY (6100 ± 1100), CHRY(200 ± 300), and Ind (3100 ± 2400) in $\mu g\ ml^{-1}$ respectively. The predicted cancer risk levels (ICLRs) based on PAH concentration in kitchen indoor air for different routes of exposure were inhalation 6.8×10^{-5}, ingestion was 3.0×10^{-5}, and via dermal contact was 0.97×10^{-5}. The levels indicates potential risk to high potential health risk criteria as per USEPA. PAH metabolites (Mean/Median) detected in urine samples of kitchen workers were higher as compared to control subject viz.1-NAP (10.69/5.86), 9-HF (1.44/ND), 3-HF (2.60/1.12), 2-HF (3.55/1.58),9-PHN (0.98/0.63), 1-OHP (3.93/2.76) and 1-NAP (4.10/2.15), 9-HF(0.36/ND), 3-HF (0.83/0.98), 2-HF (1.22/1.45), 9-PHN (0.29/ND), 1-OHP (0.38/ND) respectively. **Conclusion:** Detection of PAHs in kitchen indoor air and higher urinary PAH metabolites in kitchen workers are evidence of PAHs exposure. The ICLRs levels based on the exposure of PAHs denotes the risk of carcinogenic effects among kitchen worker. The use of efficient exhaust systems for the removal of indoor air in kitchen is suggested as a preventive measure to reduce the PAHs in the indoor air. The sources of PAHs in kitchen like cooking oil fumes and combustion activities should be reduced to minimise the emission of PAHs.

Effect Of Neurolytic Coeliac Plexus Block In Advanced Unresectable Intraabdominal Malignancies For Pain Relief : A Study Of 15 Cases

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Introduction: The celiac plexus located at the level of T12-L2 (usually L1) contains sympathetic fibers and some parasympathetic fibers and provides sensory innervation and sympathetic outflow to stomach, liver, spleen, pancreas, kidney and GI tract up to splenic flexure. Most common indication of celiac plexus block is treatment of pain caused by pancreatic cancer and from other GI malignancies from LES to splenic flexure, as well as liver, spleen and kidneys. **Methods:** Of the group of patients with intra-abdominal malignancy who were deemed inoperable due to advanced disease or recurrence, 15 patients with intractable abdominal pain were subjected to celiac plexus block. The procedure was done in prone position ,under fluoroscopic guidance. After local infiltration at 1 cm below the inferior ribs and 7 cm from the midline on each side, a 22-gauge, 5-inch-long needle was inserted and advanced to the anterolateral aspect of the superior portion of the first lumbar vertebral body on each side. After confirmation of needle position by fluoroscopic imaging and radiocontrast dye ,ten milliliters of 0.5% bupivacaine was injected ,then, 10 mL of absolute alcohol was injected through each needle. All the patients were followed up prospectively and pain intensity was noted and rated according to numerical rating scale(NRS). **Results:** Of the 15 patients , the mean survival was 5 months and 13 patients had good pain relief throughout and the NRS improved significantly, 1 patient had pain relief lasting for 15 days and 1 patient did not have any significant pain relief. **Conclusion:** Coeliac plexus block can provide significant pain relief in cases of advanced intraabdominal malignancies which also includes those which are not confined to pancreas and thus should be offered as a method of palliation and to improve quality of life.

An Analysis Of Skin Adnexal Tumors In A Tertiary Care Hospital

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Introduction: Cutaneous adnexal tumors are a large diverse group of tumors thatare commonly classified according to their state of adnexal differentiation- eccrine,apocrine, follicular and sebaceous. These tumors are usually missed clinically and often confirmed by histopathology. Although most of them are benign, it isimportant to diagnose them accurately since many of themare genetically predetermined and may represent sites ofpredilection for later development of more aggressive tumors or may be locally aggressive. **Material and methods:** A retrospective study on skin biopsies was conducted in Department of Pathology, PGIMS, Rohtak over a periodof five years. Haematoxylin and eosin stained sections and few cases with special stains like PAS were studied. The adnexal tumors were classifiedand analysed according to the patient's age, gender, site and state of differentiation. **Results:** A total of 108 cases of skin adnexal tumors were analysed. Benign tumors were common and composed of 90% cases. Mean age was 53.5 years with male preponderance (53%). These cases were further classified according to origin of tumor. Maximum cases showed follicular differentiation comprising 43.5% followed by eccrine tumors (39%). Most common site of occurrence was neck and commonest lesion being pilomatricoma. Amongst malignant tumors, five cases of sebaceous carcinoma were analysed. Two rare cases of syringocystadenomapapilliferum were also observed. **Conclusion:** Skin adnexal tumors are differentiated from other cutaneous tumors by their distinct histological morphology. Since these tumors have similar clinical presentation, their clinical diagnosis

become difficult andhistopathological examination is necessary. Tumors of follicular and eccrine differentiation are frequent. Most of adnexal tumors are benign excision provides complete treatment.

Keywords: Adnexal tumors, follicular, eccrine.

Microscopic Focally positive Basal cell carcinoma; a retrospective analysis

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Introduction: Basal cell carcinoma (BCC) is a locally invasive malignant tumor. Incidence is increasing by 10% per year;incidence of metastases is minimal, but local recurrence is common. The complete excision of the BCC allows reduction of relapse. **Materials and Methods**:Retrospective data was collected from hospital data base of the patients who were diagnosed to have BCC and underwent surgery during period of January 2006 to December 2015. The patient and tumor character'son age, primary site of tumor, tumor size, surgery and reconstruction done, pathologic diagnosis, marginal status, adjuvant therapy, recurrence and disease status at last follow-up were noted. **Results**: Total of 73 patients were treated during study period.All patients underwent wide local excision. Three patients underwent orbital exentration, who had tumor around eye and was infiltrating conjunctiva/ cornea. Margins were focally positive in 19 patients. These patients were not submitted for reexcision and were on follow up. Margins were free in 54 patients with average margin of 2.1 mm (range 1 mm – 5 mm). Three patients received adjuvant radiation as one patient had twice recurrence and other two patients had gross positive margin.At a median follow up of 27 months (range, 1 to 71 months),46 patients are on follow up. Five (10.9%) patients had recurrence. Four of five patients had focally positive margin on histopathology at initial surgery, one patient had free margin of 2mm during initial surgery. Reexcision was done in all patients with adjuvant radiation therapy in one patient who presented with twice recurrence. Twenty seven patients were lost to follow up. Of 19 patients, histopathology report showing focally positive margins, four (21 %) patients recurred at a median follow up of 22.6 months (range, 12 – 36 months). **Conclusion:**Basal cell carcinoma is locally invasive malignant tumor with indolent course. Wide excision with adequate margin is the treatment of choice. Even with focally positive microscopic margin, chance of recurrence is around 23% on long term follow up, and should be managed surgically when detected in centers where frozen section is not routinely done.

Dosimetric comparison between 2- Dimensional, 3D-conformal radiation therapy and intensity modulated radiation therapy in the treatment of posterior fossa boost in medulloblastoma

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Aim: To compare 2 Dimensional, 3D conformal radiation therapy and intensity modulated radiation therapy in posterior fossa boost in children with medulloblastoma; dosimetrically evaluating and comparing all three techniques with regard to target coverage and doses to organs at risk. **Methods and Material**: Seven previously irradiated patients of medulloblastoma were retrieved and replanned with 2 Dimensional , 3DCRT and IMRT techniques respectively. Dosimetric comparison was done by performing three plans for the posterior fossa boost for the same patient. Prescription dose , normal-tissue constraints were identical for both plans. Statistical analysis used: SPSS, version 19, statistical software package. For quantitative data, paired '*t*' test was applied to calculate the difference between two means. **Results**: Mean values of $PTV_{95\%}$ and $PTV_{5\%}$ in IMRT were 97.19% and 106.07%, for 3DCRT were 96.57% and 106.33% and for 2D-RT were 96.32% and 105.54% respectively. The dose homogeneity was better in IMRT (1.091) as compared to 3DCRT(1.100) and 2D-RT (1.095) but was not statistically significant (p=0.341 for IMRT versus 3DCRT and p= 0.731 for IMRT versus 2D-RT). Conformity index was comparable in all the plans 2D-RT (0.976) , 3DCRT(0.979) and IMRT(0.976) with p value was insignificant .IMRT plan provided reduced mean dose to cochlea relative to the 2D-RT and 3DCRT plans with p value 0.000 for right cochlea and 0.001 for left coclea (IMRT versus 2D-RT) and p value 0.032 for right cochlea and 0.020 for left cochlea(IMRT versus 3DCRT). IMRT showed no advantage over 2D-RT and 3D-CRT in sparing the anterior cranial structures where mean doses to right and left lens were 0.61Gy and 0.56Gy for IMRT , 0.14Gy and 0.11Gy for 2D-RT and 0.16Gy and 0.09Gy for 3DCRT respectively. **Conclusion**: IMRT technique was able to improve homogeneity index, spare the cochleae, but 3D-CRT plans were superior in sparing anterior cranial structures without compromising the dose to posterior fossa. As majority of children with medulloblastoma survive ,IMRT technique can be applied as posterior fossa boost to spare cochlea in these growing children .

Key words: 2D-RT(2 Dimensional Radiotherapy), 3D conformal radiation therapy (3DCRT) and intensity modulated radiation therapy (IMRT), Posterior fossa.

Impact of integrated services and neoadjuvant chemotherapy in reducing abandonment in Retinoblastoma

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Background: Abandonment in patients with retinoblastoma is the highest amongst all childhood cancers. Availability of comprehensive care under one roof is associated with better compliance. Neo-adjuvant chemotherapy before definitive treatment improves the acceptance for enucleation in our country. **Material and Methods:** Records of all patients of retinoblastoma presenting at Dr Shroff's Charity Eye hospital between January 2010 and July 2015 were reviewed.Pediatric oncology services were introduced at the center in July 2014. Data on demography, treatment given, abandonment and outcomes was collated. The main outcome measureswere effect of integrated treatment at a single-center and impact of neoadjuvant chemotherapy in improving acceptance for enucleation. **Results:** Medical records of 89 patients who presented in this period were analyzed. Of these, 20 patients were lost to follow up after the initial consultation. Of the 69 patients30 were girls and the mean age was 2 years. Bilateral disease was seen in 30% and 65% had group E disease. Over half of the patients abandoned treatment before integrated services were provided at the center. This reduced to 10% after chemotherapy services could be provided on site. Six of the 10 patients(60%) who were advisedprimary enucleation in the initial phase refused surgery and were lost to follow while only 1 of the 22 patients (4.5%) who received neoadjuvant chemotherapy refused surgery. **Conclusion:** The presence of comprehensive care under one roof in patients with retinoblastoma is associated with better compliance to treatment. Giving neoadjuvant chemotherapy is associated with better acceptance for enucleation as a treatment modality.

Re-implantation of SterilisedTumour Bone for Malignant Tumours of Long Bones – 2 years Follow Up of 12 Cases

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Background: Intra-operative Extracorporeal Irradiation (ECI) and re-implantation of the sterilized bone segment is a novel addition to the

armamentarium for Limb Salvage Surgery (LSS). The advantage of an inexpensive, anatomically size matched graft provides opportunity for all eligible patients to undergo LSS, in the Indian setup. The oncological safety has been demonstrated in various studies. This procedure has been used selectively at Regional Cancer centre Trivandrum, in LSS for malignant bone tumors since 2012. We report the oncological and functional outcomes of 12 cases. **Materials and Methods**: Prospective analysis of all patients with malignant tumours of long bones who underwent enbloc resection, extracorporeal irradiation and re-implantation in the Department of Surgical Oncology, Regional Cancer Centre Trivandrum, between January 2012 and January 2014 was included in the study. **Results:** The mean follow up was 24.5 months (13-35 months). The mean age of patients included in our study was 13 years. 83 percent were females. In 58 percent of patients the site of tumor was in tibia , and for rest of the patients the site of tumor was femur. 8 out of 12 patients had osteosarcoma, 3 patients had ewing's sarcoma and 1 patient had an adamantinoma. Average time for union of Metaphyseal osteotomy was 6.2 months (4 to 12 months). Average time for union of Diaphyseal osteotomy was 10.6 months (5 to 15 months). The mean Musculoskeletal Tumour Society Score was 28(26 to 30). 75 percent of cases had no complications and there was 1 case each of fracture, non union and plate extrusion. 83 percent of cases were disease free at last follow up , 1 patient had distant metastasis and no patient had local recurrence. **Conclusion:** Extracorporeal Irradiation is an oncologically safe and convenient technique, with a good functional outcome, for reconstruction in Limb Salvage surgeries for extremity bone sarcomas.

Pediatric Oncology Networked Database (POND) Registry Initiated in Bangladesh

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Introduction: In 2012, the estimated population of Bangladesh was 164 million with 47% under 15 years old. There is no national population-based cancer registry but using worldwide incidence rates of between 80 and 150 cancer diagnoses per 1 million children, the expected incidence rate is 6000-9000/year in Bangladesh. Only about 25% are actually currently being diagnosed. Hospital-based cancer registries are key tools to plan and monitor the quality of care and outcomes of cancer patients. **Objectives:** The aim of this study was to register definitive diagnoses of all new cases of childhood cancer in order to develop a useful and informative cancer registry using the POND database (www.POND4Kids.org), and to monitor disease patterns, treatment refusals, abandonment, and outcomes of all childhood cancers at BSMMU, Dhaka (the largest referral centre) in Bangladesh. **Material and Methods:** This prospective study was performed from January 2012 to September 2015 to reliably estimate childhood cancer incidences. All children newly diagnosed with cancer, aged below 16 years, and admitted into our department were enrolled using the POND4Kids registry (supported by a World Child Cancer Twinning Program). Data was registered by a data manager and supervised by departmental consultants and a medical officer. The registry captured a complete summary including patient demographics, tumor type and site, clinical status, initial investigation profiles, disease status, and treatment refusal or abandonment. At six-monthly intervals, each registered patient underwent a review in the outpatient department by phone to confirm current status. **Results:** About 1796 newly-diagnosed childhood malignancy patient were registered from January 2012 to September 2015. Hematological malignancies comprise 82% of cases (ALL-58%, NHL-10%, AML-9% and others-5%), and solid tumors 18%(neuroblastoma-5%, Wilms tumor-3%, RMS-2%, hepatoblastoma-3% and others-5%).Among the newly-registered patients, 89% started treatment, while 11% refused and/or discontinued treatment after diagnosis, mostly due to financial constraints. Among the children who started treatment, 55% are continuing, 15% discontinued, and 19% of patients died during treatment. **Conclusions:** ALL comprises more than half of the incidence of childhood cancer in our cohort. High treatment refusal, abandonment, and toxic deaths are the major obstacles in treating childhood cancers in Bangladesh. This registry enables us to record not only the outcomes of each patient, but also workload, changes in incidence, and is a useful tool to evaluate whether our attempts to reduce the obstacles to curability are working year on year.

Neuroblastoma: Outcome From A Tertiary Cancer Referral Centre In India.

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Introduction: Solid tumors in children are a major cause of death in the developed and developing countries. neuroblastoma, is one of the most common tumor in children, despite extensive and on-going research and clinical trials and multidisciplinary care, about 50 % of children with neuroblastoma will succumb to the disease. **Objectives:**This retrospective observational study done to evaluate the outcome of children with neuroblastoma (NB) from a tertiary cancer referral centre in India. **Material and Methods:**All children with NB registered from January 2001 to July 2015 were included in the study. INSS was used for staging. All children included in the study received chemotherapy and radiation therapy appropriate for stage. Tumor resection was done when feasible. The final outcome was overall survival and it was categorized as Complete Response (CR), Partial Response (PR); Stable disease (SD) and Progressive Disease (PD); Recurrent disease (RD). Analysis of fifteen-years outcome was done. Multivariate analysis for significance of age, site, N-Myc status and stage was performed. **Results:**Total 40 children in the age range of 0-65years(median 5years) were enrolled. Majority of the children were male 25(62.5%).30(75%) had abdominal primary and 7(17.5%)mediastinal primary at presentation. Stage distribution stage(1+2) 10(27%),stage(3) 6(16%),stage(4) in 20(54%), stage (4s) 1 (2.7%),three of them were esthesioneuroblastoma.10(27%) underwent gross complete resection,3(8.1%) got local RT because of inoperable residual disease. at the time of last follow-up,23(57.5%) were alive,14(35%) were lost to follow.8(21.6%) had CR,16(43.2%) had VGPR+PR,3(8.1) SD,3(8.1%) Progression and 1 patient was not assessed,3(8.1%) died.31(77.5%) received chemotherapy,ccg 3891-29(72.5%),1 RAPIDCOJEC and 1VAC,major toxicity was grade 3/4 neutropenia in 14(45.1%),no treatment related mortality(TRM).5(13.5%) had consolidation HDSCT with Single Agent melphlan/BLUMEL as conditioning, no TRM.2(40%) died post transplant 1 is progressed and 1 died because of dengue fever. **Conclusions:** Outcome of metastatic Neuroblastoma is continued to be dismal. There should be risk adapted therapy to improve survival and reduce long-term side effects.

Key words: Neuroblastoma, Treatment, Outcome

Role Of Pet- Ct In Staging Of Pediatric Round Cell Tumors. Can It Eliminate The Need For Bone Marrow Biopsy?

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Background: Paediatric round cell tumors (RCT) have a variable propensity to invade bone marrow. The current gold standard for detection of bone marrow metastases is bilateral iliac bone marrow biopsy (BMB). BMB is not a completely risk free procedure and although small it carries the risk of hemorrhage. In children it requires use of general anesthesia with its associated morbidity along with the morbidity of post procedure pain. Furthermore, marrow procedures on very young infants are technically difficult & up to 38% of samples may be inadequate for interpretation. In recent years PET CT has emerged as an effective functional imaging for many solid tumors .Therefore this study was planned to see whether

PET scan can substitute BMB. **Materials and methods**: Study design: Prospective observational study. The study included paediatric patients with histologically confirmed diagnoses of Neuroblastoma (NB)or Rhabdomyosarcoma (RMS). All patients underwent a routine staging workup(CT scan and I131MIBG scan for NB , CT scan and 99Tc bone scan for RMS) along with PET-CT using low dose pediatric protocol and bilateral bone marrow biopsy. In cases where there was a disparity between BMB and PET -CT result a targeted MRI was done for confirmation of marrow involvement. **Results:** There were 33 patients of RMS and 30 patients of NB in our study. NPV, sensitivity, specificity and positive predictive value(PPV) of PET CT for detecting bone marrow metastases was 97.9% , 92.3 %, 94% and 80% respectively . PET scan detected significantly more number of metastases than the conventional imaging used for staging work up.Out of 63 patients only one patient had a positive BMB and negative PET CT, while three patients had a marrow uptake on PET-CT butBMB was negative for malignancy(NB-2 and 1-RMS). Of these 3 patientsmarrow metastases was confirmed by MRI in the RMS patient, however the two NB patients were lost to follow up. **Conclusion:** PET-CT can obviate the need for bone marrow biopsy and its associated morbidities.Use of Low dose CT makes its use safe. Thus,it has the potential to be a single stop staging investigation in the work up of RMS and neuroblastoma.

Key words: PET CT, Paediatric Round cell tumor, Bone marrow biopsy

Table: Comparison of PET-CT with bone marrow biopsy

	PET – CT	
BM biopsy	**PET-CT Negative**	**PET-CT Positive**
Uninvolved	47	3
Involved	1	12
	48	15

Outcome of malignant ovarian germ cell tumor in pediatric and adolescent girls.

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Introduction: Germ-cell tumors (GCT) are the most common ovarian neoplasms in the first two decades of life. **Objectives:** To study the outcome of ovarian GCT in children and adolescents. **Material and Methods:** Retrospective chart review of all cases of malignant ovarian GCT in children up-to18 years of age was done from January 2002 to December 2015. The medical records of patients registered during this period were reviewed and the data was analysed with respect to age at diagnosis, clinical presentation, tumor markers, surgical stage, tumor histology, therapy, clinical course, and outcome. **Results:**Out of 31 patients registered at our institute during the study period, 25 underwent treatment and were subsequently reviewed. Mean age at presentation was 11.7 years (range: 3-18 years). The most common presenting feature was abdominal pain in 17(72%) patients. All but one had unilateral disease. Tumor markers were elevated in 23(92%) patients at presentation, elevated AFP in 19(76%), β-HCG in 11(44%) and LDH in 13(52%). The histology revealed mixed germ cell tumor in 11(44%), dysgerminoma in 7(32%) patients followed by yolk sac tumor in 3(12%), embryonal carcinoma and immature teratoma in 2(8%) patients each. Staging work up revealed stage I, II, III and IV in 12(48%), 5(20%), 7(28%) and 1(4%) patients respectively. Twenty (80%) patients underwent surgery prior to chemotherapy out of which 7(28%) patients presented after undergoing surgery at another centre. Fertility preserving surgery was done in 23 (92%) patients. BEP (bleomycin, etoposide, cisplatin) based chemotherapy was given; 4 cycles in 14 (56%), 3 cycles in 6 (24%),2 cycles in 2(8%) patients. There were two events, one abandoned and other relapsed that could not be salvaged with second line therapy. Rest of the 23 patients are alive and diseases free with event free survival of 96% at a median follow up of 26 months. **Conclusions:**This study confirms the excellent outcome of patients with ovarian germ cell tumors. The emphasis on fertility preserving surgery and cisplatin-based chemotherapy is the key to successful oncological and reproductive outcome.

Key words: Ovarian GCT, fertility preserving surgery.

Symptomatic central venous sinus thrombosis associated withL- asparaginasein children with acute lymphoblastic leukemia: A single Institution experience over 17 years

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Background: L-asparaginase is an integral component of acute lymphoblastic leukemia(ALL) treatment with reported incidence of cerebral thrombotic complications varying from 1-3%. Serious consequences associated with its occurrence emphasize the need for high level of awareness among treating physicians. **Material and methods:** This is a retrospective analysis of ALL patients, less than 18 year of age, treated between January 1998and December 2014, who developed symptomaticcentral venous sinus thrombosis(CVST). Clinical, radiological, treatment and outcome details of these patients were retrieved from the hospital e-medical records. **Results**: Symptomatic CVST was observed in 1.6%(8/468) of our ALL patients.Median age of the patients was 8years (range 2-17 years), 6 were male and 4/8(50%) had NCI high riskdisease. All patients received a four drug induction which included E.coliasparaginase in a biweekly schedule at doses of 6000U/m^2. Other co-existing prothrombotic risk factors observed were hyperleucocytosis (1, expired), sepsis (1) andinvasive aspergillosis (1). All events occurred during induction except one during reinduction. Median time to symptoms was 21 days (2-27) from first exposure. The clinical presentation included seizures (4/8), hemiparesis (3/8), slurring of speech/dysarthria (3/8) and headache (2/8).On MRI the most common sites of thrombosis were saggital sinus(3/8) and cortical veins(2/8). All except one patient received low molecular weight(LMW) heparin at a dose of 1mg/kg twice a day. There were two thrombosis attributable deaths. The remaining patients tolerated re-challenge with L-asparaginaseuneventfully during reinduction, undercover of LMW heparin.Complete neurological recovery was observed in all surviving patients. **Conclusion:** Incidence of symptomatic L-asparaginaseassociated CSVT at our centrewas 1.6%which is similar to published literature. High index of suspicion and early imaging(MRV) aid timely diagnosis and appropriate interventionthat are essential to reduce morbidity and mortality associated with this complication.

Our experience with neuroblastoma in infants

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Introduction: Neuroblastoma (NB) is the most common solid extracranial tumourin children. Age at diagnosis is an important prognostic factor due to high chances of spontaneous regression in infants. **Objectives:**To study the infants treated for NB at our institute over a period of 6 years. **Material and Methods:**Descriptive study by retrospective chart review. All children aged 12 months or less, treated for NB from January 2009 to December 2015 were included. The factors analysed were age at diagnosis, stage, site of primary, tumour biology, mode of treatment and outcome. Due to small sample size statistical and survival analysis was not feasible. **Results:**Out of 47pediatric NBpatients (age <18 years) managed during the study period, 13 were infants(27.6%)

and were further studied. Four boys and 9 girls had a mean age 4.4 months at presentation(range 5 days-12 months). The primary sites were adrenal (n=7),para-spinal (n=2), thoracic (n=1), cervical (n=1), retroperitoneal (n=1) and unknownprimary(n=1). The presentation was progressive abdominal distension in 6, compression of vitalorgans (spinal cord, trachea, mediastinum) in 3 andpalpable mass in 2patients. The tumour was detected incidentally in 1 and prenatally in 1 patient. Elevated urinary catecholamines were seen in 9/13 patients. Staging revealed stage IVS (n=6), stage II (n=5), stage IV (n=2) and stage III(n=1).Seven patientsunderwentsurgical excision (6 primary, 1 delayed)due to large tumour size and pressure symptoms. Histopathology was unfavourable in 5/13 patients and none had N –Myc amplification. Chemotherapy was given in 5 patients (3 neoadjuvant, 2 adjuvant) based on Philadelphia scores and staging. Close observation alone was done in 3/6 IVS patients with spontaneous regression. Both neonates progressed rapidly. Another 2 patients sought treatment elsewhere. Remaining 9 patients had a median follow-up of 10 months (range 2-64 months) with no events. **Conclusions:**Infant NB has a favourable outcome. Those presenting at birth were challenging to treat and had poor outcomes (100% mortality) in this small group.

Dengue Fever inPaediatric Oncology: Lessons Learnt

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Background: Dengue fever is an arthropod-borne viral infection, which hasa wide spectrum of clinical presentations ranging from mild febrile illness to catastrophic haemorrhagic fever. Managing dengue fever in an immunocompromised child is often challenging. The clinical presentation, course and risk for mortality is discussed here. **Methods:** We retrospectively analysedthe data of children who developed dengue fever while on treatment for a malignancy. Data of paediatric oncology patients with fever from August to November (the period wheredengue is epidemic in Delhi) from 2009 until 2015 was evaluated. Dengue fever was diagnosed based on either positivity forNS-1 antigen or IgM, or both. **Results:** We evaluated 21 patients. Male:female ratio was13:8. Age ranged from 8months to 17years. Underlying diagnoses included ALL (n=12), AML (n=2), post HSCT (n=2) and solid tumours (n=5). Nine were on intensive phase of treatment (4 had ALL, 1 was post HSCT day+17 for relapsed ALL, 1 had relapsed AML, and 3 had solid tumours). Fever was the presenting complaint in 19/21 patients, followed by vomiting, abdominal distension and unexplained oliguria and unexpected fall in platelet counts. Minimum average platelet count was 6111cells/mm^3 (range, 1000-9000) with a mean time to platelet recovery of 7days (range, 3-13) in children on intensive treatment. Patients not on intensive treatment had significantly higheraverage platelet counts of15,222cells/mm^3 (range, 1000-210,100) and shortermean time to platelet recovery of 3days (P=0.033, P=0.013 respectively). Significant bleeding manifestations andsevere illnesswith plasma leakage were found in 6/9 children on intensive treatment and 1/12 on non-intensive regimen. Twochildren died of denguehaemorrhagicfever (on induction and consolidation chemotherapy, respectively,for ALL)probably due to a delay in diagnosis of dengue fever. Investigations for dengue were sent on day 3 or 4of fever during the epidemic of 2010 while the same was done on day 1 of fever during the epidemic of 2015, contributing to early diagnosis and prompt management of dengue fever and no mortality in 2015. **Conclusion:** A high index of suspicion should be kept for dengue infection in immunocompromised children suffering from malignancy during the annual epidemics. Aggressive support is mandatory especially for those under intensive treatment phase.

Prospective study of neuroblastoma - single institutional experience

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Background: Neuroblastoma is the most common extracranial solid tumor of childhood. Neuroblastic tumors are derived from embryonic neural crest cells of the sympathetic nervous system. Common sites of origin are adrenal medulla, chest, neck and pelvic sympathetic ganglia. These tumors have a predilection for young children; 60% of cases occur before age 2 years. Choice of treatment modality depends on stage, location of tumor, associated risk factors and patient age. The purpose of this study is to study the age and site ofpresentation, histological type and treatment modality involved. **Material and Methods**: 15 neuroblastoma patients treated surgically from January 2010 to January 2016 are included in this study. All cases were assessed clinically and diagnosed by biopsy; MRI or CECT scan were done to assess local extent of tumor.Patients were followed prospectively and the data was collected on a proforma and analysed. **Results**: The mean age of presentation was 4.3years (range 1-8years). The most common site was adrenal gland (66%). The most common histological type was neuroblastoma (86%). 5/15 patients received neoadjuvant chemotherapy followed by surgery, while 10/15 patients were taken up for upfront surgery. 2/15 patients were found to be inoperable during surgery due to extensive locoregionalinfiltration (13%). 1/15 patient developed local recurrence (6%). **Conclusion**: Neuroblastoma is one of the most common tumors in children, with adrenal gland being the most common site of occurrence. The choice of treatment is decided taking the patient and tumor factors into consideration. The goal of surgery is gross total resection of primary tumor without injuring the vital organs.

Keywords: neuroblastoma, children, surgery.

Limb Conservation Surgery For Bone Tumors

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Introduction: Malignant tumors that arise from the skeletal system are rare, representing 1% of all cancer cases.Amputation had been the standard method of treatment for most of bone sarcomas until Kenneth C.Francis and Ralph C.Marcave performed original limb sparing surgery in USA in 1980 **Objectives:** To assess the feasibility, complications and shortterm outcome of limb sparing surgery in bone tumors **Material and Methods:** This is a prospective study of 25 patients with bone tumors treated with limb conservation surgery using endoprosthetic reconstruction at MNJIO&RCC . Patients are followed up for a mean period of 24 months. **Results:** In our study,majority of complication were minor wound infections. Stability and function of the prosthesis is acceptable in 24 patients except in 1 patient who had loosening and extraction of the prosthesis.Till now 4 patients had recurrence, 2 patients had local recurrence and 2 had distant recurrence. **Conclusion:** Limb conservation surgery is an available option in the treatment of malignant bone tumors in our setup. Majority of complications were minor and were comparable to other published data. Longterm followup is.

Ewing's Sarcoma – Metastasis To Mandible: A Case Report

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Background: Ewing's sarcoma is the second commonest bone sarcoma of the childhood. This round cell sarcoma is extremely malignant with high rate of metastasis. Primary Ewing's sarcoma of jaw is a rare tumor. Metastatic sarcoma to mandible is still uncommon with few case reports in the literature. Patients with mandibular metastasis usually present with advanced lesions. The curative treatment is therefore not possible. **Material and Method.** In this report, we present one such case of Ewing's sarcoma of femur that has metastasized to the mandible after completion of initial treatment. The presentation was delayed.Palliative chemotherapy was the treatment given

to him. **Conclusion:** This case can be considered unique because of the atypical presentation being metastasized to mandible after completion of initial treatment.

Limb Salvage Surgery For Bone Tumours

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Back ground: This is a prospective analysis of Limb salvage surgery with Endo-prosthetic reconstruction for bone tumors at MNJ Institute of Oncology & Regional Cancer Centre, Hyderabad. The study aimed at assessing feasibility, complications and long term complications and short term outcome of Limb salvage surgery in bone tumours. **Material and Methods**: Ours' is a prospective analysis of limb salvage surgery in 25 patients with endo-prosthetic reconstruction for bone tumours.7 patients received Custom made prosthesis and 18 patients received Modular prosthesis. The mean period of follow up is 24 months **Results:** 4 patients developed minor wound infection. 3 patients had flap necrosis out of whom 1 patient had extrusion of bush of the prosthesis and had to undergo amputation. 2 local recurrences were found & 2 distal recurrences. 1 local recurrence patient had undergone amputation and 1 local recurrence patient lost to follow up. 2 patients developed distant metastasis, out of whom one succumbed to the disease and the other was lost on follow up. No aseptic loosening or major mechanical problem were noted. **Conclusion :**The average functional outcome scale according to the Revised Musculoskeletal Tumour Society Rating Scale for Lower Extremity is 24.6(86%). Functional outcome of limb conservation surgery in our series is acceptable in terms of stability, flexion and ability to walk without support.

Resection and reconstruction with titanium mesh and PMMC flap in sternal chondrosarcoma, a rare tumor: An experience of two cases with review of literature.

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Background: Chondrosarcoma arising from the sternum is extremely rare and is often untreatable. Removal of the sternum for malignant tumor results in large defects in bone and soft tissue, causing deformity and paradoxical movement of the chest wall and making subsequent repair of the thorax very important. We present two patients withchondrosarcoma of the sternum who underwent case chest wall resection, followed by reconstruction using a titanium mesh covered with a PMMC flap. **Methods:** Both patients had massive musculoskeletal defects reconstructed with titanium mesh and PMMC flap in Kidwai memorial institute of oncology. Titanium mesh was used when the defect in the chest wall was larger than 6 cm or >2 ribs. Before surgery, chest computed tomography(CT) scan and pulmonary function tests were routinely used in all patients. The metastatic work-up was undertaken to eliminate an extrathoracic metastatic lesion. Histopathological diagnosis made by Trucut biopsy in both patients before surgery. **Results:** Both patients were extubated without paradoxical respiration just after surgery. There was no operative mortality. No signs of breakdown, dislodgment, severe depression, or deformity were seen. Neither patient developed mesh infection, pneumonia or atelectasis. Cosmetic and functional outcomes were and there was no obviously unpleasant pain and discomfort during the follow-up. **Conclusions:** Primary malignant tumors of the sternum are very rare, accounting for only nine of 2004 (0.45%) primary bone tumors in the Leeds Bone Tumor Registry. Although chondrosarcoma is the most common malignant bone tumor of the sternum, its frequency was less than 0.2%.Current therapy for chondrosarcoma requires adequate surgical excision.Radiation therapy and chemotherapy have not been shown effective. The goal of surgery is to resect the tumor with a wide margin of normal tissue, ensuring that all tumor cells have been excised and resulting in local disease control. Inadequately tumor resection is associated with a high incidence of recurrence. The exact surgical procedure depends on the location of the tumor, the extent of the disease, and the grade of the lesion. Sternal tumors are difficult to treat because of the anatomic proximity of vital neurovascular structures and the limited surgical margins that can be achieved. The adequacy of surgical resection is of paramount importance in determining clinical outcome.Reconstruction after resection is necessary to prevent respiratory deficits and to protect mediastinal structures. Various reconstruction techniques using prosthetic or homologous material have been described, including synthetic and metallic grafts, pedicled skin and muscle flaps, free skin grafts, fascia lata and autologous bone transplants, with the choice of reconstruction technique dependent on the size and site of the defect, minimizing any deleterious effects. We described a technique for the reconstruction of wide chest wall defects using titanium mesh. Its characteristics were related with light-weight, nice flexibility but excellentstrength (superior strength-to-weight ratio), good biocompatibility as well as magnetic compatibility, and itwas preferred to be used in wider chest wall defects, all of which signified safe and prospect in utilization with goodpatient outcomes.

Key words: Sternal tumor, chondrosarcoma, Wide resection, titanium mesh, PMMC flap.

Bilateral Primary Breast Angiosarcoma with abdominal wall and pulmonary metastases: An unusual clinical presentation of rare tumour – A case report with review

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Introduction: Angiosarcomas (AS) of the breast are rare constituting 1% of breast tumours.Secondary breast ASoccur secondary to irradiation following breast conservation surgery are more common. Primary breast AS are rare, accounting for <0.04% of breast tumours.In this abstract we present a rare clinical manifestation of a primary breast AS. **Case Description:** A 38 years old nulliparous lady presented with an abdominal lump of 8 months duration, bilateral breast lumps of 6 months duration, bleeding from the abdominal and left breast lump for 2 weaks (fig 1,2).She had right breast lumpectomy elsewhere 10 months ago. No history of priorbreast irradiation. Patient had symptoms and signs of severe anemia with hemoglobin of 5 g% due to bleeding. Ultrasound revealed tumors in both the breasts with spiculated margins, posterior acoustic shadowing, microcalcifications and internal vascularity with left axillary metastatic lymph nodes suggestive of malignancy.Contrast enhanced computed tomography (CECT) of the thorax and abdomen demonstrated contrast enhancing bilateral lung and anterior abdominal wall metastases (fig 3 and 4). Fine needle aspiration cytology (FNAC) from the abdominal, and bilateral breast lesions revealed malignant neoplasm with spindle cells in the hemorrhagic background (fig 5). Trucut biopsies of both thebreast tumors revealed a similar morphology of poorly differentiated malignant neoplasm (fig 6). Immuno histochemistry (IHC) study showed CD31 & CD34 positivity; CK, ER, PR, Her2neu were negative with a Ki67 of 60% diagnostic of angiosarcoma (fig 7). **Discussion:** Primary AS occur in the younger age group compared to secondary AS. It is usually intraparenchymal with occasional skin involvement.Only 3 casesof bilateral breast ASreported in the literature.Rarely they may present with bleeding and anemia as in our case.Axillary lymph nodal involvement in breast AS is uncommon. Mammogram and ultrasound do not have pathognomonic features todiagnose AS, especially in the early stages, but for magnetic resonance imaging.Our patient was falsely reassured following lumpectomy with an inadequate work up and biopsy processing due to a deceptive clinical and radiological appearance of the tumour. FNA has been often false negative in AS.A definitive diagnosis can only be obtained with histopathology and IHC studies. CD31 Endothelial marker isthe most sensitive and specific for diagnosis. **Summary:** Clinical presentation of AS is multifaceted and its harmless appearance may cause a delay and neglect by both patients and physicians. Hence, clinicians and surgeons must be aware of this disease

entity for appropriate diagnosis and treatment. CECT thorax and abdomento be considered for staging.

Limb salvage surgery for extremity tumours : Results from a tertiary care centre from south india.

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Background : Limb salvage surgery has been established as a standard care of care for extremitiytumours. However due to the diverse socioeconomic backgrounds that our indian patients come from, tit becomes significant to determine the feasibility and outcome of management of extremity tumours in them. We analysed our outcome of limb salvage surgery at a tertiary cancer centre in south india. **Materials and Methods :** A total of 29 limb salvage surgeries was performed between January 2013 - December 2015 at our centre. Appropriate oncological treatment (neoadjuvant / adjuvant chemotherapy) was delivered depending on the histopathology report. The mean follow up was 9.5 months. The patient demographics ,tumour characteristics, histopathology were studied and analysed. The final functional outcome was analysed using the musculoskeletal scoring system. **Results :** Of the total of 29 patients, 17 were male and 12 were female. IN this study with a short follow up, a better oncological outcome was seen when the postoperative tumour necrosis was > 95% and the patient was of a younger age group. The functional outcome was better in upper limbs than in the lower limbs. **Conclusion :** The oncological and functional outcome of limb salvage surgery in Indian patients were comparable with those in the literature. More prospective trials are required.

Journal of Carcinogenesis

Day-2 ACOS 2016

Combination of a COX-2 inhibitor with BCNU sensitizes glioma cells under normoxia and hypoxia

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Background: Glioblastoma multiforme (GBM) is the most malignant brain tumor characterized by neovascularization and necrosis that indicates high degree of intra-tumor hypoxia. These tumors are difficult to treat, with the median survival of 12-15 months in patients. Hypoxia is critical to chemoresistance in GBMs, which also regulates expression of many genes including COX-2. Carmustine (BCNU), one of the glioma drug, is used after surgical removal of tumor in patients but does not significantly prolong the survival due to chemoresistance. Since COX-2 is over-expressed in subset of GBM, a COX-2 inhibitor in combination with BCNU may prove to be an effective rational chemotherapy. NS-398, a COX-2 inhibitor is known to suppress tumor growth. With the above background in mind, we aimed to study the interaction of combination of BCNU and NS-398 and its effect on cell survival/death pathways under both normoxia and hypoxia. **Materials and methods:** COX-2 expression was checked in glioma cell lines (LN229, U87MG and A172) through Real time PCR and Western blotting. COX-2 expressing cell lines (LN229 and U87MG) were further used for the study. Cell viability was determined by MTT assay for the combination of BCNU and NS-398 and combination index was determined. Caspase assay as well as Propidium Iodide (PI) staining was performed to determine the efficacy of the synergistic combination. Expression of pro-and anti-apoptotic markers as well as EMT markers were checked through Real time PCR. Wound healing assay was done to check the migration. **Results:** Our results showed that glioma cells were resistant to BCNU under hypoxia. However, NS-398 was found to synergistically enhance the cytotoxicity of BCNU under normoxia as well as hypoxia in COX-2 expressing cell lines (U87MG and LN229). Increased apoptosis was indicated by high levels of caspase 3/7 activity as well as increased sub G1 phase cells (PI staining) in the combination. Addition of the caspase inhibitor further confirmed the apoptosis induced by the combination to be caspase dependent. Increased expression of pro-apoptotic (Bax, caspase 3 and cytochrome c) and decreased expression of anti-apoptotic markers (BCl2) indicated inclination of cells to apoptosis in the combination. The remaining cells showed decreased expression of EMT markers and reduced migration after the combination treatment. **Conclusion:** The *in-vitro* study showed that the combination (BCNU and NS-398) has a potential to reduce chemoresistance and metastasis of glioma cells under both normoxic and hypoxic conditions.

Key words: Glioblastoma multiforme, hypoxia, chemoresistance.

Epigenome-Wide Screening for Differential Promoter DNA Methylation in Oral Cancer reveals novel genes

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Introduction: Oral cancer is one of the most common and highly aggressive malignancies. Epigenetic factors such as DNA methylation have been known to be implicated in cancer aetiology. DNA methylation especially that of the promoter region, plays an important role in the expression of a gene. A number of studies on promoter hyper- and Hypo- methylation of oral cancer have focussed on candidate gene approach but whole genome DNA methylation profiling of Oral cancer found in Meghalaya have not been carried out till date. **Objectives:** The main objective of this study is to investigate physiognomies of Promoter DNA methylation patterns associated with oral cancer epigenome and to identify new or novel gene(s) which can be used as useful clinical diagnostic biomarkers. **Material and Methods:** Tumour and adjacent normal Samples were collected from patients in Meghalaya after getting proper consent. DNA was extracted, bisulfite converted and hybridized on the Illumina Infinium 450k Bead chip to check for differential DNA Methylation. Data was analysed using the Illumina Methylation Analyzer (IMA) package. Functional annotation for Gene Ontology (GO) and KEGG (Kyoto Encyclopedia of Genes and Genomes) pathway analysis was conducted using the Database for Annotation, Visualization and Integrated Discovery (DAVID). **Results:** CpG sites test analysis within IMA reveals 27,205 CpG sites representing ~7,336 genes ($p \leq 0.05$) to be differentially methylated (DM) between tumour and matched adjacent-normal tissues. Of these 45.7% are hypermethylated ($\Delta\beta \geq 0.2$) and 54.3% are hypomethylated ($\Delta\beta \leq -0.2$). Region level test over the genic location resulted in the identification of 3,811 Differentially Methylated Regions (DMRs) corresponding to 2,577 genes ($p \leq 0.05$). Promoter region screening reveals 55 genes to be uniformly DM. GO analysis of these 55 genes in DAVID shows enrichment of genes related to cell adhesion in term of biological process and structural molecule activity in term of molecular function. KEGG pathway analysis of individual genes shows involvement in metabolism, signaling pathway, pathways in cancer etc. Literature surveys show that some of these genes (e.g. EPB41L3, a tumour suppressor gene) have not been reported to be implicated in Oral cancer, hence a novel finding. **Conclusions:** The present study shows significant DM CpG sites and regions. The study also reveals a number of novel genes with novel DM status, some of which can serve as candidate methylation biomarkers for diagnostic purposes.

Antioxidant, Anti-Proliferative and Apoptosis Inducing Effect of Cyanobacterial Methanolic Extract: A Comparative Study.

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Introduction: Cyanobacteria are photosynthetic prokaryotes. They can accumulate various primary and secondary metabolites that have biological properties like antioxidant, anticancer, anti-inflammatory and antibiotic properties. We studied methanolic extract of 6 different cyanobacteria: *Nostoc muscorum NCCU-442, Phormidium sp. NCCU-104, Nostoc sphericum NCCU, Microchaete sp. NCCU-324, Calothrix brevissima NCCU-65 and Spirulina subsalsa NFMC*. **Objectives:** Preparation of methanolic extract and determination ofinvitro antioxidant, anti-proliferative,apoptosis inducing activity of extracts and composition of extracts. **Material and Methods:** FRAP activity, DPPH, ABTS and Superoxide dismutase radical scavenging assays were done to measure antioxidant effect. MTT assay was performed to evaluate cell death and viability. DNA Fragmentation Assay was done to study apoptosis. Chemical composition was determined by GC-MS. **Results:** Extracts of all the species possessed antioxidant potential with extract of *Nostoc muscorum*

NCCU-442 being the best for FRAP assay and for scavenging DPPH radical, where as extract of *Calothrix brevissima NCCU-65* was a better scavenger of ABTS and superoxide radical (SOR). *Calothrix brevissima NCCU-65*extract was effective against all the cell lines with IC_{50} values 241.8 µg/ml, 180 µg/ml and 210.5 µg/ml for SiHa, MCF-7 and HepG2 cells respectively. Cell death through apoptosis was confirmed by fragmented DNA pattern. GC-MS chromatogram showed various peaks of probable bioactive constituents. **Conclusions**: Cyanobacteria can be used as a cheaper and easily available source of biologically active compounds to be used by pharmaceutical industry.Methanolicextract of Cyanobacteria were found to be activeas antioxidant, anti-proliferative and apoptosis inducing agent and can be further explored for providing the treatment of cancer.

Characterization and toxicity evaluation of *Nigella sativa* extracts.

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Introduction: Natural products are being used in cancer treatments from the very ancient times. *Nigella sativa* is such an annual herb from ranunculaceae family thathas antifungal, anticancer, antibacterial, antiparasitic and anti-inflammatory properties. *Nigella sativa* seeds are used as carminative in food stuffs. The chemical constituents of *Nigella sativa* play a vital role in cancer prevention. The reason behind cancer development and progression from the very molecular level is yet to be revealed. **Objectives:** Characterization of phytochemical constituent of*Nigella sativa*extracts and its toxicity evaluation on mammalian cell line. **Material and Methods:** *Nigella sativa* seeds were procured from Agricultural University, Mannuthy, Kerala. The seeds were grounded to powder form and packed in Soxhlet apparatus. It is then extracted with Hexane for 72 hrs and successively with Methanol and filtered extracts were dried in rota-vapour. Gas chromatography coupled with mass spectroscopy (GC-MS) analysis was carried out for identification of the pure compounds in different obtained extracts.Normal ovarian cell lines (CHO) were procured from NCCS, Pune, India and cultured in DMEM and 10%FBS.The toxicity profile of the extracts were assessed by MTT (3-(4, 5-dimethylthiazolyl-2)-2, 5-diphenyltetrazolium bromide) assay, a calorimetric approach, on normal ovarian cell lines. **Results:** The hexane extract of *Nigella sativa* showed around 55 compounds upon chemical characterization. The major compounds include 9, 12 octadecadienoic acid, n-hexadecanoic acid, p-cymene and thymoquinone. The methanol extract contained about 50 compounds in which 1,2,3 propanetriol, 9,12 octadecadienoic acid, thymoquinone are the major compounds. **MTT Assay:** Results revealed that none of the Hexane and Methanol extracts of *Nigella sativa* have toxic effects (5-300µg/ml). **Conclusions:** The Hexane and Methanol extracts of *Nigella sativa* have revealed major biologically active compounds in them. Moreover since these extracts have proven to be non toxic, all these can add on to the preliminary steps in the evaluation of anticancer efficacy of *Nigella sativa* extracts.

Key words: *Nigella sativa*, Cancer, MTT Assay

Acknowledgement: Financial support for this work was provided by UGC (University Grant Commission).

Selective Transcription Inhibition of the Human High Mobility Group Box -1 Promoter with Triplex-Forming Oligonucleotides and Anticancer Drugs Targeted to *hmgb1* Positive Regulatory Region in Hepatocellular Carcinoma cell line (HepG2)

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Introduction: HMGB1(high mobility group box-1) , is a chromatin associated architectural protein with extracellular and intracellular roles. Intracellularly it plays important role in transcription, VDJ recombination, chromatin remodeling, DNA repair etc. Extracellular HMGB1 act as a cytokine to mediate inflammatory reaction through a variety of receptors including toll like receptor and receptor for advance glycation end product etc. Overexpression of HMGB1 has been reported in the development and progression of various cancers and suggested as a regulator of the tumorigenesis, metastasis, angiogenesis and associated with all the seven hallmark of cancer . Thus HMGB1 is a promising therapeutic target in the treatment of various human malignancies. **Objectives:** The present study is a comparative *invitro* binding study of Triplex forming oligonucleotide(TFO) to the promoter region of *hmgb1* and its effect on the expression of HMGB1 in HepG2. **Material and Methods:** Two potential triplex forming oligonucleotide target sequences (TTS) were selected from positive regulatory region in *hmgb1* gene promoter using TTS Mapping software. The formation of stable triplex was studied using Spectrophotometric and calorimetric technique including UV melting , Circular Dichroic technique, Fourier transform infra red Spectroscopy, and Isothermal titration calorimetry. **Results:** . Binding of TFOs with the promoter region of *hmgb1* revealed that the binding of TFO is much higher than that of potential anticancer drug. Treatment of HepG2 cell with TFOs significantly downregulated(55-60%) HMGB1 expression at the level of mRNA, protein and inhibited cell proliferation as investigated by RT-PCR, Western blot and Propidium Iodide staining. Interestingly, we found that the combination of TFO and anticancer drug , showed a additive effect on HMGB1 expression(70-78%). **Conclusions:** All these result taken together suggest that TFO based antigene strategy in combination with triplex specific ligand to inhibit HMGB1 expression could be an effective way to treat various cancer in which it is implicated to play central role.

Analyzing the effect of identified HPV-16 variants on immune response for the development of effective vaccine

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Introduction: Cervical cancer is one of the most common gynecological cancers in the world but in India, it is the top most cancer among women. Persistent infection with high-risk human papillomaviruses (HR-HPVs) is the most important risk factor. The sequence variation(s) in the most common HR-HPV i.e. HPV type 16 leads to altered biological functions with possible clinical significance in the different geographical locations. **Objective:** Identification of HPV-16 full length L1 and E6 variation and their impact on immune response for cost effective HPV vaccine development. **Material and Methods:** Altogether, 250 cervical cancer tissue biopsies were collected and processed for DNA extraction, HPV diagnosis and sequenced for variant analysis. The effect of identified major variations on the epitopes was predicted by in-silico methods and validated in-vivo. **Results:** Sixteen major variants (V1-V16) in full length L1 gene and six variants in E6 gene of HPV-16 were identified. For E6, presence of variations H78Y and L83V resulted in creation of four new epitopes for HLA-DQA1*0101/DQB1*0501. For L1, V8 predicted epitope in the reference sequence 151ISTSETTYKNTN had a score of 0.636 (with Thr having score 0.833) and in variant sequence, the predicted epitope ISTSEPTYKNT had a score of 0.630 (with Pro having score 0.796). On in-vivo analysis, L500F (V16) variation showed a significant ~2.7 fold ($p < 0.002$) increase in antibody titer, whereas T379P (V8) showed ~0.4 fold ($p < 0.328$) decrease

after final injection. **Conclusion:** The present study will provide an effective strategy to design effective prophylactic as well as therapeutic vaccine for a particular geographical region against HPV and its variants.

Modulatory role of polymorphism of genes of distinct pathways in Medullary Thyroid Carcinoma Progression.

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Introduction: Medullary Thyroid Carcinoma is an aggressive malignancy of parafollicular C cells of Thyroid. Single Nucleotide Polymorphism (SNPs) ofgenes of distinct pathways such as genes of detoxification(Cyp1A1m1,CYP1A2*F,NAT2,GSTP1) cell cycle regulatory genes (CDKN1A,CDKN1B, CDKN2A,CDKN2B,CDKN2C) &RET (G691S, S836S, S904S, L769L) are known to influence MTC behavior in terms of age of onset & its aggressiveness. The modulatory role of these polymorphisms on MTC behaviour is still unknown in Indian Population. **Objective:**To study the modulatory role of germline polymorphisms in genes of distinct pathways known to be associated with MTC on biology of MTC in terms of age of onset, tumor burden and aggressiveness. **Material& Methods:** We have chosen 13 different SNPs of 3 distinct pathways toinvestigate their role in MTC pathogenesis & screened them in 260 Indian MTC cases (42 hereditary & 218 sporadic) using RFLP/Taqman SNP genotyping approach. Clinico-pathological parameters of MTC such asage at MTC diagnosis, calcitonin levels at diagnosis & nodal/distant metastasis of the disease were collected from patients& correlated with the genotyping data of each SNP. **Results:** An association was found between disease progression & the presence of SNP inNAT2 (rs1041983), CDKN1A (rs1801270) & S904S (rs1800863) genes. Wildtype (WT) rs1041983 NAT2 patients have significantly higher serum calcitonin levels compared to the polymorphic rs1041983 NAT2 (p=0.04)& these patients presented distant metastasis more frequently (47%) than the polymorphic rs1041983 NAT2 (30%, p=0.038). Similarly, patients with polymorphic CDKN1A (rs1801270) have significantly lower calcitonin levels compared to WT CDKN1A (p=0.03) which indirectly reflects less aggressive disease associated with this SNP.Also, patients with polymorphism S904S of RET (rs1800863) presented distant metastasis less frequently than the WT (rs1800863) RET. **Conclusion:**In conclusion, wedemonstrated a protective role of RET S904S (rs1800863), CDKN1A (rs1801270) & NAT2 (rs1041983) SNPs in MTC progression &profiling these polymorphisms may help in characterizing MTC aggressiveness.

Designing therapeutic peptides as an agonists and antagonist against differentialluy expressed receptors in cancer.

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Peptides based therapy is emerging as an important strategy to combat the non-specific effects of anticancer drugs. The anti cancer peptides have high affinity towards the differentially expressed receptors on cancer cells. However, designing the highly specific peptides ligands is still a major obstacle for the development of this therapeutic class. In this study,a computational scheme of the study is proposed to design peptides against overexpressed cancer specific receptors based on the structural properties of their natural ligands. Three target receptor (TR) were selected; CXCR1, DcR3 and OPG belonging to GPCR and TNF family. To create peptides library against these receptors, the binding regions of the natural ligands of the TR were selected as a template for peptide designing. The binding regions were evaluated and validated through prediction servers, literature search, and PDB complexes structures. The binding domain of IL8 (HPKFIKELR) that is natural ligand of CXCR1 was selected as a template to design peptide. Three domains of TL1A (TDSYPEP) (TKEDKTF) (LGLAFTK) were selected for DcR3. Two regions (SIKIPSS) and (PDQDATYP) were used for peptide designing for RANKL, natural ligand of OPG. A library of peptide analog for all the three TR was generated through permutations of the template sequences. Anticancer properties of all the peptides were analyzed using AntiCp. All the peptides were dock against their TPs and analyzed based on their binding efficiencies. The peptide C9 (HPKFELY) shows best binding affinity with CXCR1 and binds with -8.4 binding energy. The peptide D1 (ADSYPFP), D6 (ADSYPQP) and D18 (AFSYPFP) show best binding energy -7.2 among all peptides. The peptide P19 (PDTYPQDP) shows good binding energy -6.9 among all other peptides. To cross check if the selected peptides have affinity to bind to receptors other then TR, homology finding was used to search highly homologues proteins and docking was performed against those proteins as well. The results indicated that peptides of CXCR1 binds with CXCR2 with less affinity but can bind with DARC affinity equal to CXCR1. The peptides of DcR3 were able to bind to TNFRSF25 and TNFRSF21 but with less affinity as compared to DcR3. Using the scheme we were able to design peptides that specifically targeted CXCR1, DcR3 and OPG. However, experimental studies are required for the validation of predicted peptides.

Keywords: Anticancer peptides; CXCR; DcR3, docking; homology modeling.

Horizontal transfer of microRNA 106b can play a role in early stages of acquisition of cisplatin resistance by regulating PTEN, SIRT1 and VDAC1.

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Introduction: The major drawback of chemotherapy is drug resistanceMost of the drug resistance mechanisms involves regulation of certain genes involved in apoptosis, cell cycle check points, DNA repair etc.. Cisplatin is one of the most effective broad spectrum anti-cancer drug. Patients initially have a good initial response to cisplatin based chemotherapy, but later relapse because of the development of cisplatin resistance. Cisplatin resistance results from epigenetic or genetic changes which affects molecular and cellular levels, and these mechanisms have recently been shown to be targeted by miRNAs. The present study was designed to analyse, whether acquisition of cisplatin resistance in cancer cells is mediated by horizontal transfer of micro RNA106b.

Objectives:

- To determine the role of miR106b in cisplatin resistance
- To analyse the expression pattern of some genes involved in drug resistance like SIRT1,PTEN and VDAC1
- To study the relation between the expression levels of miR106b and the genes SIRT1, PTEN and VDAC1
- To validate the role of miR106b in cisplatin resistance.

Material and Methods: Cisplatin resistant A431 cells were generated based on the ic_{50} value of the drug. Then the relative expression levels of some genes involved in drug resistance like SIRT1, PTEN and VDAC1 were analysed by qRT-PCR and 3'UTR analysis of SIRT1, VDAC1 and PTEN were performed using target prediction databases. Further the relative expression level of miR106b was also determined by qRT-PCR. .miR106b was cloned and overexpressed in HEK293 cells, then western blotting and real time PCR was performed to compare the levels of PTEN, SIRT1 and VDAC1 in miRNA overexpressed cells. XTT assay was performed for determining IC_{50} value of cisplatin in mir106b transfected and vector only transfected control cells. **Results:** SIRT1 and VDAC1 was found to be significantly overexpressed, whereas PTEN showed significant downregulation. The 3'UTR analysis revealed that SIRT1, VDAC1 and PTEN mRNA have miR106b response element in it. The expression level of miR106b was

decreased by 50%. From the regression curve analysis, IC50 value of cispatin was found to be higher in miR106b transfected cells when compared with vector only transfected control cells. The expression levels of VDAC1, SIRT1 and PTEN assessed by real time PCR and western analysis under conditions of miR106b overexpression showed similar results. **Conclusions:** The results obtained here suggests that horizontal transfer of micro RNA106b can play a major role in conferring cisplatin resistance to cells during the initial stages itself by regulating the genes like PTEN, SIRT1 and VDAC1 which can unveil a new chemotherapeutic strategy to combat cisplatin resistance.

microRNA-101 downregulation is prerequisite for ERK2 mediated epithelial to mesenchymal transition

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Background: Deregulation of expression of miRNAs has been linked to many pathological conditions including cancer. Global alteration in miRNAs expression has been observed in various tumour samples that have significant effect on disease development, establishment as well as progression. MicroRNA-101 has been found to be downregulated in several cancers like breast, lung, bladder cell carcinoma, prostate, colon, glioblastoma, pancreatic cancer *etc*. Restoration of miR-101, inhibits proliferation of cells either by inducing apoptosis or by senescence induction.Besides these, little is known regarding, mechanism of miR-101 downregulation in cancer and effect of miR-101 on epithelial mesenchymal transition (EMT). In this study, we investigated the regulation and role of miR-101 during EMT. **Material and Methods:** Standard cell lines were transduced with miR-101 expression vector and effect on EMT markers and cytoskeleton was monitored by western, real time PCR and phalloidin staining and wound healing assay was performed to check the effect on migration capacity of cells. Bioinformatic algorithms were used to identify the targets and further, confirmed by dual luciferase assay. Promoter activity was monitored by luciferase reporter assay to check the effect of ERK1/2 signalling on miR-101 expression. **Results:** We find that miR-101 expression decreases significantly with the increasing clinical stage and lymph node infiltration in sporadic breast cancer tumours. Accordingly, aggressive cell lines of breast and lung cancer, had lower expression of miR-101 due to decreased promoter activities of both the copies of miR-101 gene. Subsequent analysis of promoter by both in-silico and in-vitro experiments, revealed the role of ERK2 in downregulation of miR-101 expression. Loss of miR-101, even in EKR2 knockdown cells, promoted mesenchymal characters and increased migration rate in in-vitro scratch assay. Pathway enrichment analysis of miR-101 target genes also revealed the role of miR-101 in negative regulation of epithelial-mesenchymal transition by regulating several key molecules. Mechanistically, miR-101 inhibited the expression of RhoA, Rac1, Zeb1 and Zeb2 by directly binding to their 3'-UTRs, thereby affecting the cytoskeleton organisation and mesenchymal phenotypes. Analysis of sporadic breast cancer samples, disclosed the relevance of ERK2-miR-101 axis in breast cancer progression, since an increased p-ERK2 levels were observed in later stages of breast tumours. **Conclusion:** In brief, our findings delineated an oncogenic pathway that functionally links ERK2 with RhoA, Rac1, Zeb1, and Zeb2 via miR-101. Our finding that EKR2 downregulates miR-101 to increase metastasis opens up opportunities for new therapeutic interventions in cancer.

Keywords: miR-101, ERK2, Breast cancer

In-Vivo Effect of Carcinogen (Polychromatic hydrocarbon) on B-cells towards Antibody synthesis and intracellularCholesterol Homeostasis

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Introduction: Cholesterol, an integral part of the cell membrane, is maintained in the cells either by intracellular synthesis, receptor specific or non-specific endocytosis. Various studies have shown increased LDLR and SREBP2 (transcription factor) expressions as well as delayed saturation of intracellular cholesterol in malignant and proliferating cells. **Objectives:** Citation of immune suppression is common in malignancy. B cells are antibody forming immune cells. Here, we aim to explore the mechanism of action of a carcinogenvizBenzo-alpha-pyrene (mitogenic and immunosuppresive doses) along with classical mitogen and immunogen on B-cell response on its limit of antibody production and cholesterol sufficiency. **Material and Methods:** Intraperitoneal injection of carcinogen(Benzo-alphapyrene), classical mitogen(Pokeweed) and immunogen(Tetanus toxoid) to Swiss Albino mice in groups for their optimally effective dose, B-cell (CD19 & CD79a) counts by flowcytometry, ELISA for IgG estimation, western blot for protein expressions and spectrophotometry for cholesterol estimation were among the parameters studied. **Results:** The ELISA result shows a significant decrease in serum IgG level at the immunosuppressive dose of Benzo-alphapyrene (BaP100), without affecting the number of B lymphocytes against control - an outcome of flow cytometry with CD19/CD79a markers. There is significant decrease in intracellular cholesterol level in the presence of Benzo-alphapyrene. Further we analysed the expression of LDLR, a significant decrease in expressions for LDLR were observed at immunosuppressive dose of benzo-alphapyrene in mice model system. **Conclusions:** Our observation suggests that Benzo-alphapyrene leads to decrease in LDLR expression resulting in insufficient total intracellular cholesterol level. This decrease in LDLR might be a factor for the reduced B-cell response in-vivo, causing immunosupression and generation of tumor elsewhere.

Protective role of *Ocimumbasilicum*var. *purpurascens* against radiation- induced damages in mice

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Background: The present study was undertaken to evaluate the radio protective effect of *Ocimumbasilicum* var. *purpurascens*Benth. methanolic extract having profound antioxidant activity. **Materials and Methods:** Balb/C mice were treated with different doses of *Ocimum* extract (100 and 500 mg/kg body weight, intra-peritoneally) five days prior to irradiation and sacrificed at different time durations. The protective effects of *Ocimum*extract on mortality, haematological parameters, bone marrow cellularity and gastrointestinal system of irradiated mice were studied. The anti-genotoxic action of *Ocimum* extract was studied by measuring micronuclei formation, chromosomal aberrations and DNA damage (comet assay). **Results:** *Ocimum*extract administration significantly increased the life span of irradiated mice and reduced myelosuppression as evident from increases in white blood cell counts, bone marrow cellularity and the number of maturing monocytes when compared to the myelosupression in radiation control animals when injected intraperitoneally (*i.p.*) before whole body 6Gy X-ray irradiation. *Ocimum* extract significantly elevated the radiation-induced reduction in the activities of superoxide dismutase, catalase, glutathione peroxidase and glutathione in both liver and intestinal mucosa. The *Ocimum* extract treated animals showed a profound reduction in genotoxic activity which was apparent in decreases in micronuclei formation and chromosomal aberrations. Irradiation also induced damage to cellular DNA as was obvious from increases in comet parameters like tail DNA%, tail moment, tail length and Olive tail moment in the radiation control group. These parameters were decreased by *Ocimum* extract treatment. The optimum drug dose for protection was 100 mg/kg body weight. An increase in the drug dose did not increase protection. **Conclusion:** Results indicated that the radical

scavenging potential attributed for *Ocimum* extract appears to be one of the mechanisms of radioprotection by the extract.

Keywords: *Ocimumbasilicum*var. *purpurascens*, radioprotection, micronuclei, comet assay

Mitol/MARCH5/RNF153 dependent ubiquitylation negatively regulates the entry of mitochondrial replicative proteins into the mitochondria

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Background: RECQL4 belongs to RecQ family of helicases which participates in mitochondrial DNA replication by acting as an accessory factor to mitochondrial polymerase, PolgA/B2. Loss of both RECQL4 and PolgA/B2 cause decreased mitochondrial DNA replication and incorporation of mutations in mitochondrial DNA. However the molecular mechanism behind the entry of mitochondrial replicative proteins into the mitochondria has not been reported. Mitol, a mitochondrial E3 ligase in the outer mitochondrial membrane is involved in the protein quality control of mitochondria. Hence it was hypothesized that Mitol may play role in the regulation of mitochondrial replicative proteins like RECQL4 and PolgA. **Methods:** To determine the effect of Mitol on RECQL4 and PolgA, overexpression and western analysis were carried out. Enhanced ubiquitylation of RECQL4 and PolgA was observed in presence of Mitol both by *in vivo* and *in vitro* ubiquitylation assays. RECQL4 and PolgA import into the mitochondria was elucidated by in vitro import assay using isolated mitochondria. **Results:** Overexpression of Mitol causes decrease in the level of RECQL4 and PolgA, an effect which was rescued by the inhibition of the proteosmal pathway. RECQL4/PolgAubiquitylationat specific lysine residues by Mitol hampered its interaction with TOM20 receptor protein andtheir decreased its entry into the mitochondria. The complete elimination of RECQL4 from mitochondrial matrix was due to Lon peotease dependent proteolysis via PKA phosphorylation. **Conclusions:** RECQL4 and PolgAubiquitylation by Mitol negatively regulates its entry into the mitochondria. Proteolysis of RECQL4 by mitochondrial LON protease occurs via PKA phosphorylation.

Invitro evaluation of anticancer activity of ethanolic extract of *Bacopa monnieri* L. in colon cancer.

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Background: *Bacopa monnieri*is a rich source of different anti-oxidant constituents like bacoside A & B, brahmin, cucurbitacins. Currently,cucurbitacinshave also been reported for their strong anti-tumorigenic and anti-proliferative activityby inducing cell cycle arrest at the G_2/M phase and formation of multiplied cells. **Methods:** The present study was carried out to evaluate the anticancer activity of *B. monnieri*onHT-29 and Colo 320 cell lines by MTT assay and analysis of marker compound. The ethanolic extract of *B. monnieri*was prepared using soxhlet extraction method and five fractions(hexane, dicholoromethane, methanol,acetone and water) of ethanolic extracts were prepared. *In vitro* cytotoxicassay of ethanolic extract and of all fractions was carried out on HT-29 and Colo 320cell lines.The presence of cucurbitacins in these fractions was confirmed by preparative TLC and HPTLC. **Results**: TheIC_{50} values of ethanolic extract of *B. monnieri*in HT-29 and Colo 320cell lines were 74.0µg/mL and 72.0µg/mL, respectively. TheDCM fraction of*B. monnieri*showedmaximum cytotoxic activity among all fractionupto72 h and the found to be 51.0 µg/mL and53.0µg/mL, respectively. **Conclusion and Significance:** The results showed good cytotoxic activity in DCM fraction in both the cell lines may be due to presence of cucurbitacin in DCM fraction (as it is also reported in the literature) which was confirmed by TLC and HPTLC; this is the evident of marker based anticancer effect of the drug.

Key words: MTT assay, HT-29 and Colo 320

Acknowledgement: CCRUM, Department of AYUSH (Ministry of Health and family welfare)

Changes in glutathione and protein levels, antitumor activity and apoptosis induced by betulinic acid against murine ascites Dalton's lymphoma

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Background: Cancer is one of the most serious health problems to human. It is today the second largest killer in the world, next only to heart ailments. Surgery, chemotherapy and radiotherapy are the three common methods of cancer treatment. In chemotherapy, hundreds of drugs of diverse chemical nature and implying different mechanisms of action have been used against a wide spectrum of cancers. However, the extensive use of these drugs has been limited due to development of various side effects in the hosts. Thus, in an attempt to overcome the side effects of chemotherapy, the development of new drugs, using drugs in combination and the use of number of plant as well as animal-derived natural products have been tried. Natural products derivatives have thus shown great promise to have good antitumor activity with reduced toxicity/side effects in the host. 3b-hydroxy-lup-20(29)-en-28-oic acid (Betulinic acid) is a naturally occurring pentacyclic lupane-type triterpene widely distributed in the plant kingdom. It was originally isolated from the bark of the white birch (*Betula pubescens*), from which it gets its name. Betulinic acid is also found in the bark of ber tree (*Ziziphus mauritiana*), leaves of jamun tree (*Syzygium formosanum*), and leaves of tulsi (*Rosemarinus officinalis*).Antitumor activity of 3b-hydroxy-lup-20(29)-en-28-oic acid (betulinic acid) has not been assessed in murine ascites Dalton's lymphoma. Therefore the present study was undertaken. **Materials and Methods:** Drug: Betulinic acid (≥98% pure) was obtained from Sigma-chemical Co., USA. Animals and tumor maintenance: Inbred Swiss albino mice colony is being maintained under laboratory conditions keeping 5 to 6 animals in a propylene cage for the maintenance of malignant tumor model, i.e., ascites Dalton's lymphoma and also to be used in different experiments. Ascites Dalton's Lymphoma (DL) tumor, a well established murine malignant tumor model used in antitumor studies, is being maintained *in vivo* in 10-12 weeks old mice by serial intra peritoneal (i.p.) transplantation of viable tumor cells to the animals as per the established procedure in the lab. **Antitumor study:** The pattern of tumor growth and host survival etc. was determined in various groups of mice. One group of mice treated with *cis*-diamminedichloroplatinum (II) (cisplatin), a known anticancer drug, was used as positive control. The antitumor efficacy of betulinic acid was expressed in percentage increase in life span (ILS), using the formula – (T/C × 100) –100, where T and C are the mean survival days of treated and control group of mice, respectively.Trypan blue exclusion test: The DL cells were treated *in vivo* with different doses of betulinic acid and the features and viability of the cells were assessed at different time intervals using trypan blue exclusion test. **Light microscopy study:** The ascites DL cells were collected from different treatment groups and were stained with Leishman's stain. The cells in different groups were examined thoroughly and various morphological features were analysed. Apoptosis study: The DL cells at different time interval were studied for the determination of apoptosis using acridine orange-ethidium bromide staining (AO/EB) procedure. **Biochemical study:** In an attempt to understand

antioxidant related changes during betulinic acid-mediated antitumor effect, reduced glutathione estimation was done respectively in the DL cells, liver, kidney and spleen under different treatment conditions. The quantitative changes in protein in different tissues were also determined. **Scanning electron microscopy:** The DL cells collected from the animals under varying experimental conditions were processed for scanning electron microscopy. **Results:** 1. Treatment with betulinic acid was shown to protect mice against transplanted DL and led to tumor regression. Betulinic acid treatment caused about 92% increase in life span of the hosts which may suggest the potent antitumor activity of betulinic acid against ascites Dalton's lymphoma *in vivo* and *in vitro*. 2. Trypan blue exclusion test showed a significant decrease in viability of DL cells under different treatment conditions *in vivo.*3. Light microscopy showed that control DL cells were round in shape while BA treatment showed damaging changes in the membranes. Further DL cells showed the appearance of membrane blebbing and folding.4. After acridine orange and ethidium bromide staining it was observed that control DL cells nuclei were round in shape with uniform green fluorescence indicating viable cells. Green stained cells correspond to viable cells, whereas red stained cells represent apoptotic cells. Cisplatin treatment showed many apoptotic nuclei with membrane blebbing and fragmented nuclei. In betulinic acid treated mice, DL cells illustrate the appearance of membrane blebbing, folding, chromatin condensation, fragmented nuclei, and apoptotic bodies. 5. Protein content was found to decrease in DL cells as compared to control. GSH levels in DL cells were decreased significantly after treatment with betulinic acid.6. The control untreated cells showed numerous microvilli and ruffles distributed evenly over the cell surface. BA treatment showed cell membrane shrinkage, membrane blebbing, folding as observed under a scanning electron microscope. **Conclusion:** Betulinic acid killed DL cells and increased the survivability of DL transplanted mice with no toxic effects. The observations based on SEM, florescence microscopy (AO/EB staining), trypan blue exclusion test, light microscopy are good reliable indicators for confirmation of apoptotic features. Glutathione, an important cellular reluctant, is involved in protection against different free radicals, cellular peroxides, and toxic compounds in cellular systems. In case of cancer cell lines betulinic acid can alter the cellular redox balance and helps these cells towards the oxidative damage. It is clearly understood that betulinic acid maintains the normal cellular redox balance which is very much necessary for cellular metabolic process. Interestingly, mitochondrion-targeted agents such as betulinic acid does not show any side effects in the hosts, thus promising it to be a potent anti tumor agent against different types of cancers and Dalton's lymphoma in particular.

Keywords: Betulinic acid, cispatin, Dalton's lymphoma, apoptosis, antitumor activity

Evaluation of antitumor activity of propolis extract from Meghalaya in mice bearing ascites Dalton's Lymphoma

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Background – Propolis is a beehive product with a very complex chemical composition, widely used in folk medicine. Propolis has been the subject of many studies due to its diverse biological activities such as antibacterial, antiviral, anti-inflammatory, anticarcinogenic and immunomodulatory activities. Propolis is used by bees to block holes and cracks, to repair combs, to strengthen the thin borders of the comb, and for making the entrance of the hive weather tight. It has attracted much attention in recent years as a useful substance having application in medicine and cosmetics. Although antitumor activity of propolis has been extensively reported by several authors, the pharmacological properties of propolis from Meghalaya have not been studied. Thus, the present work was undertaken to evaluate the antitumor activity of methanolic extract of propolis collected from Ngunraw village of South West Khasi Hills district of Meghalaya, India. **Objectives:** To examine and evaluate the antitumor activity of methanolic extract of propolis from Meghalaya, (India) against murine ascites Dalton's Lymphoma bearing mice. **Materials and methods** Chemicals: Trypan blue, acridine orange, ethidium bromide, glutarldehyde, Osmium tetroxide, and other chemicals used in the experiments were of analytical grade and purchased from SRL Pvt. Ltd., Mumbai, India. Double glass distilled water was always used to prepare the solutions and buffers.Collection and extraction of propolis: Raw propolis was collected from Ngunraw village, South West Khasi Hills district of Meghalaya during spring and winter seasons of 2014. It was cleaned, freed from wax and its methanolic extract was prepared following the method of Nagai et al.,(2003) with slight modifications. Briefly thirty grams of raw propolis was taken and dissolves in 300ml of 70% methanol with continuous stirring for 24 hours, followed by filtration (Whitman filter paper) and evaporation. The crude extract obtained was dissolved in phosphate buffer saline (pH 7.4). Stock solutions were used to prepare the requisite dilutions. Preliminary screening for antitumor activity using different doses of methanolic crude extract of propolis (i.e., 10, 20, 50, 75 and 100 mg/kg body weight) in DL-bearing mice was conducted. Animals and Tumor maintenance - Inbred Swiss albino mice (27-30g) were maintained under conventional laboratory conditions at room temperature (20 ± 2°) with free access to standard food pellets and water *ad libitum.* Ascites Daton's lymphoma tumor is being maintained *in vivo* in 10 – 12 weeks old mice by serial intraperitoneal (i.p) transplantations of $1x10^7$ viable tumor cells per animal. Tumor transplanted host usually survived for 19-21 days. The use of animals in the present study is as per the ethical norms and has been cleared by institutional ethical committee of North- Eastern Hill University, Shillong.Antitumor study- Preliminary antitumor activities of propolis extracts were determined. Dalton's lymphoma cells ($1x10^7$ cells in 0.25 ml) were transplanted intraperitoneally (i.p.) into 10 to 12 weeks old Swiss albino mice. The day of tumor transplantation was taken as day "0". Early sign of tumor development was visible after 3 to 4 days of tumor transplantation. Tumor-transplanted animals were divided into six groups with each group consisting of 10 mice. Group I (control) animals received 0.25 ml of the respective extract vehicle, once daily for five days. Group II, III, IV, V and VI were treated (i.p., injection once daily) with 10, 20, 50, 75, and 100 mg/kg body weight/day of the crude methanol extract of propolis respectively from the day five of tumor transplantation for five days. The deaths, if any, of the hosts were recorded daily and the survival patterns of the hosts were determined for the different groups. The antitumor efficacy of propolis, was expressed in percentage increase in life span (ILS), using the formula $(T/C \times 100) - 100$, where T and C are the mean survival days of treated and control group of mice respectively Light microscopical studies - For light microscopical study, tumor-bearing mice were treated with propolis extract for five consecutive days starting from day 6 of tumor transplantation. Animals were sacrificed by cervical dislocation after 24, 48, 72 and 96 h of treatment. The ascites tumor was collected and centrifuged at 1000 rpm for 5 min at 4 °C, washed twice in PBS (0.15 M NaCl, 0.01 M sodium phosphate buffer, pH 7.4) The cell pellet was resuspended in PBS (1:4, v/v) and a drop of the cell suspension was taken on a clean slide and a thin smear was made. The smear was air dried, fixed in absolute methanol for 15 min and stained the following day with Leishman's stain. The cells were then observed and studied under the microscope.Micronucleus assay- Micronuclei were assayed in DL cells from mice in different groups following the method of Schmid (1976). DL cells were collected by centrifugation (1000xg, for 5 min, at 40C) of ascites tumor. The cell pellet was treated with a weak hypotonic solution (0.075M KCl/saline, 1:9, v/v) for 5 min. After centrifugation, cells were fixed in Carnoy's fixative (methanol/glacial acetic acid, 3:1, v/v) and repeated twice. Cells were resuspended in a small volume of fixative solution. A drop of this suspension was put on a slide, air-dried and stained with Giemsa in Sorensen's buffer (pH 6.8). One thousand cells were analyzed under the microscope for the presence of micronuclei. Trypan blue exclusion test: Cell viability of Dalton's lymphoma cells collected under different treatment conditions was checked by trypan blue exclusion test as described by Talwar et al., (1974). To analyze the comparative cytotoxity of propolis in DL cells were collected from mice at different time intervals (24, 48, 72 and 96 h) and washed twice with PBS. Aliquot of the cell suspension was mixed with an equal volume of trypan blue (0.4% in PBS) and incubated for 10 min. Viable (unstained cells) and dead cells (stained cells) were determined with a Neubauerhaemocytometer under light microscope. The percentage of viability was calculated using the formula: % viability = Number of viable

cells after treatment x 100 Number of total cells Apoptosis study: Apoptosis in DL cells from the mice under different treatment conditions was determined using acridine orange and ethidium bromide (AO/EtBr) fluorescence staining method of Baskic et al., (2006).Scanning electron microscopy - Dalton's lymphoma ascites collected from the peritoneal cavity of mice at different time points were centrifuged at 1000xg for 10 min at 4°C. The cells were washed in PBS (pH 7.4) and cell pellets were resuspended in PBS (1:4, w/v) and fixed in 2.5% (v/v) glutaraldehyde at 4°C. Fixed cells were rinsed in phosphate buffer (0.1 M, pH 7.4) and post-fixed with 1% osmium tetroxide. Cells were rinsed with PBS and dehydrated with an ascending grade of acetone (30, 50, 70, 90, and 100 % for 10 min each). The cells were then dried by critical point-drying method substituting dry acetone from the cells by CO_2 in a critical point dryer (CPD-030, BAL-TEC Co.). The dried cells were affixed to an aluminum stub with double-stick tape, coated with gold in a fine coat ionic sputter (SCD-005, BAL-TEC Co.). The cells were thoroughly viewed and photographed under scanning electron microscope (JEOL JSM – 6360). Biochemical changes: - Protein estimation- The protein content in liver and kidney was determined following the method of Lowry et al. (1951) using bovine serum albumin (BSA) as standard. Hematological studies: - SEM study of abnormal RBCs- Blood was collected from the eye orbit using capillary tube. A small drop of blood was taken in a clean micro centrifuged tube and fixed in 2.5% glutaraldehyde for 30 min at room temperature. After fixation, the blood was centrifuged for 5 min at 750xg at 40C. The pellet was washed twice in phosphate buffer and re-suspended in distilled water. A thin film of suspension was made on a clean coverslip and allowed to air dry. The cover slip was mounted on a brass stub with double-stick tape, coated with gold in a fine coat ionic sputter (SCD-005, BAL-TEC Co.). The red blood cells (RBCs) were thoroughly examined for abnormalities in RBCs under electronic microscope (JEOL JSM-6360, SEM) and photographed.Statistical analysis-All value in the present study indicates mean ± standard deviation (S.D), and all determinations were repeated three times The data were statistically analyzed using one-way analysis of variance (ANOVA) with Tukey's multiple comparison post hoc tests to compare the level of significance between control and experimental groups. A P-value < 0.05 was considered as statistically significant in all cases. **Results:** Among the different doses of the methanol crude extracts of propolis studied, the significant increase in the survival time of the hosts (ILS~ 56.41%) was observed at a dose of 50 mg/kg body wt/day. Thus, considering the observed better antitumor efficacy, propolis crude extract at a dose of 50 mg/kg b. wt. was selected for further cytoxicity and microscopical studies. Light microscopical study of control untreated DL cells showed more or less rounded shape. Propolis treatment of mice showed very little changes in DL cells, with plasma membrane damage, chromatin condensation, shedding of membrane vesicles and appearance of cytoplasmic vacuoles. Micronucleus studies of DL cells significantly decreased after propolis extract treatment and show a time - dose dependent manner. The findings from the trypan blue exclusion test and apoptosis study revealed that propolis treatment caused a significant decrease in the viability of DL cells and also induced apoptosis in tumor cells. Propolis treatment caused changes in cellular morphology, including chromatin condensation, membrane blebbing, fragmented nuclei, large size cytoplasm, and membrane vacuoles with complete loss of membrane integrity. SEM of DL cells collected from mice under different treatment conditions was done to further corroborate the results of fluorescence based apoptosis in these cells. Propolis treatment group (50mg/kg body wt.) shows deformities in DL cells which include appearance of membrane blebs and loss in microvilli from the cell surface during 24-48 h of treatment. Severe morphological alterations with complete loss in fine membrane projections, cell shrinkage and membrane folding were observed during 72-96 h which is typical characteristic features of apoptosis. Propolis extract caused a significant increased in protein concentration in liver at 24h and 48h of treatment as compared to control. In kidney, propolis treatment decreases at 48h and then gradually increased at 72-96h of treatment.SEM observation revealed the development of various types of abnormalities in RBCs of tumor-bearing mice. Different morphological abnormal types in RBCs observed include the normocytes (having smooth surface), microcytes (cells having smaller diameter than the normal erythrocytes), macrocytes (having larger diameter), echinocytes (presence of uniformly serrated projections), acanthocytes (spiculated or thorn-like cells), schistocytes (small fragmented spindle-shaped cells), spherocytes (sphere-shaped cell smaller than normal RBC), stomatocytes (elongated cells with presence of slot-like structure at the centre), ovalocytes (having oval-shaped cells) and elliptocytes (having elliptical-shaped cells). Propolis treatment at a dose of 50mg/kg body weight significantly decreased the frequency of abnormalities in the RBC of tumor-bearing mice. Conclusion- The present work describes the evaluation of anticancer efficacy of methanolic extract of propolis against murine ascites Dalton's lymphoma. Analyses of apoptosis indicate the higher frequency of apoptotic DL cells after treatment with methanol extract of propolis. From the results obtained it can be concluded that propolis could be useful as an anticancer chemotherapeutic agents.

Keywords: Propolis, Dalton's lymphoma, cytotoxicity, apoptosis, SEM, Haematological

Establishment of ex-vivo cultures of cancer associated fibroblasts from primary gingivobuccaltumors demonstrate functional heterogeneity

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Introduction: Cancer Associated Fibroblasts (CAFs) are major cell type found in tumor microenvironment. They are activated in nature and identified by expression of α-smooth muscle actin (aSMA). Recent studies have found positive correlation between activated stromal fibroblasts with poor prognosis. However, functional contribution and underlying molecular mechanism for such association is not explored in details. **Objectives:** To understand the molecular and functional role of CAFs in gingivobuccal tumors. **Material and Methods:** Gingivobuccal tumor tissues were obtained from Tata Medical Center, Kolkata after taking informed consent from patients and used for fibroblasts culture Fibroblasts grew from the tumor tissue explants and their activated nature was analyzed by immunofluorescence, immunohistochemistry and qRT-PCR. Collagen contraction ability was evaluated for matrix remodelling ability and R^2 test was performed to check the role of CAFs in invasion and metastasis. **Results:** We have established 13 cultures of CAFs directly from 13 different primary gingivobuccal tumors. CAFs showed expression of CD90 and CD44, validating their mesenchymal nature. Interestingly CAFs showed heterogeneous and higher expression of aSMA compared to normal gingival fibroblast (NOF) indicating their differentially activated behavior within the tumor even under ex-vivo culture conditions. Interestingly, CAFs showed same expression pattern of aSMA in the respective tumor tissue sections. In R^2 test, aSMA expression was very significantly correlated with expression of invasive genes *FSP1, PDGFRb, TGFb, CCL2* and *SDF1*, suggesting CAFs may play important role in tumor progression and metastasis. Further, CAFs with high aSMA expression were able to remodel the matrix much significantly than low-aSMA expressing CAFs. **Conclusions:** We have developed cultures of CAFs which maintained their in vivo behavior and might be involved in tumor invasion and metastasis.

A DNA replication protein is required for the maintenance of centrosome integrity.

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Introduction: A delicate balance of antagonistic forces exerted by motor and non-motor proteins converge on centrosomes and chromosomes during mitosis and are indispensible for maintenance of a bipolar spindle and accurate chromosome segregation. A defect in centrosomes, organelles that define spindles can lead to loss of spindle bipolarity, a hallmark of many cancers. Work over the past many years suggests an interdependency between DNA replication and mitosis. Presence of some replication proteins at centrosomes, kinetochores and midbody make them potential

candidates for regulating centrosome biogenesis and other mitotic events. **Objectives:** The study aimed at deciphering the physiological significance of the localization of a DNA replication protein, to centrosomes and its possible role in maintaining mitotic integrity. **Material and Methods**: RNAi interference experiments followed by immunofluorescence studies are utilized to examine the effects on mitosis using spindle and centrosome specific antibodies. Confocal microscopy and live cell recording assisted in gaining information on the fate of aberrated cells. Flow cytometry, western blotting, reverse transcriptase–PCR and immunoprecipitation techniques were further exploited in various phases of this study. **Results:** We observed the localization of a DNA replication protein to the centrosomes throughout the cell cycle and its absence resulted in mitotic block accompanied by highly disorganized and multipolar spindles with a concomitant augmentation in missegregated chromosomes. CENP-E, a motor protein is responsible for aligning chromosomes to the spindle equator. Cells deficient for this protein exhibited loss of centrosome integrity manifested by centriole splitting and fragmentation in a CENP-E dependent manner. **Conclusion:** Our data suggest that this factor has an as yet unknown function of providing spindle pole resistance to CENP-E-mediated forces exerted during chromosome congression and thus contribute towards centrosome stability.

"Excogitation and Anti-mitogenic response of novel BP-1M against multiple neoplasmic cells lines"

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Introduction: Cancer, a circumstance of an abnormal cell division or mitogencity, is considered as the deadliest among the disease. To maintain the tissue or cell homeostasis, normal cells carefully regulate the production and release of growth promoting factors which are responsible for the cellular proliferation through the cell growth and division cycle. In case of cancer, cells differ from most of the normal cells in a number of biochemical processes, specifically during cell growth, cell division and cell death. Cancer cells, by deregulating cell division and cell death and by up regulating intracellular self signal, achieves the uncontrollable mitogenicity, a primary hall mark of cancer. As a result, targeting mitogenicity or proliferative efficacy of the tumour cell resulting in cell death via cytotoxicity is viewed as an effective strategy for eliminating this disease. **Objectives:** To screen and identify the novel molecule having anti- mitogen activity by arresting the cell cycle process **Material and Methods: :** Anti proliferative studies-MTT, LDH, Trypan blue assay against DLA, A549, EAC,MCF-7 cell lines. Colonogenic assay to study the colony formation,FACS analysis to study the cell cycle arrest at different phases of cell cycle. **Results:** Cell based screening of novel molecule BP-1M was screened against cancer of different origin like Murine lymphoma-DLA, Murine ascites **c**arcinoma-EAC, Epithelial lung carcinoma-A549,Breast adenocarcinoma – MCF7 resulted inIC_{50} value of ~7 µM, ~10 µM, ~10 µM and ~7 µM respectively with profound inhibitory activity irrespective of cancer cell lines with three independent assay system. The cytotoxic effect resulted in inhibition of colony formation capacity in DLA and MCF-7 cells with 62.6% at 5 µM, 87.4% at 10 µM and 67.4% at 5 µM, 90.3% at 10 µM respectively in a concentration dependent manner. The cell cycle events analysis showed that compound BP-1M increased the cell cycle arrest on G2/M phase significantly indicating the antimitogenicity action of the molecule. **Conclusions:** The novel molecule BP-1M showed long term anti-proliferative effect on DLA and MCF7 cell line to form colony in a concentration dependent manner and also inhibited mitogenicity activity against cancer of different origin which could be further investigated for drug development.

Role of Vimentin in regulation of NEDD9 mediated invasive and metastasis signalling in Squamous Cell Carcinoma.

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Introduction: Invasive behavior of the tumor is due to the over expression of the scaffolding protein NEDD9 which helps in the formation of invadopodia that makes the metastatic movement by EMT signals triggered from the intermediate filamentous protein vimentin secreted during the invasion in the tumor cells. The interaction between these two proteins is expressed during the cell invasion makes the stabilization in the metastatic pathway through the expression of the downstream genes such as MMP2 and MMP9, growth factors like VEGF, FGF, IGF and PDGF etc., helps in the angiogenesis and the invasion of cancer. **Objective:** To understand the role of NEDD9-Vimentin interaction in cancer cell invasion and metastasis. **Materials and Methodology:** Identification the NEDD9 interacting proteins in Squamous Cell Carcinoma (SCC) by Co-ImmunoPrecipitation (Co-IP) and binding partners by Liquid chromatography mass spectrometry analysis (LC-MS;MS) & sequential alignment. Validation of interacting partner by Co-IP, Immunoblotting (IB) and Proximity Ligation assay. Regulation of NEDD9 complex by inhibitory studies using Withaferin A (WFA) *in-vitro*. Downstream complex alteration by ted by Zymography and IB. Pathophysiological consequences by scratch and Transwell invasion assays. **Results:** To identify NEDD9 interacting proteins/effectors large scale NEDD9 by IP studies followed by LC-MS; MS sequencing NEDD9 binding partners. Based on this approach one such protein identified is intermediate filament protein Vimentin as NEDD9 interacting protein. The specificity of this interaction was confirmed by direct Co-IP and IB analysis in addition to the use of proximity ligation assay of endogenous protein in intact SCC cells. We tested effect of treating cells withaferin A, a natural compound reported to exhibit anti-tumor and antiangiogenic properties due to induction of vimentin intermediate filamentous depolymerisation. Withaferin A treatment of cells resulted in dose dependent cleavage of NEDD9 and apoptosis without apparent effect on vimentin in these cancer cell lines is very interesting which we observed. Interaction between these two proteins necessary for invasion and metastasis. Degradation of the NEDD9 is eventually, leading to attenuation of downstream genes such as MMP-2 and –9 secretions from the cells are assessed by Zymography as well as IB assays and inferring the importance of NEDD9-Vimentin complex in invasion and metastasis. **Conclusion:** Vimentin regulates NEDD9 nexus and thereby invasive and metastatic nature of cancer creating a new target for metastatic inhibition.

Benzophenone-1B, a sharp edged sword, restricts the neoplasm of multiple origins by restraining the nuclear translocation and transcriptional activation of HIF-1α.

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Introduction: Stabilisation and subsequent nuclear localisation of HIF-1α subunits results in the activation of tumour promoting target genes such as VEGF, MMPs, Flt-1, ang-1 etc which plays a pivotal role in adaptation of tumour cells to hypoxia by activatingseveral biological processes including angiogenesis. Increased HIF-α and its nuclear translocation have been correlated with increased angiogenesis, aggressive tumour growth and poor patient prognosis leading to current interest in HIF-1α as an anticancer drug target.**Objectives:**To develop the anti- angiogenic cytotoxic molecule benzophenone-1B (BP-1B)to regress tumour growth by blocking nuclear translocation of HIF-1α. **Materials and Methods:** Screening of BP-1B

for antiproliferative effect by MTT, trypan blue, LDH leak and clonogenic assays were performed against various cancer cell lines of different origin to determine IC_{50} values. Anigoinhibitory effect of BP-1B was assessed using reliable angiogenic models such as CAM, corneal micropocket, aortic ring assays, xenograft , measurement of CD31 by IHC. Elucidating molecular signalling events by phosphorylation studies, cell fractionation studies for nuclear/cytoplasmic localization by IB, IF. Measurement of downstream activation of genes by ELISA, RT-PCR, IB and gelatin zymography. In-vivo effect was measured in solid tumour and physiological consequence at gene specific level. In-silico studies for drug and target interaction. **Results:** Antiangiogenic molecule BP-1B exhibits the minimalIC_{50}value of ~10μM in cell based screening through angiogenesis inhibitory modulation. IHC examination of CD31 proved BP-1B efficiency on antiangiogenesis in tumour induced model. Molecular signalling events study revealed the inhibition of HIF-1α phosphorylation at thr796 by p42/p44 as assessed by IB and insilico approach. This resulted in inhibition of nuclear translocation of HIF-1α, eventually leading to HIF-1 dependent transcriptional activation of VEGF-A, Flt-1, MMP-2 & -9, ang-1 was abrogated. These effects resulted in retarded cell migration and invasion. The in-vitro results were able to reproduce in *in-vivo* solid tumour models. **Conclusions:** The mechanistic validation of tumour inhibitory potential of cytotoxic molecule BP-1B resulted in altered gene expression which is due to decreased nuclear accumulation of HIF-1α. Hence, BP-1B is a target specific drug for cancer therapeutics.

Keywords: Tumour angiogenesis, HIF-1α, BP-1B and anti-angiogenesis

Mapping the research trends of glioma gene therapy from 2005 to 2014 based on co-word analysis

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Background: Glioma is the most common tumour of central nervous system which still has poor therapeutic effect and high relapse rate under the standard therapeutic schedule. Co-word analysis is a content analysis technique that is effective in mapping the strength of association between keywords.This study used co-word analysis and social network analysis to give an overview and present the thematic evolution in glioma gene therapy. **Material and Methods:** PubMed, Medline, Embase, Web of Science and the Cochrane Library wereretrieved on glioma gene therapy from 2005 to 2014. The keyword plus by ISI were used when the articlehad no author-provided keywords. Multiple words with the same meaning were merged into one relevant word. Keywords occurring in different forms, plural and singular forms, uppercase and lowercase words were standardized manually. We usedMicrosoft office Excel 2013 for data entry and organization, and setting up pivot table to count the co-occurrence frequency of keywords. The formula which demarcated high frequency from low frequency keywords was used in this study, in which "I" standed for the numbers of those keywords just occurring once in all.The co-words matrixes were put into the Ucinet6.0 software for social network analysis, and the keywords networks were displayed in two dimensional maps by the network visualization software NetDraw2.084.

GSTM1 polymorphism along with pattern of expression of EMT markers in oral cancers

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Summary: Oral cavity cancer (or oral cancer) and pharyngeal cancer include cancer of the lip, oral cavity, and pharynx (nasopharynx, oropharynx, and laryngopharynx). Ninety percent of all cases of oral cavity and pharyngeal cancer are classified as squamous-cell carcinoma. The malignant transformation of many carcinomas isassociated with loss of epithelial differentiation and gain of a mesenchymal phenotype, a process known as epithelial-mesenchymal transition(EMT) which for oral squamous cell carcinomas (OSCC) could be a predictor and a prognostic factor. The aim of our study was to investigateimmunohistochemically the N-cadherin and vimentin expression as markers of EMT process in OSCC.Thus,we analyzed 31 cases of OSCC by immunohistochemistry using the following antibodies:Vimentin and N-cadherin. When compared with the habits and antibodies, the patients with no habits were found high (35.5%) and when compared with the vimentin expression correlated with the size of the tumor. In stage 4 vimentin showed higher expression. There was no correlation found in N cadherin. GLUT1 showed an inverse correlation with vimentin. GSTM1 polymorphism was found that wild type showed 58.1% and null genotype showed 41.9%). In conclusion, the vimentin expression increases as the size of tumor increases and EMT is aggressive. From this study,we observed that, vimentin correlated with size of the tumor. Therefore the tumor is found to be aggressive because of epithelial mesenchymal transition. N cadherin does not have any correlation with the tumor size, stage, habits and GLUT expression. GLUT 1 showed an inverse correlation with vimentin. As vimentin is over expressed GLUT 1 is reduced. Patients with GSTM 1 null genotype are lacking in detoxification of carcinogens in cancer patients.

Keywords: Oral cancer, EMT, vimentin, N cadherin, GLUT 1, GSTM1 polymorphism

Differential proteomics identifies complement factor H proteolytic species as possible early breast cancer biomarkers

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Introduction: Breast cancer is one of the most common cancers among women in the world and in Taiwan. Like other cancers, detection of early breast cancer is statistically associated with limited disease, better prognosis and lower mortality. However, there are still no suitable plasma biomarkers for early detection for breast cancer. A process that most proteins undergo some form of chemical modifications during or after translation is known as posttranslational modifications (PTMs). Plasma proteins with differentially structural changes associated with disease, such as proteolytic processing, have potential to become new biomarkers for breast cancer. We have established a new analytical scheme to mine such biomarkers in blood for breast cancer. **Objectives:** Our goal is to verify proteolytic species in human blood plasma that can be biomarkers for detection of early breast cancers. **Material and Methods:** We first collected plasma samples from 6 patients before and after surgical treatment. These pairs of samples were then subjected to a modified two-dimensional differential gel electrophoresis (modified 2-D DIGE), comprising fluorescent dye labelling, macroporous reverse phase (mRP) HPLC and reducing/non-reducing SDS-PAGE. The difference protein species were analyzed with LC-MS/MS. Cleavage site-specific antibodies have been produced to perform a large-scale examination of total 379 plasma samples. These samples include 75, 74, 46, 48, and 48 patients at stage 0 ~ 4, respectively. Also, there are 29 samples from normal individuals and 59 from other cancers/diseases to serve as control. **Results:** A group of proteolytic species in some breast cancer patients were found by modified 2-D DIGE. Notably, these species disappeared from the plasma after the diseased tissue was surgically removed. A pair of complement factor H (CFH) derivatives were identified using LC-MS/MS analyses. Through a series of examination, we conclude that proteolytic removal of Arg-341 is

likely the molecular mechanism that leads to these findings. According to these data, we have generated antibodies that can specifically recognize these proteolytic products. We used antibodies to tested over 350 clinical samples and found these biomarkers can be specifically detected in plasma of breast cancer patients. It is quite encouraging that positive detection is shown in 26 patients (15~20%) with stage 0 and 1 diseases. Other 20 patients (21~22%) with stage 2 and 3 were found positive. 13 patients (27%) with metastatic tumor have also been detected. The breast cancer proteolytic marker is also confirmed by IHC in situ at tissue sections of DCIS and Stage I cancer .Surprisingly, the signal did not observe in normal individuals or patients with other diseases, strongly suggesting that these biomarkers are highly specific to breast cancer.

Effect of BMP pathway inhibitor in TNBC cell proliferation

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Triple Negative Breast Cancer (TNBC)is clinically heterogeneous & aggressive form of breast cancer with limited treatment options & lacks proven targeted therapy. Limited understanding of molecular pathways involved in TNBC poses challenges in treatment of TNBC. The conventional treatment modality for TNBC involves systemic chemotherapy; however acquired resistance and relapse is of great concern. Increasing evidence has shown that cancer stem cells (CSC) are mainly involved in development of resistance &tumor re-initiation & metastasis,in which BMP signaling pathway plays a crucial role. This pathway regulates various cellular processes including maintenance of cancer stem cells. In the present study we investigated the involvement of BMP pathway inhibitor LDN193189in the proliferation of TNBCcells using MDA-MB231cell lineby cell cytotoxicity, multi-caspase activation,clonogenicity&cell migration assays.LDN193189 exhibited significant cytotoxicity on MDA-MB231 cells with an IC50 value of 1.49uM. Higher concentrations of LDN193189 promoted caspase activation there by implying its role in inductionof apoptosis. Cells exposed tothis inhibitor for longerduration displayed reduced colony formation as indicated by the results of clonogenic assay. These results throw an insight into the possibility of developing LDN193189 as an effective targeted molecule for the treatment of TNBC.

mRNA Expression of Interleukin-1βassociation with clinicopathological feature in breast cancer patients

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Introduction: Breast cancer is one of the most common cancers among women world wide. Interleukin-1β(IL-1β) is a multifunctional pro-inflammatory cytokine which plays an important role in variety of cellular activities, including cell proliferation, differentiation, and apoptosis. The breast cancer characteristics such as tumor size, grade, lymph node and hormonal receptor status involvement are known to be the most important prognostic factors in breast cancer. The study was performed to understand the progression of breast cancer and identification of additional biomarker analysis. **Objectives:** This study, we have evaluated the mRNA expression of IL-1β genein breast cancer patients. **Material and Methods:** Tissue specimens were collected from 93 patients of breast cancer who underwent surgery at theDepartment of Surgical Oncology,King George Medical University, Lucknow (India). Informed, writtenconsent was taken from all patients included in this study. The ethical approval was taken from the instructional ethics committee before the commencement of this study. The mRNA expressions of IL-1β were evaluated by using quantitative real time PCR. **Result:** In this study, we have analyzed the association ofIL-1β with some known prognostic factors of breast cancer including patients age, menopause, tobacco, diet, tumor size, node status, ER, PR and her2/neu. However, our result indicated that mRNA expressions of IL-1β over expressed 7 fold in tumor tissue as compared to adjacent normal tissue. The high expression of IL-1β showed significant ($p<0.05$ or $p<0.01$ or $p<0.001$) association with increased tumor size, presence of lymph node metastasis, stage, hormonal status (ER, PR) and Her2/neu receptor positivity, but not correlated to age, menopause, tobacco and diet. **Conclusion:** In conclusion, our study demonstrated thathighmRNA expression level of IL-1β in breast cancer patients with tumor size, presence of lymph node metastasis, stage, hormonal status (ER, PR) and Her2/neu receptor positivity,may severe prognostic role in breast cancer.The findings of this study may be helpful in the management of breast cancer.

Keyword: mRNA expression,IL-1β, Breast cancer.

Association of cytokine profile (IL-2, IL-4, IL-6, IL-10, IL-17a, TNF-α, IFN-γ) with different established prognostic markers in breast cancer patients

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Background: Comprehensive overview of breast cancer development and progression suggests that the process is influenced by intrinsic properties of the tumor cells, as well as by micro environmental factors. If a significant relationship could be established between such markers and prognosis of breast cancer, it would aid in classifying the patients based on prognosis of the disease. **Objectives:** The purpose of this study was to trace correlation between level of cytokine markers and established prognostic markers of breast cancer. The study had the following objectives:

Methods:

1. Profiling a panel of serum cytokine (IL-2, IL-4, IL-6, IL-10, IL-17a, TNF-α, IFN-γ)
2. Profiling of genetic risk marker, BRCA1
3. Analyzing association of cytokine levels with established prognostic and genetic risk markers (ER/PR/Her-2 neu/BRCA1).

Results: The mean age of breast cancer patients in our study was 44.7. On applying unpaired t-test, difference in serum levels of IL-6, IL-10, TNF-α and IL-17a between case and control groups was statistically significant ($p<0.05$). In our study tissue incidence of estrogen receptor positivity in breast cancer patients was 40%, of progesterone receptor positivity was 45% and for Her-2/neu positive status was 87.5%. BRCA1 mutation was seen in 10% of the cases included in this study. Data for IL-6, IL-10 and TNF-α is statistically significant for all the four established prognostic markers, however correlation for BRCA1 is in opposite direction (negative correlation) to that of other three markers. We could not find any explanation for this inverse relationship between BRCA1 mutation and ER/PR/Her-2neu. **Conclusions:** Thus to summarize, trend for IL-6, IL-10 and TNF-α is statistically significant for all the four established prognostic markers, however correlation for BRCA1 is in opposite direction (negative correlation) to that of other three markers.

Wnt Signalling as a target for treating Familial Adenomatous Polyposis (FAP)

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Stem cells are the totipotent cells of the body, which when differentiates can lead to formation of whole body tissues. When these stem cells undergo alteration or mutation in their signalling pathways, it leads to the formation of cancer stem cells. These cancer stem cells (CSCs) have been defined as

cells within tumour that possess the capacity to self-renew and to cause the heterogeneous lineages of cancer cells that comprise the tumour. They have been identified in blood, breast, brain, colon, melanoma, pancreatic, prostate, ovarian, lung cancers and so on. It is often considered to be associated with chemo-resistance and radio-resistance that lead to the failure of traditional therapies. Wnt pathway is one of the cell signalling pathways that are involved in differentiation and proliferation of CSC. It comprises of 19 highly conserved glycoproteins that serve as ligands for the Frizzled (Fz) trans-membrane receptor. Wnt signalling regulates fundamental aspects of development, including cell fate specification, proliferation, morphology, motility, and survival during embryonic development. Also, regulating somatic stem cells and their niches throughout adult life. Wnt-signalling cascade comprises of three major pathways: the canonical Wnt pathway, which involves activation of β-catenin T-cell specific transcription factor (TCF) lymphoid enhancer-binding factor (LEF) transactivation complex and is implicated in tumorigenesis; the non-canonical planar-cell polarity pathway, which regulates the cytoskeleton; and the non-canonical Wnt–calcium pathway, which regulates intracellular calcium levels. Of these pathways, canonical Wnt signalling is the best understood and its inhibition has been the focus of intensive research in cancer and other diseases. Indeed, along with the Notch and HH pathways, suppression of Wnt signalling has led to the development of agents that hold promise to interfere with carcinogenesis, tumour invasiveness and metastasis. The canonical pathway leads to the accumulation of β-catenin in the nucleus and subsequent transcriptional activation of targeted genes, but this does not occur in the non-canonical pathway. Aberrant regulation of the Wnt pathway leads to neoplastic proliferation in these same tissues specifically, cutaneous CSCs require β-catenin signalling to maintain their tumorigenic phenotype. Also, mutation of APC protein coding gene have been found to cause Familial adenomatous polyposis (FAP), which is known to be the main cause of colorectal carcinogenesis. It has been suggested that Wnt signalling is also involved in the regulation of cancer stem cells (CSC), because there are many similarities in the signalling pathways that regulate normal adult stem cells and CSC. In this perspective, work has been focused on the Wnt/β-catenin signalling pathway, which is the most intensively studied and best characterized Wnt signalling pathway. This review provides with an overview on the function of the Wnt/β-catenin signalling pathway in CSC, and the possibility of the development of novel therapeutics to target this pathway.

Key words: Cancer stem cell (CSC), Familial adenomatous polyposis (FAP), Wnt.

Prognostic relevance of *SAMSN1* expression in gastric cancer

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Introduction: The prognosis for patients with advanced gastric cancer (GC) remains dismal. The identification of biomarkers relevant to the recurrence and metastasis of GC is advantageous for stratifying patients and proposing novel molecular targets. **Objectives:**To evaluate the clinical implications of SAMSN1 expression in GC. **Material and Methods:**The expression and methylation status of SAM Domain, SH3 Domain And Nuclear Localization Signals 1 (*SAMSN1*), a mediator of B-cell function, were investigated in 12 GC cell lines. Immunohistochemical staining was performed to determine the pattern of SAMSN1 protein expression in gastric tissues. The prognostic impact of *SAMSN1* expression was determined by analyzing 175 pairs of surgically resected gastric tissues. **Results:** A significant decrease in the level of *SAMSN1* mRNA was detected in six of 12 GC cell lines without promoter methylation. The mean expression level of *SAMSN1* mRNA was lower in GC tissues when compared with normal adjacent tissues, an observation that was independent of tumor differentiation. The pattern of SAMSN1 protein expression significantly correlated with that of *SAMSN1* mRNA.Low *SAMSN1* mRNA expression was significantly associated with tumor size (>60 mm) and shorteroverall survival. Multivariate analysis identified low *SAMSN1* mRNA expression as an independent prognostic factor for poor overall survival (hazard ratio 1.80, 95% confidence interval 1.08–3.03, $P = 0.023$).In patients with stage II/III GC who underwent curative surgery, low *SAMSN1* expression was associated with shorter disease free survival. **Conclusions:**Our results indicate that downregulation of *SAMSN1* transcription may affect the progression and recurrence of GC and represents a novel biomarker of GC.

Genome-wide DNA methylation analysis in stomach cancer using the Infinium HumanMethylation 450K BeadChip

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Introduction: Stomach Canceris the fifth most common cancer worldwide. In India, Mizoramhas the highest incidence of stomach cancer as per the cancer atlas of India. There is limited number of studies on Genome wide methylation changes in stomach cancer, but for the same, no information is available in relation to Mizoram. **Objectives:** The focus of this study is to understand the differential methylation patterns of the sites and their association to promoters and CpG islands. **Material and Methods:** Genome-wide DNA methylation profiling was performed on 24 samples which included 12 stomach cancer and 12 adjacent normal stomach tissues from an indigenous population of Mizoram. To query the differential methylation status between cancer and adjacent normal tissues, the Illumina Infinium HumanMethylation450 BeadChip microarray was used. DNA methylation was assessed in about 485,000 CpG sites. The raw data obtained from GenomeStudio was processed using the IMA (Illumina Methylation Analyzer) an R package specifically designed to analyse site-level and region-level methylation changes using the 450K DNA methylation microarray. The data was quantile normalized. The β values were calculated to reflect the methylation status at each site and methylation difference for each site was calculated as a beta-value difference (Δβ). Functional analysis of the differentially methylated genes was performed using the Database for Annotation, Visualization and Integrated Discovery (DAVID). **Results:** The query returned 2883 sites (~1149 genes) as differentially methylated ($p<0.05$). 2391 sites were hypermethylated ($\Delta\beta \geq 0.2$) and corresponded to 922 genes, 492 hypomethylated ($\Delta\beta \leq -0.2$) sites corresponding to 266 genes.Of these, 186 genes were associated with the promoter, 706 genes were located in CpG islands and 143 were associated both with the promoters and CpG islands. DAVID analysis on the hyper- and hypo- methylated genes showed significant enrichment for GOterms like DNA Binding, Transcription, Regulation of transcription, pathways in cancer, cell cycle etc. Literature survey shows that some of the reported genes are new and novel in term of methylation implication in stomach cancer. **Conclusions:** Considerable DNA methylation changes were observed in stomach cancer at a genome-wide level. Understanding the epigenetic changes in Stomach cancer will help better explain pathogenesis of stomach cancer and may even subsequently help to identify molecular markers for stomach cancer diagnosis and treatment.

Identification of secretory miRNAs to function as potentialearly detection biomarker for Pancreatic Ductal Adenocarcinoma (PDAC)

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Chronic pancreatitis (CP) is a progressive inflammation of pancreas characterised by fibrosis of pancreatic tissue, which eventually affects the proper functioning of the organ. We are specifically focussing on a class of CP i.e Tropical Calcific Pancreatitis (TCP). Chronic pancreatitis is one of the major risk factor for Pancreatic Ductal adenocarcinoma (PDAC). It is one of the most aggressivecancers with survival rate of only 4-5%. The reason for such low survival rate is due to delayed diagnosis as the initial symptoms of the disease are not distinct from any other gastrointestinal disorder. The detection techniques like MRI and EUS are there but they are quite sophisticated which require trained manpower and high maintenance cost. Other than that there are presently available serum biomarkers like CA 19-9 for detection but they are not very sensitive and specific. So there is an urgent need to develop a non-invasive serum based biomarker for the early diagnosis of Pancreatic Cancer. **Objective:**To analyze differential gene expression changes in pancreatic tissue from TCP patients and tumour tissue from PDAC patients and to use that information in identifying deregulated secretory proteins capable of functioning as potential biomarkers in serum of these individuals. These biomarkers will help in early detection of PDAC in TCP patients. **Study Design:** Pancreatic tissue and whole blood is being collected from TCP and PDAC patients. Comparison of the total plasma miRNA expression pattern is being done using miRNA microarray. Similarly, we also plan to compare the plasma miRNA profile to that isolated from the pancreatic tissue and correlate with the gene expression pattern obtained from gene expression microarray. Results will be validated in another set of samples. **Result:** We did a preliminary screening using miRNA microarray from plasma of normal individuals, TCP and PDAC patients (Two samples each). We have found 24 miRNAs to be uniquely deregulated among these groups. Interestingly, 11 of these miRNAs show a progressive upregulation and one miRNA shows progressive downregulation as the disease progresses from TCP to PDAC which make them good candidates for biomarkers to be tested further.

Jagged-1 mediated Notch-3 signalling alterations in the progession of HPV associated precancer, Invasive squamous cell and Adenocarcinoma of uterine cervix

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Introduction: Cervical cancer is the most common cancer worldwide including India. Limited reports are available for Notch signaling alteration(s) in cervical carcinoma which play an important role in cell proliferation, differentiation, and apoptosis. **Objectives:** The study was aimed to evaluate the role of Notch-3, Jagged-1 in cervical precancer, Invasive squamous cell carcinoma (ISCC) and Adeno squamous cell carcinoma (ADSCC). **Material and Methods:** A total of 188 tissue biopsy samples comprising of precancer (n=30), tumor specimens (Invasive squamous cell carcinoma, n=98; Adenocarcinoma, n=20) and non-neoplastic cervical tissues (n=40) were obtained from the Department of Obstetrics and Gynecology, LNJP and Safdarjang Hospitals, New Delhi. All samples were analyzed for HPV infection by PCR and for Notch-3, Jagged-1 and protein expression by Immunohistochemistry and Western blotting. **Results:** 80% (24/30) of precancerous and 87% (103/118) of cancer patients were found to be positive for HPV infection. Among them, 80% (24/30) were positive for HPV 16 in precancer and 83.8% (99/118) in cancer patients. We observed significantly up-regulated nuclear expression of Notch-3 (4.17 ± 0.39; 4.74 ± 0.18; 1.25± 0.47) and Jagged-1 (3.70 ± 0.38; 4.64 ± 0.17; 3.8 ± 0.47) in precancer, ISCC and ADSCC (p=0.001, p=0.001, p=0.001) as compared to normal controls (0.70 ± 0.20; 0.95 ± 0.21; 1.03 ± 0.29) respectively. Receiver Operating Characteristic (ROC) analysis in ISCC showed that the values for area-under-the-curve (AUC) with respect to sensitivity and specificity for nuclear Notch-3 and Jagged-1 were 0.93, 84.7%, 87.5% and 0.93, 86.7%,77.5% respectively. **Conclusions:** These findings suggest that deregulation of Notch-3 andJagged-1 proteins may play an important role in HPV associated pathogenesis of cervical cancer.

Keywords: Notch-3, Jagged-1, Cervical cancer

Prevalence of Human Papillomavirus and *Chlamydia trachomatis* infection in cervical and anal samples of sexually active women in India

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Introduction: Cervical and anal cancers often arise from precancerous dysplasia lesions. Human Papillomavirus (HPV) is considered to be the main etiologic agent for cervical cancer and Chlamydia trachomatis (CT) is one of the major cofactors in the development of cervical intra epithelial neoplasia. **Objectives:** To investigate the prevalence of HPV and CT infection in cervical and anal samples of sexually active women. **Material and Methods:** We collected 50 cervical samples and 50 anal samples and screened them for HPV and CT infection with prior informed consent. The samples were taken from Sexually Transmitted Diseases clinic of those female patients having the symptoms of genital infection including vaginal discharge, lower abdominal pain and having history of anal intercourse. Cervical and anal scrapes were used for the evaluation of HPV and CT using polymerase chain reaction (PCR). **Results:** Among the cervical cases, positivity for HPV was 36% (18/50) and CT was 42% (21/50). In anal cases, the prevalence of HPV was 4% (2/50) and CT was 2% (1/50). The most common type of HPV found in HPV positive cases was type 16 (85.7 %) followed by type 18 (14.3%). In cervical cases 28% (14/50) were co- infected, therefore in anal cases it was 2% (1/50). **Conclusions:** This study shows that HPV and CT prevalence is higher in cervical cases as compared to anal cases. There is need to continuously screen, counsel, treat and monitor trends of HPV and CT infection to make women aware about cervical cancer. Further, large population based studies are recommended to conclude this finding.

High expression of EZH2 is associated with tumor grade in human hepatocellular carcinoma

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Background: It was documented that trimethylation of lysine 27 on histone H3 (H3K27me3) has contradictory prognostic impacts in different human cancers. Recently, only few reports have documented that overexpression of H3K27me3 and EZH2 were positively associated with aggressiveness and poor prognosis in hepatocellular carcinoma (HCC) patients. Methods: Immunohistochemical analysis was used to examine protein expression of H3K27me3 and EZH2 in 67 HCC tissues. Nuclear immunoreactivity for H3K27me3 and EZH2 proteins was scored in a semiquantitative method. Results: The expression of EZH2 was significantly and positively correlated with the tumor grade (p=0.014), but not with other clinicopathological parameters. No significant correlation of H3K27me3 was found. Multivariate Cox regression analysis showed that no significant correlation of EZH2 or H3K27me3 was found. A significant positive correlation between expression of H3K27me3 and EZH2 was observed (p=0.001). Conclusion: These findings provide evidence that a high expression of EZH2 correlates

closely with the tumor grade of HCCs but fails to be of prognostic value in multivariate analysis.

Key words: EZH2 protein, Hepatocellular carcinoma

Chlorinated by- product induced Hepatocellular carcinogenesis –Abrief review

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Water chlorination has made remarkable contribution in control of water borne disease till date.In chlorine mediated disinfection process, halogen reacts with Natural Organic Matter to form carcinogenic "Disinfection by-products."Chloroform is the most prominent Trihalomethanes Species,one of the disinfection by-product formed during chlorination.Vulnerability to this hazardous by product has been found to cause severe hepatic repercussions like liver necrosis and hyperplasia. Chloroform elicits non Genotoxic-Cytotoxic mechanistic approach towards cancer. However, the level of toxicity will rely on sex, strain and routes of administration along with exposure duration. Chloroform induced cell proliferation proceeds with its oxidative metabolism with aid of CY2PE1 enzymes to form phosgene, a toxic intermediate. A carcinogenic assay on CYP2E1 knockout mouse hasexplicated its key role in carcinogenicity. However, elevated glutathionine concentration scavenges the target cell form lethal effects of Phosgene. But repeated exposure of chloroform can depletes the level of this scavenger and thus phosgene manages to interfere with the function of mitochondria which in turn leads to toxicity, necrosis followed by uncontrolled cell proliferation. There has been no evidence for possibility of Genotoxicity induced by chloroform but it has been found that this halogenated by-product alters hepatocellular apoptosis.These review insights into mechanism and level of cellular toxicity in chloroform mediated carcinogenesis due to consumption of chlorinated by- products in drinking water.

Keywords: Chlorination, chloroform, CYP2E1, Glutathionine, Hyperplasia, Phosgene.

Role of mammaglobin as diagnostic marker for Breast Cancer'

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Introduction: Breast cancer is a major problem among females all over the world. Breast cancer is known for its morphologic diversity and unpredictable clinical behavior. Immunohistochemistry has an expanding role in mammary pathology that has been facilitated by a growing list of available antibodies and a better understanding of biology. Mamma globin was first identified as a breast cancer restricted biomarker by differential screening approach directed at the isolation of novel, human breast cancer-associated genes. Mamma globin is a 93 amino acid glycoprotein with homology to other secretoglobin-uteroglobin family members. The gene has been mapped to chromosome 11q12.3-q13.1 [3]. **Objectives:** The aim of this study was to investigate immunohistochemical expression of mamma globin, and to determine the correlations with clinicopathological parameters. **Material and Methods:** Tumor block of two hundred patients ranging in age from <40 to ≥60 years were collected from Pt. B. D. Sharma University of Heath Sciences Rohtak, Haryana for this study. Out of 200 patients, only 150 were evaluated for the histological examination, 50 patients being omitted due to the incomplete information. The immunohistochemical reaction was scored on the basis of quick score (cytoplasm stain intensity) from 0 to 4. The histological parameters of all cases were reviewed by pathologist and the histological grades were determined for each case according to Nottingham modification of the Bloom and Richardson Grading System. The study protocol was approved by institutional human ethical committee (IHEC). **Results:** The positive expression rate of mamma globin biomarker was observed in 69% of breast cancer patients. Breast cancer patients were categorized in different age groups and mean age was 45 4 years. Tumor grade was found to be significantly associated with the expression of mamma globin (p=0.0017). Maximum patients (45%) were observed with tumor size 2-4.9 cm. No statistically significant association was observed among mamma globin expression, tumor size, lymph node status and histological types. **Conclusions:** Existing markers act as valuable diagnostic tools, but there is a need to further improve the sensitivity and specificity of the existing panel of breast markers. Additionally, the lack of organ specificity of these breast carcinoma markers further demonstrates the need for new markers in the diagnosis of metastatic breast cancer. Mamma globin is a highly specific marker of breast cancers, and its expression was detected in about more than half the breast cancers patients. In prognostic factor, tumor grade was significantly correlated with expression of mamma globin. Based on its breast cancer specific pattern of expression, we believe that mamma globin would be an excellent candidate for a novel and clinically useful breast tumor marker and help in management of breast cancer patients.

A case series of neuroendocrine carcinoma of the breast: A rare entity.

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Introduction: A neuroendocrine tumour is well described in the literature, but neuroendocrine carcinoma (NEC) of the breast is a very rare entity. NEC breast is not much reported in the literature so as to define the standard diagnostic, therapeutic and prognostic guidelines. It has almost similar clinical behavior; hence its diagnosis is based on histology and immunohistochemical markers. **Objective:** Our aim is to determine the clinico-pathological features, treatment and prognostic features of primary neuroendocrine breast carcinoma. **Material and Methods:** We searched the patient's records that were diagnosed with primary neuroendocrine carcinoma of the breast between 2008 and 2014 at a Regional Cancer Center in South India. We noted the demographic parameters, clinical features, diagnosis, treatment and follow-up of all the patients and we are presenting a case series study. **Results:** Eleven cases with diagnosis of primary NEC breast were admitted during the study period. All the patients were females with median age of 46±4 years. Six patients were diagnosed preoperatively on core needle biopsy while remaining cases were diagnosed post-operatively on histopathology and immunohistochemichal markers. Nine patients presented with palpable lump in the breast with average size of 3.2cm and 8 patients had palpable axillary lymphadenopathy. Three patients presented with metastases at the time of diagnosis. All except one case underwent modified radical mastectomy and 8 of these cases received adjuvant treatment. On histopathogy, seven patients had metastatic axillary lymph nodes and most of them with N2 status. All patients were ER positive, 9 were PR positive and only one patient was HER2-neu positive and two were equivocal. The common neuroendocrine markers synatophysin, NSE and chromogranine were positive in almost all patients. Average follow up was 22 months (3 to 74 months). After completion of treatment, two patients had local and axillary recurrence at 8 months and 17 months respectively. Three patients expired due to non-cancer causes. **Conclusion:** The primary neuroendocrine carcinoma of the breast in comparison with infiltrating ductal and lobular carcinoma is different in terms of hormone receptor status, staging, lymph node stage and risk of recurrence. Our study suggests that neuroendocrine carcinoma of the breast is a separate histological group and is not a less aggressive type of tumour.

Stem cell markers as predictors of response to neo-adjuvant chemotherapy in breast cancer

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Background: Neo-adjuvant chemotherapy (NACT) is an integral part of multi-modality approach in the management of locally advanced breast cancer . Cancer stem cell (CSC) has been defined as a cell within a tumour that possesses the capacity to self renewal and to cause the hetereogeneous linage of cancer cells that comprise the tumour. Various stem cell markers that have been linked to breast cancer are CD44,CD24, ALDH1 etc. Cancer stem cells have been shown to be resistant to various chemotherapeutic regimens in *in vitro* studies. **Materials and Methods:** 30 LABC patients after complete routine and metastatic work up were subjected to biopsy, immunohistochemically for stem cell markers(CD44,CD24, ALDH1). Three cycles NACT were given at three weekly intervals & patients assessed for clinical response after each cycle. MRM performed in all patients three weeks after the last cycle and the specimen were re-evaluated for any change in expression. **Results:** A statistically significant correlation was observed between clinical and immunohistochemical response to NACT. Increase in the expression of CSC indicated poor response to neo-adjuvant chemotherapy and thus a poorer outcome. **Conclusion:** These markers can be effectively utilized as predictors of response to neo adjuvant chemotherapy in patients with breast cancer and may help in tailoring the therapy and avoiding toxicity of chemotherapy in non-responders.

LICA(latissimus intercoastal artery) flap in Locally advanced breast cancer-An indian solution to indian problem.

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Background: Assessment of quality of life after surgery of breast cancer especially when BCS & MRM done is contemplated as essential part of management. Various flap techniques like LD FLAP, LICA flap ,DIEP flap, FREE flap are currently available. Main concern is of technical complexicity & donor side morbidity. **Aims and objectives**: To assess the quality of life following LICA flap reconstruction. **Materials and Methods:** 50 biopsy proven breast cancer patient underwent lumpectomy/MRM following coverage of defect by LICA flap. Quality of life – post operative cosmesis , early radiotherapy feasibility (flap vs graft), donor side morbidity, technical feasibility were assessed. **Results:** LICA flap Reconstruction was observed to provide excellent cosmesis, early radiotherapy feasibility after surgery, minimal donor side morbidities , technically easier to reconstruct the defect after surgery in breast cancer.

Quality of life assessment following LD flap reconstruction in patients with breast cancer.

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Background: Assessment of quality of life after surgery of breast cancer especially when BCS & MRM done (for larger tumour) is contemplated as assess part of management. Various flap technique like LD flap, LICA flap, DIEP flap, & Free flap are currently available. Main concern is of technical complexicity & donor side morbidity. **Aims and objective:** To assess the quality of life following LD flap reconstruction. **Material and Methods:** 50 biopsy proven breast cancer patients underwent lumpectomy/MRM following coverage of defect by LD flap. Quality of life- post operative cosmesis, early radiotherapy feasibility (flap vs graft), donor side morbidity, technical feasibility were assess. **Results:** LD flap Reconstruction was observed to be provide excellent cosmesis , early radiotherapy feasibility after surgery, minimal donor side morbidities, technically easier to reconstruct the defect after surgery in breast cancer.

Is 2D echocardiogram essential for assessing surgical fitness in breast cancer patients after anthracycline based neoadjuvant chemotherapy? Retrospective study from an apex cancer centre.

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Introduction: Cardiac toxicity is the most prominent side effect of anthracyclines. 2D Echocardiogram(2D echo) is regularly requested before and after anthracycline based neoadjuvant chemotherapy (NACT). The rationality of obtaining 2D echo on a regular basis irrespective of clinical assessment findings, has been studied in a few published series. We analysed the data from Tata Memorial Hospital to find the impact of this practice in deciding further management of these patients. **Materials and Methods:** In this retrospective study we examined clinical notes, preanaesthetic check up notes and investigation reports of 234 patients who underwent NACT in Tata Memorial Hospital from September 2013 to october 2014 for whom online reports were available. The data regarding the age of the patient, stage of cancer, chemothapeutic regimen used and number of cycles of anthracycline recieved and patient's comorbidities, ECOG performance status after completion of NACT and effort tolerance at the time of preanaesthetic assessment were noted. 2D Echo findings before and after the NACT were collected. The data was analysed using SPSS 21. **Results:** Mean age was 46.16 years(std. Deviation 9.06). 225 patients had stage II or stage III disease and 9 patients had oligometastatic disease at presentation. 229 patients recieved NACT with CEF/CAF (Cyclophosphamide, Epirubicin/Actinomycin, 5 FU) or AC/EC and 5 patients recieved trastuzumab. 24 patients had diabetes, 33 were hypertensives and 11 had more than one comorbidities. One patient had history of ischemic heart disease. The effort tolerance of 2, 3 and 4 were reported by 108, 88 and 17 patients respectively and three had an effort tolerence of ≤ 1. There were two abnormal echocardiograms with reduction of more than 10% in EF after chemotherapy. Both of them reported compromised effort tolerance of less than one, underwent planned surgery with due risk. We noticed that no patient had a change in treatment plan based on 2D echo findings alone. **Discussion:** 2D echo is regulary ordered in most oncology centers in breast cancer and sarcoma patients after anthracycline based chemotherapy. We found that no patient with an effort tolerance of 2 or more, documented ECOG performance status of 0 or 1 or Karnofsky Performance Status of ≥ 80 had a change in their treatment plan based on 2D echo findings. It is reasonable to consider 3D echocardiogram or MUGA scan which are more sensitive, as clinically indicated rather than obtaining routine 2D echo in all patients. A well designed prospective study with more number of participants is required to strengthen our findings.

DZNep countervails the effect of Nicotine in aggressive breast cancer cells

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Introduction: Emerging evidences show close association of nicotine with breast cancer. Although its relevance in inducing breast cancer is less understood, its role in increasing the breast cancer risk is broadly studied. We and other groups have shown critical involvement of nicotine in breast cancer tumorigenesis, metastasis and thus in disease progression. However, the basic mechanism by which nicotine takes the charge of carcinogen still remains unclear. Here by the use of DZNepA, an inhibitor of histone methyl transferase EZH2, we have examined that the nicotine mediated epigenetic modification can be a possible pathway for its significant association with increased breast cancer risk. **Objectives:** To check the effect of DZNepA on nicotine mediated proliferation, migration, and invasion, as well as in increased apoptosis resistance. Also to the check the possible interaction of nicotine and the polycomb group protein EZH2, thus exploring the possible underlying mechanism by which nicotine affects the breast.

Material and Methods: Using tripe negative breast cancer cells MDA-MB-231 and MDA-MB-435s and specific inhibitor of EZH2, we explored the effect of DZNepA on nicotine-mediated increased proliferation and migration. We further explored the effect of the inhibitor in inducing apoptosis in nicotine mediated apoptotic resistant cells. **Results:** In this study, we demonstrated that nicotine alters the expression of genes significantly involved in cancer progression by increasing the expression of epigenetic modifier EZH2. We further showed that nicotine mediated increased cell proliferation, migration and invasion can be inhibited by the use of DZNepA. **Conclusions:** Our study reveals the potential of DZNepA in inhibiting the effect of nicotine towards increased breast cancer risk.Also our result shows the possible interaction of epigenetic modifier EZH2 with nicotine in breast cancer tumorigenesis.

Association of CDH-1(CADHERIN) Gene Polymorphism with Breast Cancer

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Background: Mortality in breast cancer is mostly due to metastasis to distant organs. Metastatic breast cancer is progressive stage of the disease (stage-IV) and marked by expansion of cancerous cells beyond the tissue origin. At cellular and tissue level, the process of distant metastasis involves primarily differentiation from epithelial phenotype to mesenchymal phenotype, called as epithelial-mesenchymal transition (EMT). E-Cadherin (epithelial) or Cadherin (CDH1) gene (q16q22.1) provides information for making a protein called E-Cadherin, which is responsible for calcium dependent cell-cell adhesion. It has been seen that selective loss/decrease expression of E-Cadherin can cause de-differentiation and increased susceptibility of invasiveness of human carcinoma cells. Aim of this study was to screen candidate polymorphism of CDH-1 gene in metastatic and non-metastatic breast cancer patients and to study association of CDH-1 polymorphic variants with metastatic breast cancer and other clinical parameters. **Methods:** DNA was extracted from whole blood using a commercial DNA blood kit (GenElute Blood Genomic DNA Kit; SIGMA) and stored until processing for genotyping. Selected polymorphism of CDH-1 gene (SNP -616 G>C) were screened with RFLP or DNA sequencing. **Result:** In our study, total number of subjects studied were 51, which included 12 cases (metastatic breast carcinoma) and 39 controls (non metastatic breast carcinoma). Out of 12 cases studied, 3 tested positive for-616snp CDH-1 gene mutation, with genotypes GC, CC and CC. On the other hand GG was the wild genotype. Decreased E-Cadherin expression was significantly found in high-grade and metastatic (stage IV), in contrast to low and intermediate grade cancer. This seems to be in concordance with the fact that E-Cadherin alterations (lack of expression) occurs in advanced tumor stages. **Conclusion:** E-Cadherin alterations occurs in patients with age ≥50 years, high grade tumor and advanced tumor stages (metastatic breast cancer), thereby rendering it as a tumor invasion suppressor gene.

Hypofractionated Radiotherapy for Post-Operative Breast CancerPatients at Delta Hospital - an Evaluation of Clinical Experience.

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Background: As hypofractionated radiotherapy for post-operative breast cancer patients safe, effective and more convenient, it might be beneficial for patients of developing countries like ours. **Objective:** This study was done to evaluate the safety and efficacy of hypofractionated whole breast radiation therapy in patients who underwent breast conserving surgery and hypofractionated radiation therapy in patients who underwent mastectomy and axillary clearance. **Materials and Method:** This cross sectional study was conducted in Delta Hospital Ltd, Dhaka, Bangladesh, including 50 postoperative patients, (12 patients in Breast Conservation Therapy group and 38 in Post Mastectomy Radiation Therapy group), with invasive ductal carcinoma of breast treated with this hypofractionated radiotherapy protocol during the last 1.5 year. The patients were treated with 3DCRT, LINAC, 6 MV photon and appropriate electron energy. **Results:** Minimal post treatment acute morbidity was observed. Forty seven patients (94%) had grade-I acute skin toxicity and only 3 patients (6%) developed grade-II acute skin toxicity. **Conclusion:** Hypofractionated radiotherapy is as safe and effective as conventional fractionated radiotherapy and superior in terms of convenience.

Keywords: Radiotherapy; hypofractionated radiotherapy; breast cancer.

Capecitabine monotherapy in patient with recurrent and metastatic breast cancer

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Introduction: Capecitabine is highly active in the treatment of metastatic breast cancer, both as a single agent and in combination regimens. Furthermore, it is well tolerated, with favorable safety profile. **Objectives:** The aim of this study was to investigate response rate, time to disease progression and the toxicity of Capecitabine monotherapy in treatment of patients with recurrent and metastatic breast cancer. **Material and Methods:** 57 patients with recurrent and metastatic breast cancer pretreated with Taxanes and Anthracyclines at National Cancer Hospital of Viet Nam between January 2013 to December 2015 were enrolled and treated with capecitabin 1250mg/m2 administered orally twice daily (morning and evening; equivalent to 2,500 mg/m2 total daily dose) for 2 weeks followed by a 1 week rest period given as 3 week cycles; and treatment was continued until disease progression. **Results:** 57 evaluable patients were included. The average age was 49 years (range: 43 – 67). For an overall response rate of 27 % (95% confidence interval 22% to 38%), 1 patients (2%) had complete responses and 14 patients (25%) had partial responses. Time to disease progression was 8.6 months. A total of 456 cycles were given to 57 patients. Only 2 patients in the whole study had grade 3 or 4 neutropenia but without fever or infection. Common non-hematologic toxicities are fatigue, diarrhea, hand foot syndrome, and nausea but mostly grade 1 or 2.At least one cycle of grade 3 or 4 hand foot syndrome was seen in 5 % of the patients. Grade 3 – 4 nausea, diarrhea were seen in less than 1% of cycles. Alopecia was not frequently observed. **Conclusion:** The results indicated that Capecitabine was effective and well-tolerated. Moreover, this agent may offer the specific advantages, as fewer and shorter hospital visits, delayed use of intravenous chemotherapy, maintained social activities and therefore provided a good quality of life. However, a larger

Metabolic syndrome and breast cancer risk

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Introduction: Metabolic Syndrome, which is associated with increased risk of diabetes and heart disease, has recently been suggested to play a role in breast carcinogenesis. The metabolic syndrome could influence the risk of breast cancer through changes in a number of interrelated hormonal pathways, including those involving insulin, oestrogen, cytokines, and growth factors. **Objectives:** This study was aimed to assess the prevalence of metabolic syndrome in patients with breast cancer and the independent effect of metabolic syndrome on breast cancer risk. **Material and Methods:** Fifty women aged 40–80 years with breast cancer and fifty controls of similar age were screened for metabolic syndrome prevalence and breast cancer risk factors, including age at diagnosis, age at menarche, reproductive status, live births, breastfeeding, family history of breast cancer, physical activity, cigarette smoking, body mass index, and metabolic syndrome parameters. Each variable was first assessed for baseline comparisons using

the uni-variate model, and significant variables were then added to the multivariate conditional logistic regression model. **Results:** Prevalence of metabolic syndrome was 40.0% in breast cancer patients, and 18.0% in the control group (p\0.02). A positive and independent association was observed between metabolic syndrome and breast cancer risk (odds ratio=3.037; 95% confidence interval 1.214-7.597). **Conclusions:** Metabolic syndrome is more prevalent in breast cancer patients and is an independent risk factor for breast cancer.

Factors associated with Chemotherapy induced amenorrhea in premenopausal women with Ca breast.

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Background: Chemotherapy induced Amenorrhea(CIA) is defined as the cessation of menses for at least 3 months during or soon after chemotherapy. Ovarian suppression during chemotherapy is a widely occurring phenomena which is of particular significance to pre menopausal women who are concerned about their ability to conceive following adjuvant chemotherapy. CIA is dependent on the patient age(1), type(2),cumulative dose, duration and intensity of chemotherapy used(2,3). Alternatively CIA has also shown prognostic significance in certain hormone receptor positive tumors as it has been shown the gain of adjuvant chemotherapy are maximal in premenopausal women with ER+ Ca breast who undergo amenorrhea during or following chemoregimen.Here we report a retrospective cohort analysis of 30 premenopausal women diagnosed with Ca breast in our centre. **Objective:** The aim of our study was to report the incidence of CIA and the factors associated with CIA particularly the type of chemo agents used, duration, and some factors associated with reversible amenorrhea. **Method:** All women were interviewed through telephone and oral consent was taken to review their clinical data. Information was collected on age, hormone receptor status (estrogen, progesterone), HER2 status, surgical and radiation treatment, adjuvant chemotherapy (type and duration in months) and eventual endocrine therapy. The chemotherapy regimens used were as follows: i) 5-FU 600mg/m2, epirubicin75mg/m2, cyclophosphamide 600mg/m2 (FEC) ii) Docetaxel-75mg/m2 ; doxorubicin-50mg/m2 ;Cyclophophamide-500mg/m2mg. iii) Doxorubicin-60mg/m2; cyclophosphamide-600mg/m2. When prescribed, adjuvant endocrine therapy consisted of tamoxifen 20mg/day for 5 years. **Result**: Average age of patients with Ca breast in our sample was 40.8 and the mean age of patients with recovery of amenorrhea was 37.4 and patients without recovery or menopause was 44.5 there was statistically significance between the two groups ($p<0.05$).There was no significance between the recovery of amenorrhea and patients undergoing multiple lines of treatment or duration of chemotherapy in our sample.There was a significant association between the onset of amenorrhea and whether or not patients were started FEC regimen$\chi 2$ (1) = 6.86, $p < .05$. Average age of women in this group was 41.8yr. This seems to represent the fact that, basedon the odds ratio, the odds of having amenorrhea was 16.25 times higher if patients were given FEC regimen than those without.Identifying proper risk factors for onset of amenorrhea and recovery following onset couldn't be properly defined due to small sample size and limited variation in chemo regimen in our sample. 90% of patients receiving FEC regimen had onset of amenorrhea following initiation of Chemotherapy. **Conclusion:** Amenorrhea in premenopausal women with Ca breast undergoing FEC regimen is quite high. Patients are invariably anxious about the change in menstrual cycle following chemotherapy. Recovery of amenorrhea is not dependent on multiple lines of Chemotherapy but rather on age. However Risk factors that determine the onset of amenorrhea during chemotherapy couldn't be accurately identified to due to small sample size and lack of variation in chemo regimen used in our center.Disclaimer: No relevant conflicts of interest to declare.Reference:1) Torino F, Barnabei A, De Vecchis L, et al.Chemotherapy-induced ovarian toxicity in patients affected by endocrine-responsive early breast cancerCrit Rev Oncol Hematol. 2013 Aug 13. pii: S1040-8428(13)00158-3. doi: 10.1016/j.critrevonc.2013.07.0072)Molina JR, Barton DL, Loprinzi CL.FIChemotherapy-induced ovarian failure: manifestations and management.DrugSaf. 2005;28(5):401-16.3)Bines J, Oleske DM, CobleighMAReview Ovarian function in premenopausal women treated with adjuvant chemotherapy for breast cancer.JClinOncol. 1996 May; 14(5):1718-29.

Prognostic Factors determining the survival in patients presenting with *de novo* Metastatic Breast Cancer: Experience from a tertiary cancer center in southern India

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Background: Metastases is the most common cause of breast cancer mortality. Incidence of patients presenting with *de novo*metastases is relatively higher in India compared to West, due to less effective screening programs and various other socio-economic and cultural factors. **Materials and Methods:** This is a retrospective analysis of *de novo* metastatic breast cancer patients presenting to our institute from 2007 to 2011. All the patients were diagnosed with a trucut biopsy, underwent complete staging workup including receptor status. Patients who progressed on or after initial chemotherapy were excluded from the study. Chemotherapy protocols used were, 3wkly Docetaxel and Epirubicin, 3wkly Adriamycin and Cyclophosphamide followed by weekly Paclitaxel, 3wkly 5FU,Adriamycin and Cyclophosphamide. Hormonal therapy was given as required. **Results:** Of the 925 patients, 118(12.75%) presented with*de novo* metastases. The median age of presentation was 52years. Most common presentations were breast lump(81%) and backache(13%). Thoracic vertebrae(42%) was the most common site of metastases. Of the Patients with single site, two sites, and three sites of metastases had a median overall survival(OS) of 32,14 and 12 months respectively with a significant statistical difference(p value<0.0001).Patients with solitary bone metastases had a median progression free survival of 72 months. The median OS of patients with karnofsky performance status 0&1 and 2&3 were 28 and 14 months respectively. **Conclusion:** Thoracic vertebrae(Bone) is the most common site of metastases. Prognostic factors determining the survival advantage were number of sites of metastases and performance status of the patient. There is no survival advantage based on receptor status and type of chemotherapy regimens. Patients with Solitary bony metastasis had prolonged progression free survival.

Study of estrogen and progestrone receptor (er/pr) status and its correlation with various risk factors in early carcinoma breast cases coming to rims, ranchi – An institutional study

SumeghaRana

Introduction: Globally breast carcinoma is the second leading cause of cancer related deaths. Estrogen and progesterone play a central role in regulating growth kinetics of a variety of epithelial lining like in breast and endometrium and is a powerful predictive marker. **Background**: To Correlate the expression of prognostic factors like age of patient, menarche, menopause, parity, tumour size, number of lymph nodes, histological grading with ER/PR status.

Materials and Methods: Study was carried out among carcinoma breast patients admitted over a period of two years in RIMS, Ranchi. A total of 75 patients were included in the study. **Results**: This prospective study was done among 75 diagnosed cases of carcinoma breast, Estrogen receptor

positive cases were 50 and negative were 25. Whereas progesterone receptor positivewere 49 and negative were 26. ER and PR were correlated positively with increasing age and was not statistically significant (p= 0.6364 & p=0.95 respectively). Age of menarche had no correlation with ER but had significant correlation with PR. PR positive cases had low age of menarche. Menopausal status had positive correlation with ER & PR receptor. Post menopausal cases had more positivity for both ER & PR. Parity had a significant positive correlation with both ER & PR (P=0.0012 & P<0.0001 respectively). Tumour size, number of lymph nodes and histological grade of tumour had an inverse correlation with ER & PR positive receptor which were statistically significant. **Conclusion:** According to data, a statistically significant correlation of ER/PR was found with menopausal status, parity , tumour size, number of lymph nodes and tumour grade whereas age of menarche had significant correlation with PR receptor. Hence ER/PR status is highly important predictor in cases of carcinoma breast which necessitates routine evaluation of hormonal status even in early cases of carcinoma breast.

Assessment of training needs of medical graduates in Clinical Breast Examination.

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Background: The incidence of breast cancer has been growing steadily over the years in India. In order to be able to provide screening for breast cancer to women CBE needs to be explored as an option as quality mammography facilities are not available all over the country. Training needs of fresh medical graduates was assessed in CBE in order to find a way to address this issue. **Material and Method:** This cross sectional study was conducted in the year 2014 among medical graduates in various hospitals of Delhi. Sample size of 400 was calculated and information regarding existing knowledge of CBE and training needs was assessed after collecting data by a semi- structured questionnaire. Data was entered in Excel sheet and analysed using SPSS version 21 software package. **Results:** Mean age of the participants was 23.8years. Out of a total of 410 participants 402(98%) mentioned that they knew how to perform a Clinical breast exam whereas 08(1.95%) said they did not know how to do it. Majority of 322 (80.1%) responded correctly that they would examine the lymph nodes in sitting position. Knowledge of group of lymph nodes to be examined was poor at 128(31.8%). Only 154(38.3%) knew about correct posture of doing palpation of the breasts. A low proportion, 84(20.9%) actually knew the correct perimeter of the breast. Out of 392 who stated they further wanted training main reasons cited were that as a part of general; practice this skill is required 248(61.7%),cancer is on the increase and hence one must learn CBE191(47.5%),half of the women are patients54(13.4%).301/392(74.9%) said they would like to teach the women about breast self-awareness while doing a CBE whereas 91/392(22.6%) were apprehensive that either the lady might not understand or they might not have enough time to explain the procedure to the lady who comes to them. On being enquired about how would they like to improve their CBE skill responses were by practicing on patients 214/392(54.6%), 174/392(44.4%) by practicing on models/mannequin and 98(25%) by seeing videos. There was no statistically significant difference between the knowledge of students from government college as compared to private colleges and also between females and males p>0.05. **Conclusion:** There is a need to formulate a structured CBE training programme for medical graduates in India.

Key words: Clinical breast examination, training needs assessment, India, medical graduates

Molecular Characterization of Breast Cancer in West Bengal, India

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Breast cancer is the most frequently diagnosed cancer in women, resulting from genetic and environmental interactions. The prevalence of BRCA1/2 gene mutations in breast cancer differs between ethnic groups. The present study attempts to understand the molecular heterogeneity of BRCA1 and BRCA2 genes and to understand the association of various lifestyle and reproductive variables for the Breast Cancer risk. A total of 110 breast cancer patients and 128 controls were included in the study. DNA sequencing revealed 10variants of which 6 were novel. The environmental and genetic factors augment the risk of breast cancer. Certain lifestyle and reproductive factors vindicated as significant predictors (p<0.0001) for breast cancer risk. The present study being the first report of molecular heterogeneity of BRCA1 and BRCA2 genes among the Bengalee Hindu Female Breast Cancer Patients of West Bengal, envisaged that the identification of the mutations and modification of the lifestyle factors might be valuable in early prognosis of the disease to minimize the risk among the studied population.

Unusual skin oligometastasis from breast cancer mimicking melanoma

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Pigmented lesion in breast carcinoma is rare presentation mimicking melanoma. NCCN has characterized only four features of skin involvement as edema, ulceration, peau d' orange appearance and skin nodule, but *pigmentation in skin with contiguous tumor is not mentioned in literature*. That's why in our case it was mimicking melanoma with deep vertical spread in breast tissue due to dark black to brown pigmentation. Finally immunohistochemistry helped out for diagnosis confirming its breast origin and managed assuming it as systemic disease with upfront chemotherapy following the excisional biopsy of isolated skin metastasis.

Identification and Characterization of Biomarkers in Triple Negative Breast Cancer

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Breast cancer is the leading cause of cancer deaths in women worldwide, ranging >1.6% deaths. Breast cancer risk in India is 1 in 28 women during her life time. Rapid advances in breast cancer research in last decade have identified erbB2 (Her-2), Estrogen receptor (ER) and Progesteron receptor (PR) as biomarkers and therapeutic targets, which considerably decreased the mortality rate in these group of women. There are no specific regimens or targeted therapies for basal triple negative breast cancer (TNBC) except chemotherapy. These tumors are highly destructive and the majority of deaths occur in the first 5 years. The biology and the molecular mechanisms which drive the growth and metastasis of Her-2 negative breast cancer are still unknown. In this respect our recent study reported the over-expression of Annexin A2 and Annexin A2 mediated EGFR downstream signaling in the progression of TNBC. Our group also verified the efficacy of Annexin A2 antibody as the therapeutic molecule using TNBC cell lines. In our recently reported study we have demonstrated the importance of Annexin A2 glycosylation, its translocation to the membrane surface and there its interaction with animal lectin, galectin-3 further its role in the progression of breast cancer. Our molecular mechanism study yielded in purifying one plant lectin and using this Annexin A2 specific plant lectin we could dissociate Annexin A2-galectin-3 interaction and down-regulate all associated carcinogenic functions. In pursuing our study in TNBC, we have also noticed that there are about 10% TNBC phenotypes where in addition to known triple markers, Annexin A2 is also absent. We could identify over expressed Annexin A1 in these highly invasive phenotypes. Our current study revealed that reciprocal regulation of Annexin A2 and A1 in these clinical

cases.EventhoughAnnexin A1 is an anti-inflammatory and antiapoptotic protein, but in these phenotypes it acts as oncogenic and is the reason for the high invasiveness. In the current study we have characterized the p53 mediated reciprocal regulation of Annexin A2 and A1 in these TNBC cell lines. Specific targeting of over-expressing Annexin A2 or Annexin A1 could help in managing these highly invasive TNBC progressions.

"Sentinel Lymph Node Evaluation in Carcinoma Breast".

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Introduction: Sentinel node evaluation in breast cancer is initial alternative to routine complete axillary lymph node clearance for patients with early-stage breast cancer with clinically negative axillary nodes. Completion ALND remains standard treatment for patients with axillary metastases identified on SNB. Appropriately identified patients with negative results of SNB, when done under the direction of an experienced surgeon, need not have completion ALND. **Objective:** To localize sentinel node by injecting 2.5% Methyleneblue dye around the primary tumor , to assess the reliability of technique in predicting axillary lymph node status and to study the incidence and prevalence of positive axillary lymph nodes in Indian population with breast cancer. **Material and Methods:** It is a prospective observational study done in 35 patients in 2012 to 2015. 3-5 ml of Methylene blue dye was injected 10-15 minutes before surgery into the adjacent breast tissue surrounding the primary tumor after cleaning and draping the patient. Then axilla was explored after 10-20 minutes and sentinel lymph node was detected by its blue colour and by tracing the afferent lymphatic vessel and was removed and sent for imprint cytology and routine histopathology. Modified Radical Mastectomy was completed and whole of the breast tissue along with axillary contents labelled as L1, L2, L3 were sent for histopathology along with sentinel lymph node in separate container. Result of sentinel lymph node imprint cytology and histopathology compared with histopathology of other axillary lymph nodes. **Result:** The sentinel node localization rate was 94.29%. In our study, sentinel node imprint cytology were positive in 8 cases out of 35, with sensitivity of 72.7%, specificity 100% with diagnostic accuracy of 91.43% and p –value (Fisher's extract test) is <0.001 which is significant. There are 2 cases [post NACT] where sentinel lymph node was negative but other axillary nodes were positive. In cases in stage T1 –T2, sentinel lymph node biopsy sensitivity, specificity and accuracy is 100%. **Conclusion:** Sentinel-node biopsy is a safe and accurate method of screening the axillary nodes for metastasis in women with a early breast cancer with negative axilla.

Serum IL-6 level as a predictor of response to neo adjuvant chemotherapy in patients of carcinoma breast

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Background: Breast cancer is the most frequently diagnosed cancer and is the leading cause of cancer death among women worldwide. Several randomized prospective studies on breast cancer patients have proved the safety and efficacy of neoadjuvant chemotherapy. In recent years, there has been considerable interest in whether IL-6 level can be used to predict the response to the neo adjuvant chemotherapy of breast cancer patients. **Objective:** To evaluate serum IL-6 level in all diagnosed cases of locally advanced carcinoma of breastreceiving neo adjuvant chemotherapy. **Material and method**: Serum IL-6 levels were assessed in 30 women with breast cancer by ELISA before commencement of treatment (Baseline) andafter 2 weeks of each cycle of Chemotherapy (CAF Regimen). **Results:** The relationship between baseline level of serum IL-6 and response to neoadjuvant chemotherapy was statistically significant (p value=0.023). **Conclusion:** Serum interleukin-6 can be used as predictor of response to neoadjuvant chemotherapy (anthracycline based) in advanced breast cancer.

Key words: Breast cancer, Neoadjuvant chemotherapy, IL-6

Comparative Study between Triple Assessment and Dynamic Magnetic Resonance Imaging for the Evaluation of Breast Lumps

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Background: Breast cancer is the leading cause of cancer death among women in developing countries and the second leading cause of cancer death among women in developed countries.In spite of medical advances and assuring treatment regime, a reduction in morbidity and mortality due to breast cancer has seen no significant changes in India. Hence early detection by imaging modality comes handy in determining the progression of the disease. **Aims and objectives**: To compare the sensitivity and specificity of thetriple assessment of symptomatic breast lesions with contrast-enhanced dynamic MRI. **Methods**: All patients with palpable lesions underwent clinical evaluation, mammography, USG, FNAC and DCE-MRI of breast. **Results**: 80 patients with a mean age of 42years were recruited in study,70 malignant and 10 benign. MRI proved to be most sensitive modality for diagnosis of malignant lesions with 95% sensitivity, while FNAC, mammography and ultrasonography had sensitivity of 98.5%, 77% and 68% respectively. Combined triple assessment had sensitivity of 85.2% with specificity of 87.2%.MRI has specificity of around 70.59%. **Conclusion**: DCE-MRI is a highly sensitive and specific tool for diagnosis of symptomatic breast lesions.MRI has the ability to improve surgical outcomesby better evaluation of tumour extent and providing 3D information and therefore decreasing the need for re-operations leading to lower recurrence rates. Addition of MRI in evaluation of breast lump we can have reliabilityin diagnosis and accuracy in intervention.

Key words: Breast cancer, Breast lumps, Magnetic resonance imaging.

Reciprocal Regulation of BRCA1 &Annexin A2 in Sporadic Breast Cancer

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Introduction: Breast cancer (BC) is the leading cause of deaths in women worldwide, ranging >1.6% deaths. The majority of BC cases are sporadic and only few proportions have been to germ line mutations in predisposing genes. So there is need to understand and reveal mechanism of tumorogenesity in women with sporadic BC. BRCA1 protein known for its multiple vital functions such as tumor suppressor activity, DNA damage repair processes, DNA damage responsive cell cycle check point regulation of a set of specific transcriptional pathways and apoptosis. Lower or undetectable levels of expression of the BRCA1 protein have been observed in sporadic BC. Recent

reports had shown that the epigenetic silencing by cysteine Methylation, promoter hypermethylation, hypoacetylation of histones and chromatin condensation indicating that these mechanisms act together to reduce BRCA1 gene expression and it is regulated by mRNA binding proteins, the identity of which is unknown. HuR is an RNA binding protein already proven to play role in the post-transcriptional regulation of BRCA1. As like HuR other mRNA binding protein like Annexin A2 (AnxA2) expression is more in basal BC where BRCA1 expression is very low or null. AnxA2 is a multifunctional calcium dependent phospholipid binding protein. AnxA2 shows functional diversity like it regulates membrane traffic and cytoskeleton organization, extracellular activities and targeted gene disruption. AnxA2 is highly expressed in the surface of human tumor cells and promotes cell migration and invasion by activating plasminogen and cleaving extracellular matrix. AnxA2 stimulates cell proliferation, angiogenesis and invasion and can be a prognostic indicator in human cancer. **Objectives:** The Role of AnxA2 in theregulation of tumor suppressor BRCA1 genein the development and progression of sporadic breast cancer. **Material and Methods:** BRCA1 &AnxA2 expression in TNBC tissue samples & different cell lines was analyzed by IHC, Western Blotting. AnxA2 knock down study in MDA MB-231 cells was analyzed by western analysis. **Results:** In the present study, we analyzed TNBC paraffin embedded tissue specimens for BRCA1 &AnxA2 expression. We observed BC tissue samples of low BRCA1 expression showed high expression of AnxA2 and vice versa. The different BC cell line models also revealed reciprocal regulation of BRCA1 &AnxA2 expression. To validate reciprocal regulation of these proteins, we induced low AnxA2 expressing MCF 7 cell lines and we found AnxA2 over expression, down regulated BRCA1 expression. Further, AnxA2 knout down in MDAMB-231 cell lines showed, BRCA1 upregulation. **Conclusions:** In thepresent study, we demonstrated that BRCA1 &AnxA2 are reciprocally regulated. Currently we are studying the molecular mechanism of AnxA2 mediated down regulation of BRCA1 in Sporadic Breast Cancer cells.

A Clinico demographic Study of Receptor status in Carcinoma Breast

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Key words – breast, metastatic profile , receptor status

Introduction - India with a population of 1.2 billion is the most populous democracy in the world. Although the incidence of breast cancer has increased globally over the last several decades the greatest increase has been in Asian countries.Estrogen (ER) and progesterone receptors (PR) are found positive in only 20-45% of Indian patients. ER-positive rates are lower in Indian patients than those in western countries. Breast cancer patients of Indian origin tend to be younger, tumours are often large when first diagnosed, and of a high grade as compared to Western countries. **Aims and Objectives -** To study the clinico- pathological and demographic profile of Carcinoma Breast and co relation with the receptor status in a tertiary care center and to study the metastatic profile of breast cancer. **Materials and Methods**: This is a prospective observational study done on 208 patients with histologically proven breast cancer treated at Army Hospital R & R, Delhi Cantt. between May 2013 and April 2015. Data was collected by a questionnaire, filled at the first visit and at subsequent follow ups on a Microsoft Excel worksheet All data including age, menopausal status, and pathological characteristics, stage of the disease were recorded. The ER, PR and Her2Neu status of all patients was recorded and those without these were excluded from the study. In cases where Her2Neu status was equivocal (2+) by immunohistochemistry, analysis of HER2Neu by FISH was undertaken at an outsourced laboratory.The chemotherapy used in the study was based on age, nodal status, performance status, co-morbidities and receptor status of the patient. **Results:** 208 patients were included in the study. The age of the patients ranged from 27 to 82 years with a median of 49.9 years. ER expression was seen in 123(59%) patients,PR expression was seen in 111(53.4%) subjects and Her2Neu expression was seen in 84(40.3%) patients.Invasive Ductal Carcinoma's accounted for 181(87%) of the cases. IDC grade III tumors were seen to have lesser ER/PR positivity and more percentage of TNBC and HER2+ subtypes compared to grade II tumors. Luminal type (ER+, PR+, ER & PR+) accounted for 90 (43%) of all tumors. ER and PR positivity was higher in the 46 – 55 yr (65% and 52%). HER2neu positivity was maximum in the 46-55yr age group 35.8% (28cases/78 cases). The metastatic profile showed 40(19.2%) patients had/ developed lung metastases and 36 (17.3%) developed skeletal metastases. brain metastases were seen in 22.8% of HER+ cases and 18% of Luminal HER+ (E /P+, HER+) cases. In metastatic patients who were either Luminal subtype, 56.7% of metastases was skeletal. . In patients with triple negative breast cancer, 37.1% and 31.4% had lung and liver metastases.

In Nonmetastic Breast cancer patients,comparison study of Docetaxel and Paclitaxel in terms of toxicities,delay&dose reduction.

Background: In breast cancers patients , docetaxel and paclitaxel likely to have differnt toxicity profile.Although both have better result in different dosing schedule. **Aims:** This study has examined the two taxenes, their severity of toxicities in breast cancer patients of different BMI and age(Body Mass Index) retrospectively. **Materials and Methods:** From january2014 to August 2015, in two group severity of toxicities as well as the dose reduction, dose delay, granulocyte colony stimulating factor (G-CSF) in 80(40 in AC-D and 40 in AC-P group) patients with operable lymph node-positive (tumor stage T1, T2, or T3 and nodal stage N1 or N2) and high risk, node-negative (T2 or T3, N0) breast cancer without a distant metastases who received adjuvant chemotherapy – 4 cycles adriamycin, cyclophosphamide 3 weekly, followed by 4 cycles docetaxel 3 weekly (AC-D) and 4 cycles adriamycin, cyclophosphamide 3 weekly, followed by 4 cycles paclitaxel 3 weekly (AC-P)- were studied. **Results:**The patients in the AC-P group suffered from peripheral neuropathy frequently(P=.025), than those in the AC-D group. Febrile neutropenia was significant in AC-D group(P=.003). A decreasing body mass index was associated with an increased risk of febrile neutropenia(P=.008) and Increasing age was associated with an increased risk of anemia(P=.003) , fatigue(P=.008)and pain(P=.004). Dose reduction and delay occurred due to febrile neutropenia and an increase in aspartate aminotransferase (AST)/alanine aminotransferase (ALT) were more in AC-Dgroup during Docetaxel infusion. So dose reduction was only significant in the AC-D group(P=.001). **Conclusion:** In our regional cancer centre, most of the patients are malnourished and from poor socioeconomic status, they poorly tolerates 3 weekly docetaxel leads to dose reduction and delay of next cycle chemotherapy as compared to 3 weekly paclitaxel. Also not follow the weekly paclitaxel.So AC-P preferred over AC-D.

AC-P	Dose delay	Dose reduced	Anaemia	TLC reduced
Patients	17	2	9	11
Age	≤7-50		≤2-50	3-50
	≥10-50		≥7-50	8-50
BSA	1.6≤12		≤1.6-7	≤1.6-10
	1.7≥5		≤1.6-2	≥1.6-1

Synthesis, structural characterization, and anticancer activity ofa novel pregnenolone acetate-based tetrazole derivative against C33A cervical cancer cells

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Introduction: Cervical cancer is the third most common cancer that affects women worldwide and a leading cause of cancer-related deathsin developing countries. Therefore, development of new chemotherapeutic agents is required. **Objectives:**Unlike normal cells, cancer cells contain elevated copper levels which play an integral role in angiogenesis. Copper

is an important metal ion associated with the chromatin DNA, particularly with guanine. Thus, targeting copper via copper-specific chelators in cancer cells can serve as effective anticancer strategy. Keeping in view these facts, we synthesized a new pregnenolone acetate-based tetrazole derivative (ligand-L) against human cervical cancer C33A cells. We evaluated the cytotoxic effect of ligand-L on C33A cells and also explored the underlying molecular mechanism. **Material and Methods:** Multiple approaches were employed to evaluate efficacy and study molecular mechanism such as cell viability, cell cycle analysis, Annexin V-PI apoptosis,intracellular ROS generation, DNA fragmentation, mitochondrial function and western blotting analysis. Further, we also usedinteraction studies (UV and fluorescence spectroscopy) and computational approaches such as molecular docking and simulation studies to ascertainits binding and stability with DNA. **Results:** Ligand-L showed significant in vitro cytotoxic activity against cervical cancer C33A cells. Ligand-L inhibited cell proliferation and induce apoptosis in C33A cells, and such cell death was prevented to a significant extent by cuprous chelator neocuproine and antioxidant N-acetyl cysteine (NAC). It also induced cell cycle arrest at the G1/S phase, mitochondrial membrane depolarization, up-regulation of p53 and p21 and caspases 9/3 activation. All these effects induced by ligand-L were attenuated by neocuproine and NAC. This indicates that ligand-L cytotoxicity is due to redox cycling of copper to generate ROS which leads to pro-oxidant cell death. **Conclusions:** This is the first report wherewesynthesized pregnenolone acetate-based tetrazole derivative against C33 cell line that targets cellular copper to induce pro-oxidant death in cancer cells. These findings will provide significant insights into the development of new chemical molecules with better copper chelating and pro-oxidant properties against cancer cells.

Keywords: copper chelation;redox cycling; anticancer.

Sodium Butyrate induces growth inhibition and epigenetic reactivation of a tumor suppressor gene DIRAS1 in Xp11.2 translocated Renal Cell Carcinoma cell lines

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Human Renal cell carcinoma (RCC) is the most common kidney cancer constituting approximately 2-3% of all cancers worldwide and is responsible for 1.5% of cancer deaths globally. According to 2004 WHO classification of kidney tumors, Xp11.2 (TFE3) translocation RCC subtype was officially recognized. Common feature of Xp11.2 translocation cancer is chromosomal translocations leading to the formation of TFE3 fusion with different partners and TFE3 fusion protein expression. Aim of the present study was to understand the anti cancer impact of Sodium Butyrate (SB) using Xp11.2 translocated UOK146 & UOK109 RCC cell lines as in vitro model system. SB showed antiproliferative property against UOK146 & UOK109 as measured by MTT assay. FACS analysis followed by Acridine Orange staining and real time PCR of LC3, P62, BAX & BCL2 showed the autophagy & apoptosis in UOK146 & UOK109 respectively. RT-PCR showed that SB upregulate DIRAS1, a tumor suppressor gene in both the cell lines which was also epigenetically reactivated by Trichostatin A, demonstrating SB's role as epigenetic regulator. These observations indicate the role of SB as potential therapeutics for cancer treatment operational through epigenetic regulation.

Identification of [6]-Gingerol molecular targets and study their interaction using structure-based molecular modeling approach

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Chemoprevention by numerous phytochemicals derived from edible plants has been established as an accessible and promising approach for cancer control and management. [6]-Gingerol, a natural active component of ginger, is known to exhibit anti-oxidant, anti-inflammatory and anticarcinogenic properties by interacting and modulating the structure conformation of target proteins. However, the precise underlying mechanism by which [6]-Gingerol exerts chemopreventive effects are poorly understood and molecular targets of this plant-derived component is largely unknown. In the present study, we have identified a list of (n=85) potential 6-Gingeroltarget proteins using rational drug design approach integrated with publicly available potential drug target databases. The identified target proteins were mapped on pathways and disease association databases integrated in DAVID functional analysis tools. Significantly enriched biological pathways were VEGF signaling pathway, progesterone-mediated oocyte maturation and steroid hormone-mediated signaling pathways etc. linked to cardiovascular disease and various cancer types. We further assessed conformational flexible binding mode of [6]-Gingerol to the protein structure of topmost candidates identified in this study using *in silico* molecular dynamic (MD) simulation. Our preliminary analysis of [6]-Gingerol-protein complex (bound model) MD trajectories revealed higher flexibility of the active site region and local secondary structure modulation induced by [6]-Gingerol binding to protein as compared to the native (unbound model) structure. We believe that our present study could provide important clues for elucidating the underlying molecular mechanism of various chemo-preventive drugs or metabolites and may lead to the identification of newer anti-carcinogenic drug molecules.

BP-1T, an antiangiogenic benzophenone-thiazole pharmacophore, counteracts the HIF-1 signaling through p53/MDM-2 mediated HIF-1α proteosomal degradation.

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Introduction: Tumour microenvironment is an important module to promote angiogenesis;invasion and metastasisby inducing HIF-1α pathway. HIF-1a is overexpressed in many solid tumours where pVHL is mutated or silenced. Inactivation of pVHL pathway results in the up-regulation and nuclear accumulation of HIF-1α. Alternatively, HIF-1α ubiquitination and stability is regulated by p53 and E3 ubiquitin ligase-MDM-2 opening a new gateway of target for cancer therapy by promotion of p53/MDM2 pathway for proteosomal degradation. **Objectives:** To develop the anti-angiogenic small moleculeBP-1T (benzophenone-thiazole hybrid) to degrade HIF-1α by activating p53/MDM-2 proteosomal pathway. **Materials and Methods:** Cell based screening of BP-1T cytotoxic nature screened against multiple cancer types by MTT, LDH release and colony forming inhibitory efficiency by clonogenic assay.Effect of BP-1T on neovascularisation was verified by in-vivo & ex-vivo CAM, rat corneal & aortic ring assay, tumour induced peritoneal angiogenesis and CAM Xenograft byvisual and IHC.Mechanism of BP-1T on CoCl2 induced HIF-1a studied by RT-PCR, IB, and p53/MDM-2 pathway by MG132 proteosome inhibition, siRNA gene silencing, IB and cell fractionation. Altered downstream gene expressions were studied by IB, zymogram, migration & transwell invasion assay and ELISA.Pathophysiological

consequences on solid tumour growth parameters by in-vivo and molecular response underlying BP-1T effect measured by RT-PCR, immunoblot,IHC, gelatin zymogram and ELISA. **Results:** BP-1T exhibitspotent cytotoxicity at ~5μM against A549, MCF-7, SCC-9 and DLA with prolonged activity and effectively regressed neovessel formation both in reliable non-tumour and tumour angiogenic models where it reduced endothelial cell specific marker CD31 count in microvessels.Validation of antiangiogenic effect resulted in degradation of HIF-1α in p53 WT expressing cells such as A549, MCF-7 and DLA but not in p53 mutant SCC-9 cells inferring involvement of p53, as verified by siRNA approach. Mechanistically, BP-1T induced remarkable expression of p53 and MDM-2 which recruits the HIF-1α for proteosomal degradation as validated by MG132 proteosome inhibition and thereby down regulating HIF-1α dependent angiogenic genes such as VEGF-A, Flt-1, MMP-2 & -9, as a consequences migration and invasiveness is abolished. In-vivo solid tumour study mimics *in-vitro* results. **Conclusions:** A small cytotoxic molecule BP-1T, an effective phamacophore, degrades HIF-1α by activating the p53/MDM-2 pathway and thereby restricts HIF-1α leading to tumour angiogenesis which could be translated into a drug for cancer therapeutics in near

Treatment Outcome Of Radical Cystectomy For Carcinoma Urinary Bladder: An Indian Experience

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Aim: To assess the treatment outcome in patients treated with Radical cystectomy and bilateral pelvic lymphadenectomy for carcinoma urinary bladder. **Material and Methods**: In the present study 68 patients of diagnosed case of carcinoma urinary bladder who had undergone treatment between January 2009 to March 2013 were evaluated. The tumor staged from cT2-T4a and had initially undergone transurethral resection of bladder tumor. 53 were males and 15 were females. The age ranged between 46-70 years. Histopathology was transitional cell carcinoma. All patients underwent CECT Chest, and MRI Abdomen as a part of staging work up. All the 68 patients were counselled and underwent Radical cystectomy. Ileum was used as urinary conduit in 61, jejunum in 5 and sigmoid colon in 2 patients respectively. Patients were referred for adjuvant Chemotherapy and or Radiotherapy on the basis of histopathological findings. A preformed checklist was prepared and various parameters about the conduit and quality of life were recorded. **Results:** Histopathological stage varied from pT2N0-pT4aN0-2. Median follow up period was of 2 years. Ileal conduit offered minimal postoperative side effects in contrast to jejunal or sigmoid conduit. 29 patients had urinary tract infection. 2 patients required re-exploration for urinary leak. No mortality occurred. Postoperatively patients were referred for adjuvant chemotherapy and or Radiotherapy. 5 developed distant metastases (4 bone,1 brain and lung). **Conclusion:** Radical cystectomy and pelvic lymphadenectomy provide durable local control in patients with carcinoma urinary bladder. Ileal conduit emerged as the conduit of choice for urinary diversion.

A very rare case of neuroendocrine carcinoma of the stomach

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Introduction: We herein report a very rare case of Neuroendocrine Carcinoma of the stomach known for its aggressive behaviour and poor prognosis. To the best of our knowledge, only few cases have been reported in world and India till date and our case may be second such one in India. Gastric neuroendocrine neoplasms (NENs) are relatively rare tumors that account for less than 1% of all gastric tumors and Neuroendocrine carcinoma (NECs) of the stomach are rarer, representing less than 10% of gastric NENs. Neuroendocrine carcinoma (NEC) of the stomach has been recognized as a highly malignant tumor; however, because of its rarity, limited information is available regarding its clinico-pathologic characteristics and appropriate treatment modalities. **Objectives**: The objective of presenting this case is to bring out the challenges in dealing with a rare case like this, the lines of therapy given and the response. Due to its rarity, there are no standard guidelines on management of such a disease. It was a diagnostic and therapeutic challenge for us. **Materials and Methods:** This is a prospective study of a sporadic case of Neuroendocrine Carcinoma of the stomach with the endeavour to highlight the natural history of the disease including the clinical presentation, evaluation, overall course, multimodality treatment given and the response to treatment. **Result**: A 42 years old male presented with vague abdominal discomfort and significant weight loss. Upper gastrointestinal endoscopy revealed ulcero-proliferative growth in pylorus. Computed tomography abdomen showed thickening of the pylorus with loco-regional lymphadenopathy. A Radical Distal Gastrectomy was performed. Post-operative histopathology revealed High Grade Neuroendocrine Carcinoma of stomach with CK, EMA and Chromogranin positivity on immunohistochemistry. He has been treated with adjuvant Etoposide Cisplatin based chemotherapy followed by radiotherapy and has shown significant response to treatment. **Conclusion**: We reported a case of sporadic Neuroendocrine Carcinoma of stomach which are very rare, representing less than 10% of gastric NENs and such rarity has made it difficult to understand precisely their biological nature and to establish optimal treatment options. By reporting this case we want to get suggestions and feedbacks from oncologists of all three branches on approaching a rare tumor as this.

Keywords: Neuroendocrine Carcinoma of stomach, Gastric neuroendocrine neoplasms, immunohistochemistry

Changing patterns of colorectal cancer in young patients in india:have we been underlooking?

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Introduction: Colorectal cancer (CRC) is the 3rd most common cancer in men &2ndin women worldwide. In sharp contrast to overall trends, the incidence of CRC in young patients appears to be increasing. **Objectives:** This study was undertaken to evaluate age of presentation, histopathological features, AJCC stage, prognosis in terms of mortality rate in young patients(<40years) of colorectal cancer. **Material and Methods:** It is a Hospital based retrospective study comprising of 43 patients studied between Jan 2013 to Oct 2014 in Department of Surgery & Chemoradiotherapy at a Tertiary Care Hospital. **Results:** The incidence of colorectal cancer in our hospital in Central India is 38%.Majority of the young colorectal cancer patients were in 30-40 years age group(43%)& youngest to be 15 yrsold.At the time of presentation, most of them had stage III disease(41%) & stage II(37%) according to AJCC score. Almost 51% patients had poorly differentiated adenocarcinoma.Definitive surgery was possible only in44% patients. Similarly, chemotherapy was received by only 37% patients with or without surgery. Mortality rate was found to be 4% within a span of 2 years. **Conclusions:** The idea of colorectal malignancies being a disease of old age is not true anymore. Comparing the statistics with the previous studies around the globe, the incidence of colorectal malignancies in young patients is much higher in Central India. Moreover,colorectal cancer in young patient presents with specific clinico-pathologic characteristics that are worthy to be explored and managed differentially.Increased awareness,high degree of clinical suspicion among health care professionals & in general population along with better screening techniques are needed to identify these young patients at an early stage of malignancy. For younger patients who have poor survival, especially those with stage III and IV disease, more aggressive adjuvant therapies are recommended.

Key words: Colorectal, Adenocarcinoma, Young

Case series of primary GI carcinomas in children and adolescents

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Background: Primary GI carcinomas are extremely rare cancers in childhood. They are associated with high risk features and worse outcomes than adults. The low index of suspicion and aggressive histological subtype leads to delay in diagnosis and poor outcomes. **Case Series:** Our series describes 9 cases of primary GI carcinomas seen at our center in last 8 years. This cohort comprised of 2 cases of gastric, 3 cases each of colonic and rectal and 1 case of metastatic carcinoma in the abdomen with an unknown primary. The age ranged from 12 to 18 years. Patients presented with symptoms ofrecurrent pain abdomen, anorexia, altered bowel habits, weight loss and vomiting of duration ranging from 10 days to 8 months. Only one of the nine, with a diagnosis of gastric carcinoma, had associated polyposis. All the patients presented with stage III disease, except 2 with stage IV disease. Out of the nine, two are currently on treatment, one of them has received concomitant chemoradiation for rectal carcinoma and is planned for a sphincter saving surgery. Four underwent upfront surgery followed by adjuvant chemotherapy and 1 patient received only palliative chemotherapy. Five children expired because of progressive disease and 2 abandoned treatment in view of poor prognosis and eventually died. **Conclusion:** GI carcinomas, a rare entity in children pose a diagnostic challenge and carry a grave outcome. Most patients present with advanced disease and are treated based on adult protocols.

Metastatic Breast Cancerto stomach: Report of Five Cases and Review of the Literature

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Introduction: Breast cancer is most common cancer in women worldwide andin India. Breast cancer is known to spread to bone, lung and liver commonly. However, spread to gastrointestinal tract is rare. As compared to other parts of the gastro intestinal tract, stomach is the most commonly involved metastatic site. Information is very sparse regarding the management of patients with cancer breast metastasizing to stomachas there are very few case series and reports that are available in literature. **Objectives:**. Primary gastric cancers must be differentiated from metastasis to stomach as the later condition is underdaignosed and the management of both conditions are different and associated with poor prognosis.We present a case series of five is patients of breast cancer with mixed pathology metastasising to stomach with review of literature. **Material and Methods:** Spread to the gastro intestinal tract(GIT) is of special mention due to its uncommon spread and diagnostic dilemma. The presenting symptoms may be from the absence of symptoms to non specific abdominal pain, nausea, vomiting and obstruction. The treatment can be curative or palliative, in the form of chemotherapy, surgery or best supportive care. **Results: Conclusions:** Gastric metastasis from breast cancer is very rare. Due to its non specific symtoms it posses a challenge to the treating surgeon both in making a correct diagnosis and planning treatment. A high index of suspicion must be maintained while treating a patient with gastric symptoms , especially with history of previous breast cancer.clinical expertise along with endoscopic, radiological and pathological evaluation with IHC is essential to discriminate primary gastric cancer from breast cancer metastasis to the stomach which will result in optimal outcome in such cases.

Long-term Outcomes after treatment with surgery with or without radiation therapy for Anorectal malignant Melanoma: Data From a regional cancer center in south India.

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Background: Malignant melanoma of the rectum is an extremely rare and very aggressive disease.This entity constitutes only 0.54% of all anorectal malignancies and less than 1% of all melanomas.Patients, predominantly women, typically present with local symptoms in the fifth or sixth decade of life.Anorectal malignant tumors are increasing in frequency for unknown reasons. Surgery is the principal treatment, and the role of adjuvant therapy has not been defined. The aim of this study is to present the experience and outcomes of the treatment for the patients with anorectal melanoma from our institute, Kidwai memorial institute of oncology, a regional cancer center in south india. **Material and Methods:** This is a retrospective study conducted between 2005 to 2013 at Kidwai memorial institute of oncology. Records of 32 registered patients with anorectal malignant melanoma (ARMM) were analyzed and patients with metastatic disease were not included. Patients were treated with surgery (abdominoperineal resection or wide local excision) with or without radiotherapy. Comparison was done with special reference to survival, and local recurrences. **Result:** Of 32 patients, 18 were male with mean age at diagnosis of 60 years and 14 were female with mean age at diagnosis of 62 years. 22 patients underwent abdominoperineal resection, 10 patients underwent wide local excision and 5 patients received pelvic irradiation in conjunction with surgery.The 2year survival rate of the all patients with anorectal melanoma was 20% with a 5 year survival rate of 21 patients treated before 2010 was 12%.The overall median survival was 12 (range from 3–61)months. The difference between survivalwas not statistically significant between the groups. Local recurrence was significantly more in WLE group.Of the 10 patients treated initially with local excision, six required reoperation and two underwent salvage abdominoperineal resection. Depth of invasion had significant effect on survival and was found to be an important prognostic factor influencing survival. Radiation therapy did not decrease local recurrence rate in studied patients. **Conclusion:** At time of diagnosis systemic dissemination is almost universal in patients with

Age	Pathology	TNM	Other Metastasis	Receptor status			IHC			Treatment	Survival after metastasis (months)
				ER	PR	her2	her2	GCDFP-15	mammaglobin		
56	IDC	pT2N2M0	Bone, liver	+ ve	- ve	+ ve	+ ve	+ ve	+ ve	Sx,CT,RT,HT	18
61	IDC	pT3N1M0	Bone,Lung	- ve	- ve	- ve	- ve	+ ve	+ ve	Sx,CT,RT	6
51	ILC	pT2N2M0	Bone, Liver, brain, Peritoneal carcinomatosis	+ ve	- ve	+ ve	+ ve	+ ve	+ ve	Sx,CT,RT,HT	16
63	ILC	pT3N2M0	Lung, Brain	+ ve	- ve	- ve	-ve	+ ve	+ ve	Sx,CT,RT	14
48	ILC	pT3N1M0	Bone, lung, skin	+ ve	+ ve	+ ve	+ ve	+ ve	+ ve	Sx,RT,HT	11

AMM. Improving local control is important sincesome patients will survive up to 5 years. Complete or R0 resection is the first choice of treatment for anorectal melanoma and early diagnosis is the key to improved survival rate for patients with anorectal melanoma.Survival of patients with anal melanoma is similar after local excision, rectal resection or radiotherapy irrespective of whether patients have localized or regional disease.

Identification of genetic polymorphisms for Gastric cancer in South Indian population

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Background: Gastric cancer is the fourth most common cancer and the second major cause of cancer related deaths worldwide. Gastric cancer is one of the most common cancers in South India. Most of the gastric cancer cases are presented at the advanced stage and this makes it difficult to provide a successful treatment. A predictor that helps in identifying the risk of developing a disease in a population will be useful to detect the group that is susceptible to the disease. Hence, a case control study was undertaken to investigate the role of Single nucleotide polymorphisms (SNPs) in Gastric cancer. **Materials and Methods:** A case-control study (n=180 cases and 320 controls) was undertaken to investigate the role of 4 SNPs in-TGFβ C-509-T, TGFβ T-869-C, XRCC1 Arg-194-Trp and IL4 C-590-T in Gastric cancer risk. Genotyping was done using Taqman Allelic discrimination assay. **Results:** Taqman allelic discrimination assay was performed for TGFβ C-509-T, TGFβ T-869-C, XRCC1 Arg-194-Trp and IL4 C-590-T in 180 cases and 320 healthy controls. The genotypic frequencies obtained are listed in Table 1, 2, 3 and 4. Genotypic frequencies were compared between the cases and controls. Genotypic frequencies were also compared within the cases between the genders, type of gastric cancer and their grades. Chi square analysis was performed using Epi info software at 95% CI, α=0.05 to find the association between the different parameters. There was no relationship observed in our study while comparing the genotypic frequency between the cases and controls, between the genders, between the type of gastric cancer and between the grades. **Conclusions:** Our results indicated that the four SNPs did not have any relationship with predicting the risk of the disease. Further correlation on SNP data and lifestyle, dietary habits of the cases and controls has to be done to find whether they can be used to predict the gastric cancer susceptibility in South Indian population.

Table 1: Genotypic frequency for TGFβ C509T

	Homozygous CC	Heterozygous CT	Homozygous TT
Cases	0.165	0.476	0.359
Controls	0.190	0.437	0.373

Table 2: Genotypic frequency for TGFβ T869C

	Homozygous AA	Heterozygous AG	Homozygous GG
Cases	0.006	0.229	0.765
Controls	0.02	0.231	0.749

Table 3: Genotypic frequency for XRCC R194W

	Homozygous TT	Heterozygous CT	Homozygous CC
Cases	0.017	0.313	0.670
Controls	0.013	0.228	0.759

Table 4: Genotypic frequency for IL4 C590T

	Homozygous TT	Heterozygous CT	Homozygous CC
Cases	0.017	0.313	0.670
Controls	0.013	0.228	0.759

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A prospective non-randomised study of total robotic 3 stage esophagectomy for carcinoma esophagus-single institute indian experience

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Background: To evaluate the safety and technical feasibility of robotic assisted three stage esophagectomy. We also aimed to analyze short term oncological outcome of this procedure**. Material and Methods:** It is prospective non randomised study from July 2011 to June 2014; we included thirty five consecutive histologically proven surgically resectable(T1-3, N0-1, M0) carcinoma esophagus patients. All underwent total robotic assisted transthoracic and transperitoneal three stage esophagectomy. **Results:** Median age was 61 years (range 38-72). Majority 74.29% (n=26) were squamous cell carcinoma and remaining were adenocarcinoma 25.71% (n=9). The most common location of the tumour was mid thoracic esophagus 51.43% (n=18). Total docking time, thoracic docking time, total operative time, thoracic phase operative time and blood loss in the initial 10 cases were 67.9±13.24 min, 32.2±9.74 min, 429.2±57.65 min, 96.6±20.33 min and 433.20±48.72 ml respectively and in the subsequent 25 cases, 33.20±4.16 min, 13.76±3.43 min, 321.13±13.75 min, 57.04±9.15 min and 256.32±17.52ml respectively. Median number of lymph nodes dissected was 32. Major complications were in 3 patients (diaphragmatic hiatal hernia, azygos vein bleeding and anastomotic leak). One case converted to open method. Two cases required one day ventilator support, with ICU stay for 1 day in 15 cases, 2 days in 5 patients. Median hospital stay was 8 days. There was no in-hospital or 30 day mortality. All had microscopic negative resection margins. In the median follow up of 24 (2-45) months, one patient recurred in cervical and mediastinal lymph nodes. **Conclusion:** Robotic assisted three stage esophagectomy has the benefits of minimally invasive surgery and immediate oncological outcomes are comparable to conventional open surgery. Robotic surgery gives 3-dimentional and magnified view and endowrist gives better dexterity with intuitive movements. These technical advantages make oncologically sound surgery. Therefore total robotic three stage esophagectomy is a safe and feasible technique for the treatment of esophageal cancer.

Key words: Total robotic esophagectomy, minimally invasive esophagectomy, three stage esophagectomy

Peri operative management of Hyperthermic intraperitoneal chemotherapy (HIPEC) for peritoneal surface malignancies- single institute Indian experience

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Introduction: Cytoreductive surgery (CRS) and hyperthermicintraperitoneal chemotherapy (HIPEC) has shown better oncologic outcomes with acceptable morbidity in peritoneal surface malignancies (PSM). CRS+ HIPEC is a unique clinical situation in which post operative events due to complex pathophysiological changes happen during the procedure. We evaluated the perioperative toxicities of extensive CRS+ HIPEC in PSM and effective management of toxicities. **Methods:** In our prospective observational study from February 2013 to June 2015 fifty sevenPSM patients with ECOG 0/1 either primary or previously treated by surgery and systemic chemotherapy were submitted to CRS & HIPEC. We included peritoneal confined ovarian carcinoma 57.1%, colorectal carcinoma 16.1%, pseudomyxoma 12.5%, mesothelioma 3.6%, and gastric carcinoma 3.6% without extra abdominal disease. HIPEC was done by dedicatedteam of surgeons, anesthetists, intensivists and medical oncologists, usingFDA approved Belmont® hyperthermia pump with temperature of 42°C for 30-90 minutes. The chemo regimes were based on type of primary malignancy.Perioperative outcome data were collected and analysed. **Results:** Among 57 patients, 73.7%were females and 26.3% were males. Median duration of surgery including HIPEC was 9 hours. Median hospital stay was 13.96 days. Median time for gastrointestinal recoverywas 5.35 ± 1.4 days. Extended ICU stay required for 19.7% patients. Recurrent disease ($p=0.028$) and closed method ($p<0.001$) associated with more adverse outcomes. Closed method also associated with more wound related complications ($p<0.001$) and ARDS ($p=0.005$). Most common grade 3 & 4 complications were hypocalcemia 32.1%, hypokalemia 32.1%, anemia 21.4% and thrombocytopenia 7.1%. Multivisceral resections associated with increased infections ($p=0.04$), longer hospital stay ($p=0.005$), prolonged GI recovery ($p=0.039$) and ventilator need ($p=0.008$). Major surgical morbidity occurred in 8.9% patients requiring surgical intervention. Sixty days operative mortality was 1.8%. **Conclusion:** We suggest plenty of oral liquids and decreased roughage intake and early start of total parenteral nutrition to reduce the subacute intestinal obstruction. Preoperative chest physiotherapy and high protein diet will lessen adverse events significantly. The expectant management of dyselectrolytemia with improved anesthesia management, critical care, and post- op rehabilitation will improve perioperative outcomes.

Key words: Peritoneal surface malignancies, Cytoreductive surgery, Hyperthermicintraperitoneal chemotherapy, HIPEC.

Retrospective study of clinicopathologic features and prognosis of neuroendocrine carcinoma of the esophagus

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Background: Esophagealneuro-endocrine carcinoma(NEC) is a rare but aggressive neoplasm known to have a poor survival outcome.In 2010, the WHO proposed new diagnostic criteria for this disease that mainly depend on the rate of cellular proliferation. Owing to their rarity, an optimal treatment strategy has not been established and various combinations of surgery, radiotherapy & chemotherapy have been described. **Objective:** To analyse the clinico-pathologic features and prognosis of neuroendocrine carcinoma of esophagus. **Material and Method:** This is a retrospective study of cases of neuroendocrine carcinoma of esophagus from a regional cancer institute in south India over a period of five years from 2008 to 2013. **Results:** Out of thirty- two patients treated over the period of five years, 24 were male &8 female, having median age of 62 years. Twenty patients had large-cell NEC and 12 had small-cell neuroendocrine carcinoma. Synaptophysin was positive in all the cases while chromogranin was positive in 23 cases. Fourteen patients had locoregional disease and 17 had distant metastasis. Patients with locoregional disease were treated with chemoradiation with or without surgery or with surgery only. Patients with distant metastasis were treated with systemic therapy. Overall survival was better in patients with non-neuroendocrine component than with pure NEC($P=0.03$). There was no difference in prognosis between patients with large-cell NEC and those with small cell NEC. **Conclusion:** EsophagealNEC is an aggressive tumor and patients with mix NEC have better outcome.

Keywords: Esophagus carcinoma; neuroendocrine; small cell;mixed

Prevalence And Predictors Of Apical Lymph Node Involvement In Locally Advanced Rectal Cancers In The Era Of Combined Modality Therapy: Prospective Study

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Introduction: Lymph node status is a major prognostic factor for survival in patients with rectal cancer. The incidence of metastatic nodes at the origin of Inferior Meseneteric Artery (Apical nodes) has been reported to be relatively low in several studies, ranging from 0.3 to 8.6 percent. In this era of standardized Total Mesorectal Excision and Neoadjuvant cheomoradiotherapy there is a need to study the rationality for apical nodal retrieval and its oncological safety. **Materials and Methods:** With the primary aim of finding the incidence of apical lymph node involvement in locally advanced rectal cancer (stages II & III) taken up for surgery after neoadjuvant chemo radiotherapy, the study was undertaken in Department of Surgical Oncology at Regional Cancer Centre. During surgery apical nodes were sampled and sent separately for pathology. **Results:** From Nov 2013 to Sep 2015 , apical node was sampled in 140 cases. Of these lymph nodal tissue was identified in 51.4% (72/140). Two cases (2/72)had positiveapical nodes (2.8 %). First one had pathological complete response in the specimen but at apical node and the next had p T3N2 with ECS, PNI and close CRM. Three cases had prolonged bladder drainage. (2%). **Conclusion:** The incidence of apical node involvement remains low in locally advanced rectal cancers operated after neoadjuvantchemoradiation.

Diagnostic Accuracy of Raman spectroscopy for Colorectalcancer: A Meta-analysis

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Background: In global, colorectal cancer is the third most commonly diagnosed cancer in males and the second in females, with approximately approximately 1.4 million new cases and700,000 deaths per year. Raman spectroscopy (RS) is fast, non-invasive, relatively specific, widely available and convenient, which can provide important biochemical macromolecules information including nucleic acids, proteins and lipids based on the inelastic light scattering. RS has been a potential method for colorectal cancer early diagnosis.This work aims to determine, in a meta-analysis for the first time, the diagnostic performance of RS contrast with biopsy in patients with colorectal lesions. **Material and Methods:** Relevant studies published from January 2000 to June 2015 were identified through a comprehensive search of PubMed, Medline, Embase and the Cochrane Library. The search

terms were combinations of the relevant medical subject heading (MeSH) terms, key words, and word variants for "colorectal cancer" or "colon cancer" or "rectum cancer" and "Raman spectroscopy". Studies evaluating the diagnostic performance of RS in patients suspected of having colorectal cancer who underwent RS and biopsy were reviewed. We included studies using biopsy as a reference standard. The pooled weighted sensitivity and specificity were calculated and a summary receiver operating characteristic curve (SROC) was rendered by using Meta-Disc Version 1.4 and STATA 12.0. Further subgroup analysis was conducted in this work. We conducted Deeks ' funnel plot asymmetry test to investigate publication bias. The quality of the studies was rated with the QUADAS 2. **Results:** The search strategy produced 113 hits after duplicates removed. Finally, 14 studies were included in this meta-analysis. A total of 1274 patients and 1660 lesions were assessed. Pooled weighted estimates of sensitivity and specificity were 0.87 (95% confidence interval: 0.86 - 0.89) and 0.89 (95% CI: 0.88 - 0.90), respectively. The pooled diagnostic odds ratio of RS in the diagnosis of colorectal cancer was 66.42 (95% CI, 32.90 - 134.08).Symmetric SROC curves showed an overall area under the curve of 0.9578. There was no significant publication bias all around the world (P =0.34). When we grouped by country, the pooled sensitivity, specificity and DOR for Chinese patients were 0.85 (I^2=87.6%, P=0), 0.89 (I^2=88.1%, P=0) and 88.11 (I^2=84.7%, P=0), while for other countries, the pooled data were 0.90 (I^2=84.2%,P=0), 0.89 (I^2=89.4%, P=0) and 57.46 (I^2=79.6%, P=0), respectively. When we grouped by modalities of RS, the pooled sensitivity, specificity and DOR for studies using NIRS were 0.89 (I^2=82.9%, P=0), 0.90 (I^2=87.9%, P=0) and 55.62 (I^2=77.1%, P=0), while the pooled data for studies using SERS were 0.96 (I^2=77.4%, P=0.0041), 0.98 (I^2=69.6%, P=0.0196) and 865.04 (I^2=61.9%, P=0.0489), respectively. When we grouped by samples, the pooled sensitivity, specificity and DOR of RS performed on tissues were 0.91 (I^2=83.6%, P=0), 0.90 (I^2=89.9%, P=0), and 76.14 (I^2=78.3%, P=0), while the pooled data for studies using blood were 0.89 (I^2=85.3%, P=0), 0.94 (I^2=82.8%, P=0) and 159.57 (I^2=83.2%, P=0), respectively. When we grouped by diagnostic algorithms, the pooled sensitivity, specificity and DOR of PCA/LDA were 0.88 (I^2=89.0%, P=0), 0.91 (I^2=90.6%, P=0), and 87.96 (I^2=84.4%, P=0), while the pooled data for studies using PLS/LDA were 0.86 (I^2=65.5%, P=0.0206), 0.88 (I^2=30.5%, P=0.2183) and 48.83 (I^2=71.6%, P=0.0071), respectively. When we grouped by in vivo or ex vivo, the pooled sensitivity, specificity and DOR of in vivo were 0.87 (I^2=72.6%, P=0.0121), 0.88 (I^2=44.4%, P=0.1447), and 52.25 (I^2=75.5%, P=0.0066), while the pooled data for studies ex vivo were 0.88 (I^2=88.3%, P=0), 0.91 (I^2=90.0%, P=0) and 78.67 (I^2=83.5%, P=0), respectively. When we grouped by frequency of RS, the pooled sensitivity, specificity and DOR of low frequency were 0.87 (I^2=88.0%, P=0), 0.90 (I^2=90.0%, P=0), and 66.53 (I^2=82.4%, P=0), while the pooled data for high frequency were 0.93 (I^2=0.0%, P=0.8836), 0.88 (I^2=0.0%, P=0.6353) and 101.95 (I^2=0.0%, P=0.6128), respectively. **Conclusions:** RS has considerable sensitivity and specificity in the evaluation of colorectal lesions. RS is a promising, reliable method for differential diagnosis of benign and malignant colorectal lesions, especially NIRS and SERS modalities, and the PCA/LDA diagnostic algorithm also increase diagnostic accuracy of RS. Concerning low frequency/high frequency and in vivo/ex vivo, the accuracies are still controversial. Further studies are still required to confirm our findings.

Keywords: Raman spectroscopy, colorectal cancer, diagnostic accuracy

Correlation of ClinicopathologicalParameters with Presence of HER2 in Gastric Cancer

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Background: Gastric cancer is one of the common cancers with poor prognosis having overall five year survival less than 30%. Important factors for poor prognosis are advanced disease at diagnosis, histological grade, perineural invasion, and lymphovascularinvasion. Recently human epidermal growth factor receptor2 (HER2) has been studied as a prognostic marker for gastric cancer. HER2 overexpression has been correlated to poor outcomes and more aggressive disease. Moreover it provides the rational of anti-HER2 therapy in gastric cancer. This study was conducted to evaluate the role of HER2 as a prognostic factor in gastric cancer. **Methods**: A prospective observational study was conducted on all patients with gastric adenocarcinoma admitted in Tribhuvan University Teaching Hospital, Kathmandu, Nepal over ten month period (January 2015 to October 2015). The clinical and pathological parameters including age, sex, chief complaints, perioperative outcomes, grade, stage of tumor, lymph node involvement, CEA level were recorded. HER2 was examined on surgical or endoscopic specimen by Immunohistochemistry or FISH method.Patients were divided in two groups based on the presence or absence of HER2 and their clinical and pathological parameters were compared. **Results:** There were total of 41 patients included in the study. Twenty six (63%) were male and 15(37%) were female. Mean age was 58.4±13.4 years. Twenty four (58.5%) of the tumor were in distal third of the stomach. Thirteen (31.7%) patients were at stage IV of the disease. Seven patients (17.1%) were positive for HER2 antigen. Raised CEA level was found in (54%) gastric cancer patients.In comparison to HER2 negative patients, HER2 positive patients had significantly higher CEA level (p: 0.04), more poorly differentiated tumors (p: 0.02) and more nodal metastasis (p: 0.001). There was no significant difference in age, tumor size, tumor location, perineural and lymphovascular invasion between two groups of patients. **Conclusion:** HER2 was positive in 17% of Nepalese gastric cancer patients. HER2 positive tumors were associated with poor prognostic parameter like more nodal metastasis and higher grade of cancer.

Key words: Gastric cancer,HER2, Prognostic factors

Scenario of minerals in etiology of gastric cancer patients

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Introduction: Gastric cancer (GC) continues to be the second most common malignant neoplasm around the world with varied regional incidences due to different factors and in Kashmir among all the cancers GC has been reported to be a highly prevalent malignancy,constitutes about 30%-40% of all malignancies. Various studies have been done on incidence rate and distribution of gastrointestinal cancers in Kashmir, but there was no information regarding the mineral status of the GC patients till date. Since the beginning of the 1970s the minerals has received a lot of attention as per the variations of mineral concentration in serum has been related to increased risk for various types of cancer in humans. **Objectives:** To study the role of minerals in gastric carcinogenesis. **Material and Methods:** In this studyserum of three hundred blood samples were used to analyze the status of concentration of Selenium (Se), Copper (Cu), Zinc (Zn) and Iron (Fe) in gastric cancer (GC) patients and healthy individuals by using atomic absorption spectrophotometer. **Results:** There was a significant ($p<0.05$) decline in the concentration of Se in serum samples of GC patients as comparison with the healthy individuals and on comparison within the genders among GC patients the level of Se concentration remained insignificant. Concentration of Cu in serum samples of GC was increased significantly ($p<0.05$) as comparison with the healthy individuals and on comparison within the genders among GC patients there was a significant ($p<0.05$) decline in the concentration of Cu in male as comparison with the female group, There was a significant ($p<0.05$) decline in the concentration of Zn in serum samples of GC patients in our study as comparison with the healthy individuals and on comparison within the genders among GC patients the level of Zn concentration remained insignificant $p>0.05$. Level of difference of Fe remain insignificant ($p>0.05$) in serum of GC patients and within gender among GC patients. **Conclusion:** There is under or overtake of minerals by malignant cells as per there requirement and may be the cause of increase or decrease of particular mineral concentration in serum of gastric cancer patients which may be one of the

Significance of Circulatory Serum Interleukin 18 and 10 levels in Locally Advanced and Advanced Metastasis Stage of Prostate Carcinoma

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Background: Prostate cancer is one of the most common cancer afflicting men today. Prostate biopsy, an invasive technique is normallyutilized for diagnosing this cancer. Efforts are being made for accurate and precise non-invasive biomarker. Diagnostic accuracy and precision of prostate specific antigen (PSA) has been well recognized. IL-18 is a pro-inflammatory cytokine expressed on several cells including prostate gland elements, and is a vibrant mediator of immune responses with anti-cancerous properties. IL-10 is an anti-inflammatory cytokine that is associated with tumour malignancy which causes immune escape. Serum interleukin-18 (IL-18) and interleukin-10 (IL-10) have shown their diagnostic ability in other cancers but not explored well in prostate cancer. This study, thus decides the diagnostic and prognostic significance of PSA, IL-18 and IL-10 prospectively in patients with carcinoma prostate. **Methods:** A total of 285 patients, aged 40-84 years were investigated during 2007 to 2013 and recruited for this study after Institutional ethical approval. Total 285biopsy approved patients were included in study and grouped into various stages as per TNM classification. Peripheral blood samples of all patients and age matched control subjects were obtained at baseline and estimation of PSA, IL-18 and IL-10 was done by enzyme linked immunosorbent assay (ELISA). Data were analyzed with appropriate statistical tools like ANOVA and Graph PAD. **Results:** The baseline levels of PSA, IL-18 and IL-10 in all groups of carcinoma prostate were found to be significantly ($p<0.05$) higher than Control. The levels of IL-18 and IL-10 also found to be elevated significantly in stage T3 ($p<0.05$) and T4 ($p<0.05$) as compared to stage T2. The levels especially of IL-18 is found to be well associated with progression of the disease of various groups ($r=0.80$, $p<0.05$). In contrast, IL-10 showed significant direct association with progression of carcinoma ($r=0.82$, $p<0.05$). Study concluded that serum IL-18 has to be a better diagnostic marker with higher specificity and sensitivity and IL-10 may be valuable as a prognostic marker than PSA in carcinoma prostate.

Key words: Prostate specific antigen, interleukin-18, interleukin-10, prostate cancer,

Menadione Downregulates Wnt Signaling Pathway and Reverses EMT in Colorectal Cancer Cells

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Introduction: Colorectal cancer is the third most common cancer in men and the second in women worldwide(1).Although colorectal cancer incidence has been steadily decreasing in U.S and Canada,the incidence is rapidly increasing in Japan, Korea and China (2Activating mutations inthe Wnt signaling pathway are necessary for the development of colorectal cancer followed by additional mutations accumulated due to two possible courses: (a)-Chromosomal instability associated with KRAS point mutation andloss of chromosomal region that encompasses p53 and other tumor suppressors on18q and17p. (b)- Defect in DNA mismatch repair, resulting in high microsatellite instability(3).Epithelial-mesenchymal transition (EMT) is a process which facilitates the process of cancer cell invasion and metastasis(4, 5). Activated Wnt signaling pathway is a known inducer of EMT in different cancers(6).Menadione is a naphthoquinone and is also a synthetic analogue of vitamin K (vitamin K3).Menadione has been found to exhibit anti-cancer activity in cancer of liver, cervix, nasopharynx, lung, stomach and breast and also in leukemias and lymphomas. Menadione has also been shown to act as a radiosensitizing agent, increasing the survival time in inoperable bronchial carcinoma patients(7).It also increased the cytotoxicity of mitomycin C and modulates the resistance of advanced gastrointestinal cancer (particularly colorectal cancer) to mitomycin C in a phase II clinical trial on patients(8). **Objectives**: To study the effect of menadione on Wnt signaling and EMT in human colorectal cancer cells. **Materials and Methods**: **Reagents-** Menadione was purchased from Sigma (St.Louis,MO,USA).A stock solution of 5mM menadione was prepared in dimethyl sulfoxide (DMSO) and diluted in cell culture medium to get the different working concentrations. Dulbecco's Modified Eagle Medium (DMEM) and Fetal bovine serum were purchased from GIBCO (Invitrogen,Carlsbad,USA). Polyvinylidene difluoride membrane and Enhanced chemiluminescence kit were obtained from BIORAD (Hercules, CA,USA).β-Actin antibody was obtained from Sigma whereas CTNNB1 and CCND1 antibodies were obtained from Santa Cruz (CA, USA) and horseradish peroxidase conjugated secondary antibody was obtained from Jackson ImmunoResearch Inc. (PA, USA).CRL-1790 cells were a kind gift from Dr. Kundan Sengupta (ISSER, Pune). **Cell Culture**: SW480 and SW620 cells were cultured in complete Dulbecco's Modified Eagle Medium (c DMEM) and CRL-1790 was cultured in Eagle's Minimum Essential Medium (EMEM) supplemented with Streptomycin (100µg/ml), Penicillin (100 U/ml) and 10 % FBS. Cells were maintained in a humidified incubator at 37°C with 5% CO_2. **MTT Assay:** Cells were seeded in 96-well plate at a density of 8000 cells/well and grown overnight. Cells were then treated with increasing concentrations of menadione. After 24 and 48 h of drug treatment 10µl of 5mg/ml 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) made in phosphate buffered saline (PBS) was added in each well and incubated at 37°c with 5% CO_2 in a humidified incubator for 3 h, followed by dissolution of formed formazan in 100 µl of dimethyl sulfoxide (DMSO).The optical density was measured at 570 nm with 655 nm as background reference. **Clonogenic Assay:** 1000 cells were seeded in 12-well plate and kept in incubator for overnight. Next day, cells were treated with drugs and incubated for 12 days in incubator at 37°C with 5% CO_2. Cells were washed with PBS and fixed in 3:1 ratio of methanol and acetic acid for 5 minutes. After removing the fixing reagent, 0.5% of crystal violet (in methanol) was added and kept at room temperature for 15 minutes. Cells were washed with tap water and kept on room temperature for a day to get dry. Cells were scanned to get the image and counted. **Protein Isolation and Western Blotting:** After 24 h of drug treatment, cells were washed with PBS and total protein was extracted using RIPA lysis buffer (20 mM Tris, pH -7.5), 150 mM sodium chloride, 1mM ethylene diaminc tetra acetic acid (EDTA),1mM phenyl methane sulfonyl fluoride, 20mM sodium fluoride, 1% protease inhibitor, incubated for 1 h and centrifuged.Bradford assay was used to estimate the concentration of protein and 50µg of protein was loaded in SDS-PAGE and transferred to polyvinylidene difluoride (PVDF) membrane. The membrane was incubated with primary antibodies against CTNNB1, CCND1, CDH1, SNAI1, VIM (1:1000 dilution) and ACTB(1:10,000 dilution) overnight and incubated with an HRP-conjugated secondary antibody (1:5000 dilution). Protein bands were detected by Enhance Chemiluminescence Detection Kit and visualized by VersaDoc System (Bio-Rad). **Wound Healing Assay:** 1 million of cells were seeded in a 48-well plate and incubated for overnight in incubator. A scratch was made on the confluent layer of cells using 10 µl pipette tip gently washed with media, treated with DMSO/menadione and maintained in serum free DMEM for 48 h. Migration of cells was measured by comparing the surface area of wound at 0 h and 48 h of drug treatment. Image was taken at 4X magnification and area measured using ImageJ software. **Cell Cycle Analysis:** Cells treated with menadione were washed with PBS-EDTA and then harvested using 0.25 % trypsin EDTA and suspended in c DMEM. Cells were centrifuged and washed twice with PBS. Cells were fixed in 70% ethanol made in PBS and left overnight. Fixed cells were centrifuged, washed with 0.1% FBS in PBS and re-suspended in 300µl PBS.3µl of RNase (20µg/ml) was added and incubated for 1 h at 37°C. 3 µl of 2µg/ml propidium iodide was added and stored at 4°C in dark until analysis. **Results**: Menadione Induced Differential Inhibition of Cell Proliferation Following the 24 htreatment of cells with menadione,the IC_{50} for SW620 and SW480 cells were found to be 10.65 and 16.07 µM, respectively.In all further experiments 10 µM of menadione was used to treat the cells. Even the highest concentration of menadione used for cancer cells showed very less toxicity in the normal colon cells. These results indicate that menadione had preferential toxicity towards colorectal cancer cells compared to normal

colon cells. **Menadione Suppresses Clonogenic Potential of Human Colorectal Cancer Cells:** Menadione treatment was found to decrease the number of colonies formed compared to the control untreated cells. **Menadione Inhibits Wnt Signaling Pathway:** Menadione (10μM) was found to decrease the β-catenin at protein level as well as Cyclin D1, the downstream target of Wnt signaling pathway. Effect of Menadione on Cell Cycle Distribution Menadione treatment of human colorectal cancer cells SW620 and SW480 was found to increase the cell fraction in subGo andGo/G1 phase in SW480 cells while in SW620 cells,SubGo and G_2/M cell fraction was significantly increased. **Menadione Reverses the Process of EMT:** Menadione (10 μM) significantly enhances the expression of E-cadherin, a membrane protein, and represses the expression of cytoskeleton EMT marker protein vimentin and transcription factor snail which are involved in the regulation of EMT. Menadione Inhibits Cell Migration Menadione treatment of cells maintained in serum free medium and monitoring the scratched surface of confluent cells by microscopy indicated that menadione inhibits the migratory potential of colorectal cancer cells as revealed by the measurement of area covered by cells in drug treated and untreated control cells. **Conclusions:** Our data provide novel findings that menadione shows preferential toxicity towards human colorectal cancer cells.It inhibits the Wnt signaling pathway and reverses the process of EMT.Menadione may therefore be a potential chemopreventive agent in human colorectal cancer.

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Key words: Menadione, Colorectal cancer, *Wntsignaling*

Recurrence of CEA secreting colorectal malignancies; Can 18F-FDG PET-CT detect recurrent disease earlier than serial serum CEA estimation – A multi-institutional prospective study.

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Aim: To determine the diagnostic capability of 18F-FDG PET-CT scan in colorectal malignancy recurrence. **Material and Methods:** A prospective study of 28 consecutive treated patients of colorectal malignancy with normal serum CEA was carried out using whole body FDG PET-CT scan. All patients were biopsy proven cases of CEA secreting colorectal malignancies, appropriately treated for the primary malignancy, were in remission and on surveillance. They were with or without any suspicious symptom(s) with normal serum CEA level (less than 4 ng/ml). FDG avid lesions were subjected to histopathology or interval FDG PET-CT scan within 8-20 weeks with serum CEA determination to confirm recurrence. Negative PET-CT studies also had interval PET-CT scans 8-20 weeks later and serum CEA measurement to confirm absence of recurrent disease. **Result:** FDG PET-CT detected metabolically active lesions in 13 patients, out of which 11 were true positive and 2 were false positive for recurrence. False positive lesions had histological evidence of granulomatous abdomino-pelvic lymphadenopathy, possibly tubercular in etiology. All FDG negative patients (total 15) had an interval FDG PET-CT scan performed along with measurement of CEA. 9 (out of 15) patients showed no significant interval change (True Negative). 5 (out of 15) patients had new FDG avid lesion(s) in the second scan with raised CEA values (True Negative). One patient had normal serum CEA with FDG avid solitary serosal deposit along anastomosis in second scan, which though present in the first scan, was missed probably due to small size and intense physiological FDG uptake along adjacent bowel mucosa (False Negative). On comparison of two scans, the lesion showed increase in size and metabolic activity. Overall FDG PET-CT showed 91.7 % sensitivity, 87.5 % specificity, 84.6 % positive predictive value and 93.3 % negative predictive value in detecting colorectal malignancy recurrence prior to rise in serum CEA. **Conclusion:** Serum CEA is widely used as the only colorectal tumor marker in the post treatment surveillance. However normal CEA value does not completely rule out recurrence. FDG PET-CT as an isotropic metabolic imaging modality shows promise to be one stop approach in the surveillance of large bowel malignancy.

Key words: FDG PET-CT, CEA, Recurrence, Colorectal Malignancy

Surgical management of malignant gastric outlet obstruction

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Introduction: The etiology of the gastric outlet obstruction (GOO) has been changing universally from benign to malignant disease. The extent of the surgical treatment of malignant GOO depends on stage and type of malignancy, and the anticipated prognosis. The aim of this study was to analyze the presentations of the malignant GOO, treatment modalities and outcome in patients treated at a tertiary care hospital in Nepal. **Materials and Methods:** A retrospective review of all 86 patients with diagnosis of GOO, admitted for surgical treatment at the Department of Surgery, Tribhuvan University Teaching Hospital, Kathmandu, Nepal for the period of September 2007 to August 2012, was carried out. **Results:** Out of 86 patients with GOO, 61 (70.9%) patients had malignant disease. The mean age of presentation was 57.40 years and the male: female ratio was 2:1. Gastric cancer **was** the most common etiology 54 (88.5%) followed by duodenal carcinoma 5(8.2%), advanced carcinoma gall bladder 2(3.3%). Out of 54 patients of gastric cancer, 19 (35.2%) patients were of stage IIIB followed by 13(24.1%) patients of stage IIIC and the remaining patients (40.7%) had metastatic disease.Of 54 patients with gastric cancer, Surgery with curative intent was undertaken in 32 (59.3%) patients, out of which subtotal gastrectomy was done for 26 (81.3%) patients and total gastrectomy was done for 6 (18.3%) patients. Out of 22 (36.1%) patients with advanced gastric cancer, palliative subtotal gastrectomy was done for 8 (36.4%), gastro-jejunostomy for 11 (50%), feeding jejunostomy for 2 (9.1%) and one patient was discharged on request of patient party. Similarly 5 (8.2%) cases of duodenal carcinoma, 2(3.3%) advanced carcinoma gall bladder underwent gastro-jejunostomy. Post - operatively, 2 (3.3%) patients had bleeding (1 patient required re-exploration), 5(8.2%) patients had surgical site infection, 2(3.3%) had anastomotic leakage and 2 (3.3%) mortalitiesin gastrectomy done for carcinoma stomach. **Conclusion:** GOO is a common entity with diverse etiology, gastric malignancy being the most common cause with advanced disease. Patient education and early detection is necessary for curative treatment.

Key words: Gastric Outlet Obstruction, Malignant Etiology, Surgical Management

Radical Surgery for Gallbladder Cancer: A Single Team Experience at University Teaching Hospital

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Background: Gall bladder cancer is one of the highly prevalent gastrointestinal cancers in the northern part of India and Nepal. However, only limited number of patients undergo surgery with curative intent as majority of them present in advanced stage requiring some form of palliation, either endoscopic or surgical. Many at times, in patients resected with high suspicion of cancer preoperatively turns out to be some form of

benign pathology in postoperative histology. Here we intend to present our experience of managing gallbladder cancer with curative intent. **Materials and Method:** All patients with preoperative diagnosis of gallbladder cancer, either on imaging or histology and undergoing radical resection with nodal dissection over five years period (2010 Dec- 2015 Nov) were analyzed. All the surgeries were performed by two surgeons (RSB and PJL) both gastrointestinal surgeons trained in HPB surgery. Disease presentation, diagnostic methods, type of surgery performed, postoperative histology, perioperative outcome and postoperative management were studied. **Results:** During the period, total 19 patients underwent standard surgery for gallbladder cancer. Total 13 patients had preoperative suspicion of cancer while 6 were incidental gallbladder cancers detected on cholecystectomy specimen (5 laparoscopic, 1 open). All patients with incidental gallbladder cancer underwent completion extended cholecystectomy (Segment 4b and V) with nodal dissection. Among those suspected preoperatively (13 cases), none of them had preoperative histological diagnosis. Out of 13, total 4 patients required bile duct excision, 1 had right extended hepatectomy and remaining 8 had extended cholecystectomy. All patients had standard lymphadenectomy. Out of 13, total 4 turned out to be xanthogranulomatous, 1 was tuberculosis, and 2 chronic cholecystitis while remaining 6 were carcinoma gallbladder. Perioperative outcome was excellent with no mortality. All patients with confirmed carcinoma in postoperative histology were referred for adjuvant therapy. **Conclusion:** Despite high incidence, only limited number of gallbladder cancers present at resectable stage. Thus, any patients with high index of suspicion of gallbladder malignancy should undergo a formal cancer surgery, the perioperative outcome of which remains excellent.

Keywords: Gallbladder cancer, extended cholecystectomy, Xanthogranulomatous

Multimodality treatment of hepatoblastoma & its outcome- a tertiary centre experience

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Introduction: Hepatoblastoma is the most common malignant tumor of the liver in children. Surgery remains the primary means of curative therapy, but the role of chemotherapy in both the adjuvant and neoadjuvant setting has become increasingly important over the past three decades. New insight has also been gained into the molecular biology of hepatoblastoma. **Material And Methods:** This Is A Retrospective Study of 39 Patients of Hepatoblastoma At Our Centre In Last 10 Years From 2005-2015. Their Presentation, Treatment Offered, Prevalence, Surgical And Medical Treatment Approach, Complications And Follow Up Were Studied. Neoadjuvant Chemotherapy Was Given In 33 Out Of 39 Patients In The Form Of Cisplatin + Adriamycin And Reassessment Was Done After 1-3 Cycles, In Case Of Inadequate Response Maximum Of 6 Cycles Were Given. **Results:** Median age of presentation in our study was 36.4 months with male: female ratio of 2.2:1. Almost, all patient showed change in resection margin after chemotherapy, which was confirmed by ct scan. Six patients underwent primary surgery as they were having small lesions. Both neoadjuvant and adjuvant chemotherapy were well tolerated but there were two mortalities: one patient died on the first post operative day and another patient died 15 days after surgery,5 days after being discharged from the hospital.Follow up varied from 6 months – 108 months with a mean follow up is 25.63 month. survival at 2 year is 96.7%. **Conclusions:** Our study concluded that multidisciplinary approach to hepatoblastoma is justified as it decreases the resection margin, increase tolerance to surgery, decrease morbidity and improves the outcome of patient.

Dual primary gastric and colorectal cancer – An uncommon entity

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Introduction and Objectives: The incidence of multiple primary malignant neoplasms is said to increase with age and the occurrence of a second malignancy in a patient with a known malignant tumor are not uncommon. Theyare being encountered mainly because of an increase in the number of elderly patients, improvements in diagnostic techniques and prolonged survival of patient's treated for malignancy. However this phenomenon is still considered to berare. Herein, we present a case of synchronous gastric and ascending colon cancer and a case of metachronous transverse colon and gastric cancer treated in our centre. **Material and Methods:** We reviewed the records of 67 patients who underwent surgery for gastric cancer in our department from January 2013 to December 2015. Synchronous double primary cancer was defined as an extra gastric cancer diagnosed within a 6-month interval of the detection of gastric cancer. **Results:** Synchronous and metachronous double primary cancers were identified in 1 patients each. The extragastric site of the primary tumor in patient with synchronous gastric cancer was in ascending colon and with metachronus gastric cancer in transverse colon respectively. Synchronus cancer patient underwent D2 gastrectomy with extended right hemicolectomy and was discharged with uneventful recovery while the second case underwent extended right hemicolectomy post D2 gastrectomy. Unfortunately he developed anastomotic leak and hospital acquired pneumonia and succcumbed to death on 17th post operative day. **Conclusions:** Although double primary gastric cancer associated with colon cancer in patients are very rare, the possibility of synchronous lesions or the occurrence of metachronous cancer should not be overlooked and colonoscopy should be advised when suspicious. Combined resection should be applied whenever possible while periodic examination including colonoscopy and proper follow up is necessary to rule out metachronous cancer.

SILS-Single Incision Laparoscopic Sigmoid colectomy.

Ravishankar K Diddapur

Gleneagles Hospital and Mount Elizabeth Novena Hospital

With the marriage of surgery and technology, applications of laparoscopic surgery/minimal access surgery are increasing exponentially. Laparoscopic cholecystectomy was first performed in 1985 and popularized since 1987. Over the last 4 year single incision laparoscopic cholecystectomy & surgery has become popularized as instrumentation for the same has been available. This surgery has the advantage of not leaving behind any visible scars since the incision is made within the umbilicus and heals without any noticeable scars. The pain associated is also less as it is from 1 incision rather than 3 or 4 incisions as shown in some of the RCT's. In this talk I will cover the development and practice of recent advances in SILS – Single incision video laparoscopic surgeries with emphasis on SILS Hemicolectomy. Scar less surgery in the form of NOTES (Natural Orifice Transluminal Endoscopic Surgery) has been in a developmental stage over the last 4-5 years. However this carries a risk of peritonitis though only in a small percentage if there is a leak at the enterotomy site. Peritonitis needs laparotomy (Long incision) and carries a risk of mortality albeit in a small percentage. The instrumentation and technology is novel. In contrast SILS surgery being done through the umbilicus and does not have the risk of peritonitis due to leak from closure of enterotomy site. Umbilicus being central gives good access to all the four quadrants of abdomen. Instrumentation is well developed. We will see video clip SILS laparoscopic sigmoid colectomy. I offer this surgery in elective as well as selected emergency cases.

SILS-Single Incision Laparoscopic Right Hemicolectomy.

Ravishankar K Diddapur

Gleneagles Hospital and Mount Elizabeth Novena Hospital

With the marriage of surgery and technology, applications of laparoscopic surgery/minimal access surgery are increasing exponentially. Laparoscopic

cholecystectomy was first performed in 1985 and popularized since 1987. Over the last 4 year single incision laparoscopic cholecystectomy & surgery has become popularized as instrumentation for the same has been available. This surgery has the advantage of not leaving behind any visible scars since the incision is made within the umbilicus and heals without any noticeable scars. The pain associated is also less as it is from 1 incision rather than 3 or 4 incisions as shown in some of the RCT's. In this talk I will cover the development and practice of recent advances in SILS – Single incision video laparoscopic surgeries with emphasis on SILS Hemicolectomy. Scar less surgery in the form of NOTES (Natural Orifice Transluminal Endoscopic Surgery) has been in a developmental stage over the last 4-5 years. However this carries a risk of peritonitis though only in a small percentage if there is a leak at the enterotomy site. Peritonitis needs laparotomy (Long incision) and carries a risk of mortality albeit in a small percentage. The instrumentation and technology is novel. In contrast SILS surgery being done through the umbilicus and does not have the risk of peritonitis due to leak from closure of enterotomy site. Umbilicus being central gives good access to all the four quadrants of abdomen. Instrumentation is well developed. We will see video clip SILS laparoscopic right hemicolectomy. I offer this surgery in elective as well as selected emergency cases.

Carcinoma of urinary bladder -our experience in ilealconduit as ueinary diversion - A retrospective study

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Introduction: Urinary Bladder carcinoma is the second most common cancer of Genito - Urinary Tract. Radical cystoprostatectomy in male patients and Anterior Pelvic Exenteration in female patients with Enbloc Pelvic lymphadenectomy is the standard procedure in muscle invasive bladder carcinoma in the absence of metastatic disease. For more than 30 years ,ileal conduit has been considered the standard urinary diversion for Bladder Carcinoma patients subjected to Radical Cystectomy. **Materials and Methods:** A Retrospective study was done from January 2014 to December 2015 at our Regional Cancer Centre Kidwai Memorial Institute Of oncology. All patients with Histopathologically proven Muscle Invasive Bladder Carcinoma between age group 18 - 80 years were considered as inclusion criteria. Those patients with advanced disease and who were unfit for surgery were excluded. **Results:** In my study we had 30 cases of Muscle Invasive Bladder Carcinoma in 2 years. Male : Female ratio was 23 : 7. **27** patients were identified with Transitional Cell Carcinoma and**3** patients with Squamous Cell Carcinoma. Radical cystectomy was done in 29 patients and Palliative cystectomy in 1 patient, within 2 1/2 to 3 hours {short duration of surgery }. All 30 cases were High Grade Tumors. We came across complications like uretero - ileal leak (9 patients) and mortality (2 patients). **Conclusion:** Majority of the patients we came across were elderly patients above 60 years . Though we had T2 and T3 cases for whom we could have considered NACT / CTRT, we opted for surgery as per MRC , EORTC and Randomised Trials. Our experience suggested that Ileal Conduit is a simple and standard surgical technique ,with acceptable complications that could be managed conservatively and also with short duration ofsurgery with satisfactory post operative quality of life.

ExophyticJejunal Growth:Jejunal Adenocarcinoma,A Rare Case

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Introduction: Small bowel tumours are rare consisting of only 1-2% of all Gastro intestinal neoplasms. Out of all small bowel neoplasms,nearly 60% are malignant and rest are benign. Benign tumours include leiomyoma,lipoma,adenoma and hemangioma. Malignant tumours include adenocarcinoma,GIST and sarcomas. Most common site of small bowel malignancy is duodenum. The most common type of malignancy is Adenocarcinoma .Mean age of presentation of adenocarcinoma of small bowel is above 65 years of age. Predisposing factors includes FAP, HNPCC and Chrohn's disease. **Case Report:** A 25 year old male patient presented in the Surgery Department with a complain of abdominal pain since 1 month, intermittent,colicky in nature with no other bowel bladder complaints. Patient also complains of anorexia over the month with history of significant weight loss over past few months' .No similar family history. On examination, per abdomenwas soft, non-tender. A7*7cm firm, non tender mass having smooth surface was palpable at left hypochondriac region extending into the epigastric region. There was no hepatosplenomegaly, no ascites Contrast Enhanced Computed Tomography shows soft tissue lesion involving the transverse colon with an exophytic component involving the small bowel,no evidence of liver metastasis. On surgical exploration, a 7*7 cm conglomerated mass was found 10cm distal to duodenojejunal junction with flimsy adhesions to the surrounding bowel and firm adhesion to the mid portion of the transverse colon. No plane of dissection was found in the midportion of the transverse colon. Pylorus, greater curvature of stomach and 1st part of duodenum were free from the mass. Resection of thejejunal mass along with 5cm of normal jejunum on either side of masswith itsmesentery done followed by end to end jejunojejunal anastomosis. En-block dissection of the mesenteric lymph nodes done upto the level of the origin of superior mesenteric artery. Similarly,the adherent mid portion of transverse colon was resected along with its mesentery followed by end to end colo-colic anastomosis. No evidence of peritoneal seeding, liver metastatic deposits or mesenteric lymph nodes were found. Histopathological examination shows adenocarcinoma of jejunal mass with tumour free margins .No malignant cells were found in the transverse colon. **Discussion:** G.I. malignancy is leading cause of death in the World .Small intestinal malignancy is rare of all the G.I. malignancy and in that common site is duodenum.We here present a case having exophyticAdenocarcinoma of the jejunumwhich is very rare and very few case are reported in literature.Commmonlyadenocarcinomas present as intraluminal mass with patient presentation being that of obstruction.Mainstay of treatment is complete surgical resection of the tumour mass,role of chemotherapy or radiotherapy is unclear.Small bowel malignancies are detected late due to their rarity,unclear presentation and diagnostic difficulties.No screening methods are available for small bowel malignancies unlike colorectal malignancies.Hence in our case,we were able to completely resect the tumour with macroscopic and microscopic tumour free margins.We want to highlight that adenocarcinoma can present as exophytic growth in the small bowel without intestinal obstruction.

Utility of pet-ct scan for evaluating raising cea levels after surgical resection of colorectal cancer

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Background: As per existing guidelines, during the follow-up of surgically resected colorectal cancer, PET-CT is indicated when there is elevation of CEA>5ng/ml and no obvious site of recurrence on clinical examination and basic imaging. As an instituitional policy, PET CECT scan was being performed at our institute whenever 1) CEA levels rose above 5 ng/ml and 2) whenever there was doubling of CEA value (even if CEA was <5 ng/ml). **Aim and Objective:** To correlate CEA elevation in the follow-up period with positive findings on PET-CECT scan by calculating the rates of PET positivity at various pre-determined cut-off levels of raised CEA. **Methodology:** Study period was from January 1,2013 to December 31,2014. We retrospectively analysed all cases where a PET-CECT scan was performed for elevated CEA levels during the follow-up period after complete resection of the primary tumour with adjuvant/neo-adjuvant therapy. **Results:** A total of 106 patients underwent PET-CECT scan for the above mentioned indications. Overall 49% of the patients had metabolically active lesions. At CEA level < 5ng/ml, 5.1-10 ng/ml, 10.1-15 ng/ml, 15.1-50 ng/ml and >50 ng/ml, PET scan showed presence of disease in 9.1%, 33.3%,63.2%,

76.5% and 90.9% respectively. **Conclusion:** PET scan is good at identifying the source of raising CEA level in colorectal cancer patients on follow-up. Even when CEA elevation is in the range of 5.1-10ng/ml, about one third of the patients would have a PET detectable recurrence and hence >5 ng/ml is an appropriate cut-off for performing PETCECT scan in these patients.

Assessment of HER-2/neu expression in TCC of Urinary Bladder

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Contest: Assessment of HER-2/neu expression in TCC of Urinary Bladder. **Objective:** To evaluate and compare the over-expression of HER-2/neu in TCC of Urinary Bladder and to evaluate the correlation between the Her-2/neu positivity and its intensity of over-expression with tumour aggressiveness. **Design:** Prospective study with a minimum follow-up of six months. **Study Group:** patient presenting with hematuria (macroscopic/ microscopic) in Surgical OPD/ Casualty at Northern Railway Central Hospital, New Delhi from March 2010- December 2011. **Sample Size:** A total number of 70 patients with TCC of Urinary Bladder were included in the study. 30 patients having benign bladder lesion were considered as the control group. **Methodology:** A total of 100 patients, 70 cases and 30 control were included in the study who presented with painless hematuria. Patients were evaluated by routine investigations including routine Urine examination; urine culture and sensitivity; urine cytology for three successive days; NMP-22; abdominal ultrasonography followed by CT abdomen to look for local extravesical spread/ invasion. Metastatic work up was done in all patients which included a CBC; LFT; Alkaline phosphatase; Chest radiograph and Bone scan. All patients underwent cystoscopy and TUR/ Biopsy for histopathologicalconfirmation and Her-2/neu receptor status. **Results:** Significant number of patients of TCC of Urinary bladder (68.6%) showed HER-2/neu positivity. All the patients (30 out of 70) showing high grade were HER-2/neu positive. 18 (60.0%) patients in high grade showed HER-2/neu 3+ expression while rest 12 (40.0%) patients were HER-2/neu 2+. Total 28 patients showed invasive tumour out of which 24 patients were HER-2/neu positive but on co-relating with the case group, the association between the HER-2/neu expression and stage of tumour was not significant($p=0.137$). **Conclusion:** HER-2/neu over-expression was significantly co-related with the TCC of Urinary Bladder.HER-2/neu positivity was co-related with the grade of tumour and increase in intensity of HER-2/neu expression is associated with the increase in tumour grade. However, there was no significant association between the HER-2/neu over-expression and muscle invasion and stage of tumour.

Transhiatal oesophagectomy –a single institute experience

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Background: The optimal approach for Carcinoma at lower Oesophagus and OG Junction remains controversial. Despite Oncological advances, Surgical resection is the only treatment that has repeatedly been shown to prolong survival, albeit in only 30% of patients. Transhiataloesophagectomy is often advocated as the preferred surgical approach in patients with early tumours (or) the patients with more advanced disease who would not tolerate a thoractomy. Transhiataloesophagectomy has been favoured operative approach in our Institution for managing on carcinoma of oesophagus below the level of carina and type I and type II tumours of OG junction. **Aim of the Study:** The aim of the study was to assess a single unit experience and outcome of transhiataloesophagectomy in an era when the use of systemic oncological therapies has been increased dramatically. **Materials and Methods:** Between July 2008 and December 2015, 154 consecutive patients (91 males, 63 females, median age = 57 years) underwent transhiataloesophagectomy. A further 13 patients underwent transthoracic oesophagectomy during the same period and were excluded from analysis. Invasive Squamous Cell Carcinoma in 92 patients, Adenocarcinoma in 58 patients, malignant melanoma in 1 patient and adeno squamous cell 3 patients. 68 patients received Neo adjuvant chemotherapy. **Results:** There were no operative and peri operative mortality within one month after surgery. Major complications included: Respiratory complications in sixteen patients, clinically apparent anastomotic leak in ten patients, recurrent laryngeal nerve neuropraxia in seven patients and hiatus hernia in three patients. Median length of hospital stay was 10 days. Roresection was achieved in all patients except in three patients who had multicentric disease. **Conclusion:** Transhiataloesophagectomy is an effective operative approach for tumours of the infra carinal oesophagus and the oesophagogastric junction. It is associated with low mortality and morbidity and two year survival rate of nearly 50% when combined with neoadjuvantchemotherapy.

Esophageal Cancer: A five-Year Single Centre Study Reflecting Daily Practice

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PT. BDS, PGIMS, ROHTAK

Background: Esophageal cancer is the eighth most common cancer and sixth leading cause of cancer deaths in the world, with the majority of cases occurring in developing countries . Most of the tumours of esophagus are malignant and the diagnostic symptom, dysphagia, occurs very late. The overwhelming majority of esophageal malignancies are classified as either squamous cell carcinoma (SCC) or adenocarcinoma (ADC). SCC comprises 60–70% of all cases of esophageal cancer worldwide, while ADC accounts for a further 20–30%. The incidence of the two main types of esophageal cancer varies greatly between different geographical areas. In general, ESCC is more common in the developing world, and EAC is more common in the developed world.The remaining 5% represent rare malignancies and metastases from other organs. **Material and Methods:** We examined all pathology reports, endoscopy records, and patient files from PT BDS PGIMS ROHTAK Hospital from January 2011 through 2015 to identify all patients with a histologic diagnosis of EC. During this 5 year period, 494 biopsies were taken endoscopically for suspicious carcinoma. Out of which 77 were non conclusive and 417 were identified to be positive. The positive cases were classified further for the type of EC histopathologically. We reviewed the following from the records of these patients: age at diagnosis, sex, tumor histology, endoscopic site, clinical or medical records to identify the risk factors involved. **Results:** From 417 patients, 89.6% were squamous cell carcinoma, 5.03% were adenocarcinoma. EC was more prevalent in males than females.To date, no single factor could be identified as the main cause of the excess incidence of SCC as compared to other types. Three main components emerged as important risk factors: smoking and alcohol consumption were more prevalent in patients with SCC and adenocarcinoma patients had GERD as most common risk factor. Other varieties like small cell carcoinoma, signet ring adenocarcinoma, adenosquamous carcinoma, sarcomatoid carcinoma constituted 0.2% only. Poorly differentiated carcinoma comprised 1.1%. **Conclusion:** In summary, this case series describes the large number of EC patients reported to date, and it highlights the uniqueness of the EC experience in tertiary centre of northern india.

Key words: Esophageal carcinoma; Esophageal adenocarcinoma; Esophageal squamous cell carcinoma; epidemiology; Risk factors

SPINK1 confers chemoresistance in Colorectal Cancer by upregulating Metallothioneins

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Background: Colon cancer is the leading cause of cancer associated malignancy and mortality in both men and women worldwide. SPINK1 over-expression has been associated with many cancer types, including lung, breast, colon, and prostate. SPINK1 (Serine Protease Inhibitor Kazal type 1) is known to be one of the major drivers of oncogenesis in colon adenocarcimona. Due to its homology with EGF, SPINK1 is known to behave as an autocrine and paracrine growth factor mediating the downstream effects through EGFR signalling across multiple cancers. Here, we explore the mechanism of SPINK1 mediated oncogenicity and resistance towards chemotherapeutic drugs in colorectal cancer. **Material and Methods:** Stable knockdown of SPINK1 was performed in a colon adenocarcinoma cell line, WiDr, using lentivirus based small hairpin RNAs (shRNAs). Microarray of SPINK1 knockdown cells and scrambled control cells was carried out using Agilent Whole Human Genome Oligo Microarray. Microarray data was analysed by using Ingenuity pathway analysis (IPA) software and DAVID (Database for Annotation, Visualization and Integrated Discovery) to identify the differentially expressed genes. IC50 value for chemotherapeutic drugs was determined using WST Assays. **Results:** Global gene expression profiling data revealed that various isoforms of Metallothioneins (MTs) were upregulated upon SPINK1 knockdown. DAVID analysis showed that knockdown of SPINK1 is associated with up-regulation of important pathways regulating tight junction assembly, regulation of translational initiation and cellular response to metal ions such as zinc and cadmium. Further, SPINK1 knockdown cells showed augmented sensitivity towards chemotherapeutic agents as compared to isogenic scrambled control WiDr cells. **Conclusions:** Our study shows an important role of SPINK1 in colon cancer progression. Over-expression of SPINK1 during the course of cancer progression leads to downregulation of different isoforms of MTs, thus imparting chemotherapeutic resistance. Hence, this study provides a strong rationale for using SPINK1 as a potential therapeutic target in treatment of SPINK1- positive colon cancer.

CELIAC DISEASE AND COLON CANCER

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Background: Celiac disease (CD) is a chronic immune-mediated disorder of small intestine that occurs in genetically predisposed populations.It is characterized by permanent intolerance to wheat gliadins and other cereal prolamins in the small bowel mucosa. It is characterized by anti-tissue transglutaminase (anti-tTG) antibodies. The epidemiology of CD has iceberg characteristics as there are far more undiagnosed cases than diagnosed cases. Celiac disease is associated with an increased risk of lymphoma and small bowel malignancy, but most studies have found no increased risk of colorectal cancer. Aim of this study is to compare the prevalence of colorectal adenomas in celiac disease patients. **Methods**: We identified all celiac disease patients who underwent colonoscopy at our institution. **Results**: Biopsies from a total of 100 consecutive cases of suspected CD on the basis of clinical and serological profile after ruling out other causes of malabsorption formed the study group. The biopsy was taken from second part of duodenum through eosophagoduodenoscopy. Histopathological diagnosis was established on routine haematoxylin and eosin stained sections. Representative section was also subjected for immunohistochemical staining with antihuman CD3 antibody for evaluating intraepithelial lymphocytes. The histopathological grading was performed as per modified Marsh grading.Comparison of these grades with the serological (anti tTg levels) and other clinical parameters (symptoms, weight, endoscopy and hemoglobin levels) was done. The colonoscopy done in patients showed sigmoid colon malignancy in three (3/100) of the total patients. **Conclusions** The celiac disease is associated with various complications including malignancies. There are 3 types of cancer associated with celiac disease: enteropathy-associated T-cell lymphoma (EATL), non-Hodgkin's lymphoma, and adenocarcinoma of the small intestine mainly. Colon cancer due to celiac disease is quite rare.

Key words: Celiac disease, sigmoid colon, colon adenocarcinoma

Comparison of serum biomarkers CYFRA 21-1 with CA 19-9 in the assessment of biliary tract cancers

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Background: Biliary malignancy is common in various parts of Asia and has high fatality. Since surgical resection in early disease remains the only potential cure, timely diagnosis is very crucial. CA 19-9 has been used in biliary malignancy but it can be raised in benign obstructive jaundice as well. However, its expression depends on Lewis phenotype and hence it has no value in 7 – 10 % of patients who are negative for lewis antigen The lack of a reliable marker to aid in timely diagnosis and advancement in treatment modality are the main reasons for limited survival in patients with this neoplasm. In a developing country like Nepal with limited resources where proper imaging facilities are not readily available and are quite expensive, biomarkers such as CYFRA 21-1 can have an important role in patients with biliary tract cancer. **Objective:** The objective of the study is to compare the accuracy of biomarkers CYFRA 21-1 with CA 19-9 for the diagnosis of biliary tract cancers and to correlate the level of biomarkers with the stage of the disease. **Patients and Methods:** This is a cross-sectional observational study conducted at Department of Surgery and Department of Biochemistry of Tribhuvan University Teaching Hospital, Kathmandu, Nepal, over a period of 2 years (13 April, 2012 to 14 April, 2014). Patients with histopathological diagnosis of biliary tract cancers were enrolled in the study. Measurement of serum CK 19 fragments was performed using the CYFRA 21-1 EIA KIT (Fujirebio Diagnostics, US) and was compared with CA 19-9. Demographic characteristics, physiological variables and laboratory values of these patient population were analyzed. **Results:** There were 61 patients included in the study. The mean age was 53.41±12.5 years. There were 34 females (56%) with sex ratio of 1:1.25 (Males: Females). Amongst the biliary malignancies, carcinoma of the gallbladder was the commonest followed by hilar cholangiocarcinoma. Most of the patients (64%) were in the middle age group (40 to 60 years) and majority of the malignancies were in advanced stage (Stage III and IV). CYFRA 21-1 had sensitivity of 80.3% and CA 19-9 of 68.9 % for the detection of Biliary Tract Cancers. Comparing the means of CYFRA 21-1 and CA 19-9 for stage of the disease progressive rise of CYFRA 21-1 with the rise in stage of the disease was observed ($p < 0.03$). **Conclusion:** CYFRA is a more reliable test than CA 19-9 in all stages of biliary malignancy and can assist in distinguishing early and advanced malignancy. Amongst the biliary malignancy, higher values of CYFRA 21-1 is present in carcinoma of gallbladder

"Role of Molecular Markers in Biliary Tract Malignancies".

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Introduction: Biliary tract cancers (BTC) comprise a heterogeneous group of neoplasms including gallbladder cancer, intrahepatic cholangiocarcinoma, extrahepaticcholangiocarcinoma and variably, ampullary carcinoma. Identification of reliable molecular markers may provide important prognostic information, and facilitate adequate treatment plans and targets for a novel therapeutic approach. **Objective:** To study distribution of molecular markers such as ER, PR, P53, cyclin D1, Muc1, Muc4, Muc2, her-2/neu, K-Ras among patients with biliary tract malignancy Role of molecular marker in outcome, prognostic indicator, histological grade and type of biliary tract malignancies. (their by determining their role as prognostic indicator in BTC).Material and method:Prospective observational study done in radiological suspicious 35 patient in department of surgery between 2013 to 2015. Specimen sent for HPE, result of molecular markers are compared with outcome , grade of malignancy and their distribution among malignant and benign disease is studied. **Result:** Conclusion: In our study when expression of molecular markers was observed as per grade

Histopathology →	Positive		Negative		p-value	Sensitivity %	Specificity %	PPV %	NPV %	Diagnostic accuracy %
	n	%	n	%						
Mucin 1	8	53.33	5	25.00	0.043	53.33	75.00	61.54	68.18	65.71
Mucin 2	3	20.00	2	10.00	0.201	20.00	90.00	60.00	60.00	60.00
Mucin 4	8	53.33	6	30.00	0.082	53.33	70.00	57.14	66.67	62.86
Cyclin D1	11	73.33	6	30.00	0.006	73.33	70.00	64.71	77.78	71.43
P53	10	66.67	4	20.00	0.003	66.67	80.00	71.43	76.19	74.29
ER	1	6.67	0	0.00	0.121	6.67	100.00	100.00	58.82	60.00
PR	8	53.33	5	25.00	0.043	53.33	75.00	61.54	68.18	65.71
Her-2 Neu	10	66.67	9	45.00	0.101	66.67	55.00	52.63	68.75	60.00
Krasmutaion	8	53.33	1	5.00	<0.001	53.33	95.00	88.89	73.08	77.14
ER/PR/Her-2 Neu	13	86.67	9	45.00	0.006	86.67	55.00	59.09	84.62	68.57
Mucin1/2/4	12	80.00	8	40.00	0.009	80.00	60.00	60.00	80.00	68.57

of malignancy it was that expression of Muc-4, K-ras and PR significantly (p-value <0.05) correlates with grade of malignancy, were expression of Muc-4 and K-Ras is more frequent in high grade malignancy and PR in low grade malignancies. Expression of Muc1 is also more frequent in high grade malignancy, whereas expression PR, Muc-2, Cyclin D1 and Her-2 is usually associated with low grade malignancy but is statistically insignificant.

A study of Her2/neu expression in Carcinoma Gallbladder and its Clinico-pathological correlation

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Introduction: Her2/neu, proto-oncogene is amplified and overexpressed in a number of human adenocarcinomas. Overexpression of Her2/neuc-erbB-2 is indicated as a worse prognostic factor and associated with neoplastic progression in various adenocarcinomas. Gallbladder cancer is the most common cancer of the biliary tract and has a particularly high incidence in Chile, Japan, and Northern India. With high incidence and poor prognosis, there is necessity for improved understanding of the molecular carcinogenic mechanisms of carcinoma gallbladder which may lead to improved therapeutic regimens. **Objectives:** Objective of the study is to studyHer2/neu expression in patients with carcinoma gallbladder and study its correlation with clinical presentation and with pathological features. **Material and Methods:** Tumor specimens from 60 gallbladder cancer patient were examined for HER-2/neu expression by immunohistochemistry (IHC), with scores of 2+ or 3+ defined as positive. Tissue were obtained from radical cholecystectomy specimens and Ultrasound guided needle biopsy of inoperable gallbladder cancer patients. The relative frequency of Her2/neu positivity was scored and correlated with other histological parameters of the tumor among two groups of gallbladder patients-curative setting(those with operable disease at presentation) and palliative setting (those with inoperable disease at presentation). **Results:** Among total 60 patients, 42 belonged to palliative group and 18 belonged to curative group. 11 out of 42 patients (26.1%) in palliative group had positive Her2/neu in tumor. 2 out of 18 patients (11.11%) in curative group had positive her2/neu in tumor. **Conclusions:** A positive Her2/neu in carcinoma gallbladdercorrelates with advanced inoperable disease at presentation and therefore with overall survival. Hence, it may have a role in progression of disease.

Comparison of the outcomes between locally advanced cervical adenocarcinoma and squamous cell carcinoma patients treated with definitive chemoradiation

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Background: Squamous cell carcinoma and adenocarcinoma are the two most common histology of carcinoma carvix. We aim to present comparison of survival outcomes between locally advanced adenocarcinoma and squamous cell carcinoma patients treated with definitive chemoradiation. **Materials and Methods:** It is a retrospective analysis and direct comparison between adenocarcinoma and squamous cell carcinoma cervix treated from January 2011 to December 2015. Of 73 patients analyzed 61 had squamous carcinoma histology and remaining 12 had adenocarcinoma. Inclusion criteria were patients with locally advanced stage (IIA) who have completed definitive chemoradiation and were available for response evaluation at 3 months of completion of treatment. Endpoints for the study were disease response evaluation at 3 months, progression rate, median progression free survival, median recurrence free survival, median loco-regional control, median distant metastasis free survival, median overall survival. **Results:** There was no significant difference between the two histology groups with respect to rate of achieving complete response (78.6 vs 75 %, p = 0.718) and rate of disease progression (36% vs 50%, p = 0.517). There was no significant difference between median PFS (57.75 vs 17.74 months; p = 0.964), median RFS (not reached {NR}vs 66.03 months; p = 0.876), median loco-regional control (not reached for both; p = 0.315), median DMFS (NR vs 66.03 months; p = 0.438) and median OS (NR vs 66.13 months; p = 0.884). **Conclusions:** Locally advanced squamous cell carcinoma and adenocarcinoma treated with definitive chemoradiation have similar outcomes. Small sample size is the limitation of this study.

ROLE OF MRI IN THE EVALUATION OF GYANECOLOGICAL MASSES. A prospective study

NehaJaglan

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Background: Magnetic resonance imaging (MRI) offers high contrast resolution, provides good tissue characterization, and has capability of multiplanar imaging better delineates and characterizes normal uterine anatomy along with focal and diffuse uterine conditions and also because it is non-invasive, carries no risk of radiation, requires no anesthesia and is less operator dependent, hence, it is becoming a useful modality for the evaluation of gynecological pathology. **Objectives:** To determine the origin and to characterize gynecological masses on MRI and stage the gynecological malignancies. **Material and Methods:** It was a prospective study in patients

with gynaecological mass lesions over a period of two years subjected to a multiplanar, multisequential MRI Scan of the pelvis on a MAGNETOM AVANTO 18 Channel 1.5 Tesla TIM MR Machine by Siemens India Ltd. Informed and written consent and detailed relevant history has been taken from each patient. The final diagnosis and staging confirmed by the histopathology report. **Results:** We included in our study 94 cases, all underwent MRI and histopathological evidence was available only 82 patients. 38 out of 82 were malignant. MR imaging diagnosed with an overall accuracy for the malignant masses of 93%. The MR imaging findings that were most predictive of malignancy were necrosis in a solid lesion (odds ratio, 104) and vegetations in a cystic lesion (odds ratio, 47). On MRI, the sensitivity for the mass of ovarian origin was (94.7%) and specificity was (75.1%). The diagnostic accuracy was (92.1%). For the mass of uterine origin, MRI had a sensitivity of (77.1%) and diagnostic accuracy of (98.1%).

Keyword: gynecological mass; MRI; diagnosis; staging

A PROSPECTIVE RANDOMISED STUDY OF OPEN VERSUS ROBOTIC ASSISTED LYMPH NODE DISSECTION IN ENDOMETRIAL CARCINOMA .

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Introduction: To evaluate the technical feasibility of robotic assisted surgery and evaluate the surgical out come of robotic surgery in terms of adequacy of staging, blood loss ,lymph node harvest, hospital stay, complications. **Material and Methods:** The study included 50 patients diagnosed with endometrial carcinoma. They were divided into two groups one open and other robotic. All patients underwent Type I Pan Hysterectomy + B/L Pelvic lymphadenectomy + Para-A ortic node dissection upto renal veins bilateral. Patient in robotic arm underwent surgery with the Da Vinci Robotic system state of art facility. All patients were followed up for complications. **Results:** Out of 50 patients included in study 25 were in first arm who had open surgery and 25 in other arm who had robotic assisted surgery.The average blood loss in open arm was 234ml vs 81.28ml in robotic arm. In open surgery on average 27.6 nodes were harvested when compared to 30.56 nodes in robotic arm. Duration of hospital stay for open group was 5.54 days vs 1.94 days for robotic arm.. with respect to complications patients in open arm had no intraoperative or post operative major complications whereas 5 patients had minor post-op complications , in robotic arm 1 patient had intra-operative complication and none had post-operative complications. **Conclusion:** This study showed results indicating robotic assisted surgery had equal oncologic outcome as compared to open technique. Minimal blood loss , shorter hospital stay, less pain helped in quicker recovery and early return to normal activities. Robotic assisted surgery had better clinical outcome and patient satisfaction when compared to open technique.

Tele-cytology: An innovative approach for cervical cancer screening in resource-poor settings

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Objective: Carcinoma cervix remains a leading cause of cancer mortality among women in countries lacking any screening program. The existing screening policy and approach via conventional cytology centered mainly in Tertiary Care Center, is totally unaffordable to Indian women, especially in the remote areas. This suggests the need of depolarizing the resources via generating the near real time modalities which could be used at the door step of the needy ones. For any screening modality to be effective it should be adequately sensitive, specific, reproducible, cheap, simple, affordable, and the most important is should be real time to ensure wide coverage and curtail loss to follow-up. Incorporating telecytology as a screening tool could make the dream come true. **Methods:** Telecytology is the interpretation of cytology material at a distance using digital images. Use of mobile telecytology unit housed in a van carrying satellite equipment and the automated image capturing systems is the central theme behind this idea. The imaging equipment would be carrying out the imaging of Papanicolaou smears prepared at the screening site and sending the images to the central laboratories situated at some tertiary care level. **Results:** This concept could overcome the hindrance of trained cytology infrastructure in the resource poor settings and could provide an efficient and economical way of screening patients. **Conclusion:** There is possibility that the designed approach may not detect the entire women positive for the disease but if the desired objective was to diagnose as many cases as possible in resource poor setting, then this process offers an advantage over no screening at all.

Keywords: Cervical cancer, screening, telecytology

Laser induced breakdown spectroscopy (LIBS) in cervical cancer screening: A proposed tool

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Objective: Cervical cancer, one of the few highly preventable cancers through successful screening, is the most common cause of death from cancer in women in the developing world. This brief hypothesis postulates a screening tool aimed to have a real time screening of cervical cancer using LIBS modality. **Methods:** Laser Induced Breakdown Spectroscopy (LIBS) is a spectrochemical method for determining the elemental composition of various samples present in any phase, by simultaneously vaporizing and exciting the sample and thus it improves the spectrochemical techniques by eliminating the requirement of sample pre-treatment. LIBS system focuses a high peak power laser pulse onto a targeted material to produce a laser spark or microplasma. Elemental line spectra is created, collected and analyzed by a fiber spectrophotometer since nano- to micro-grams of material are ablated in femto- to nano-seconds (depending on the laser pulse duration), the whole process can be considered as minimally destructive and real time. **Results:** The postulated hypothesis is aimed to use laser induced breakdown spectroscopy (LIBS) in the screening of cervical cancer as trace mineral elements acts as biological signature in tissues like bones, teeth, hair, blood, etc., from the living phase and store information regarding habitat, nutrition, and other environmental conditions. Previous researches have shown significant differences in concentrations of trace elements between normal and cancerous tissue cells. **Conclusion:** The technique is exemplified by suggested use of LIBS in studying biological samples such as tissues, gall stones, biological aerosols and in vivo cancer detection.

Keywords: Laser induced breakdown spectroscopy, cervical cancer, screening.

Prognostic value of lymphocyte-to-monocyte ratio in Epithelial ovarian cancer patients

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Background: Ovarian cancer is associated with high morbidity and mortality due to late presentation and high recurrence rate following treatment. The two important prognostic factors-ie stage and residual disease left after debulking will be known only after surgery. Currently there are no well established clinical or biologic markers including, CA-125, that can predict survival of patients with epithelial ovarian cancer prior to surgery. Clinicians and researchers have made widespread efforts

to identify biomarkers that predict progression of the disease, response to treatment and survival. Inflammation is recognized as a hallmark feature of cancer development and progression. The aim of our study was to evaluate the prognostic significance of the preoperative haematological marker – lymphocyte-to-monocyte ratio (LMR) in patients with ovarian cancer. **Method:** Electronic medical records of epithelail ovarian cancer patients who underwent surgery between January 20011 and December 2013 at Amrita Institute of Medical sciences, Kochi were reviewed. Demographic, Clinicopathological and complete blood count data were collected. The optimal predictive value of lymphocyte-to-monocyte ratio to predict advanced stage, suboptimal surgery, and survival was determined and compared with those of thrombocytosis. Preoperative lymphocyte-to-monocyte ratio were evaluated in 100 patients and the prognostic significance was then determined by univariate analysis using SPSS 20. **Results:** A total of 100 epithelial ovarian cancer (EOC) patients were included in this study. Lymphocyte to monocyte ratio of <2 yielded better predictive values than those have High preoperative lymphocyte to monocyte ratio >2 was significantly associated (p=0.085) with poor survival using univariate Cox survival analysis. The median overall survival in patients with lymphocyte to monocyte ratio >2 was poor - 24 months (95% CI 32.918-38.439; p=0.085) compared to patients with lymphocyte to monocyte ratio<2 having - 29months (95% CI 15.975-38.775). **Conclusion:** In this study we have shown that elevation of the lymphocyte to monocyte ratio is an independent prognostic marker for poor survival in patients with epithelial ovarian cancer along with age and FIGO stage. Lymphocyte to monocyte ratio is a readily available and inexpensive biomarker with independent prognostic value in epithelial ovarian cancer.

Title:Diagnostic role of Interleukin-6 serum level in ovarian carcinoma patients: A case-control Study

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Introduction: Environmental and genetic factors are playing key role in the development of ovarian carcinoma. Evidence suggests that chronic inflammation is involved in the regulation of cellular events in ovarian carcinogenesis, including disruption of the immune response and regulation of the tumour microenvironment. Cytokines may contribute to metastases by promoting angiogenesis, enhancing tumor cell adhesion, inducing proteolytic enzymes and their levels have been investigated as diagnostic and prognostic markers in cancers.Interleukin 6 (IL-6), is secreted by T cells and macrophages to stimulate immune response.IL-6 acts as both a pro-inflammatory cytokine and an anti-inflammatory myokine. **Objectives:** The aim of this study was exploring the role of Interleukin-6 and its significance in ovarian carcinoma patients. **Material and Methods:** A total of 220 patients, aged 20-60 yrs were enrolled for the study after approval of the Institutional ethics committee. Of the total of 110 patients had biopsy proven ovarian carcinoma (TNM stage: T2=26, T3=35 and T4=49). Peripheral blood samples of all patients and 110 age matched control subjects were obtained at baseline and estimation of IL-6 serum level was done by enzyme linked immunosorbent assay (ELISA) and significance of difference between two groups was calculated by using the student t-test. **Results:** The baseline levels of IL-6 in all groups of ovarian carcinoma were found to be significantly (p<0.01) higher than the control group. The levels of IL-6 found to be elevated significantly in stage T3 (p<0.07) and T4 (p<0.03) as compared to stage T2. It also showed its increase value in patient with advanced stage and metastasis. **Conclusions:** These findings show that serum IL-6 may be used as diagnostic biomarker in patients but still more studies on larger sample size is needed for its validation.

Keywords: Interleukin-6 – Diagnostic Marker - Ovarian carcinoma

A resection of an unusually large renal cell carcinoma: A gentle giant in hand

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Back ground: Renal cell carcinoma is a great mimic among the malignancies so much so that it is called an intern's tumor. However, there is also another part of the spectrum where the malignancy just grows and grows pushing boundaries but never crossing them. We herein report a case with such a presentation that would deter many surgeons considering an upfront surgical approach and risk writing off the patient labeling them "bad tumor biology". It is being reported to join the database of precedent cases to provide a case for Exploration in such presentations. **Material and Methods**: A 66 year-old gentleman presented with heaviness in the right side of the abdomen for two months. He was otherwise unperturbed. On palpation, a mass was more than obvious in his abdomen occupying the entire right side. He was duly evaluated with MRI urography, CECT chest, abdomen and pelvis. The imaging revealed a mass arising from the mid and lower pole of the right kidney. There was no thrombus in the inferior vena cava or enlarged lymph nodes but lung masses with spiculated margins were noted suggestive of metastases. He was planned for cytoreductive surgery after a board discussion. He was taken up for Right radical nephrectomy and right pulmonary metastasectomy in the first stage followed by left pulmonary metastasectomy four weeks later. Post resection, the specimen was 17 x 16 x 15cm and cut section revealed the tumor to be 17 x 16 x 14cm. It weighed at 5.018kg. Seven nodes were harvested with the specimen and all were negative for malignancy. All the pulmonary metastasectomy specimens were also negative for malignancy as well. This case is being reported to add to the notoriety of unusual and unpredictable behaviour of renal cell carcinoma. It was such a huge mass that would deter the boldest of surgeons yet it was complacent with its location inside the kidney. The endemic prevalence of TB in India throws many a red herring in the lungs. **Results**: A right radical adrenal sparing nephrectomy was done along with right pulmonary metastasectomy. The tumor on cut section measured 17 x 16 x 15 cm and weighed 5.018kg. The post op histopathology report revealed a papillary renal cell carcinoma – type I with Fuhrrmann nuclear grade I.Left pulmonary metastasectomy specimens were also negative for malignancy placing him under Stage II (T2bN0M0). **Conclusion**: All these present a case for an exploratory laparotomy and possible cytoreductive surgery irrespective of the results of the RCTs being done to examine the role of surgery in stage IV renal cell carcinoma. This is especially true in TB endemic areas where lung lesions mimicking metastases are dime a dozen. The patient is suddenly now placed in a lower stage and has undergone curative resection. Many a patient have benefitted from such wishful thinking of their doctors to give them the best chance

A rare case of small cell carcinoma urinary bladder

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Introduction: Small cell carcinoma of the bladder (SCCB) is rare, highly aggressive and diagnosed mainly at advanced stages. Hematuria is the main symptom of this malignancy. The origin of the disease is unknown; however the multipotent stem cell theory applies best to this case. Histology and immunohistochemistry is almost same as small cell lung carcinoma. The overall survival rate at 5 years does not exceed 8%. At the time of presentation 59% of patients have clinical stage >T2 and 56% show metastatic disease. In 50% of the patients, fatal progression occurs within 6 months. Local recurrence after radical surgery occurrs in 50-70% of cases. **Objectives:** To sensitize the audience regarding the diagnosis, workup and management of this rare disease. **Material and Methods:** We report a patient with small cell carcinoma bladder with nodal metastases. A 32 year old male presented with hematuria in March`2014.On evaluation, CECT abdomen and pelvis was suggestive of malignant neoplastic lesion in urinary bladder. Biopsy from bladder growth was suggestive of small cell carcinoma bladder. PET CT was suggestive of supraclavicular and abdomino-pelvic lymph nodes.

He was managed with two lines of palliative chemotherapy. Post two lines of palliative chemotherapy till April`2015 patient presented with large conglomerate lymph nodal mass in left supraclavicular lymph node. FNAC from the same revealed metastatic deposits of small round blue cell tumor. **Results:** He was managed with palliative radiotherapy to the nodal mass to a dose of 30 Gy/10#. The patient showed good symptomatic response. The details of the case will be presented in poster form. **Conclusions:** In the absence of a prospective study, and because of the rarity of the disease, the best treatment for small-cell bladder cancer remains uncertain. Neoadjuvant chemotherapy with platinum regimen plus aggressive surgical approach will be the treatment of choice. The association of chemotherapy and radiotherapy should also be considered.

River flow incision for decreasing morbidity of Ilio-inguinal dissection

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Introduction: Ilio-Inguinal Lymph node dissection is an important component of surgical treatment for a variety of below umbilical malignancies ranging from Carcinoma of Penis, Vulva, Primary cutaneous cancer, soft tissue sarcoma, melanoma etc. Skin flap necrosis is one of the most common complications after Ilio-inguinal Lymph node dissection (ILND). Established surgical principles of preserving Great Saphenous vein (GSV) have decreased lymphedema associated with ILND .However with reported frequency up to 65% in published literature, skin flap necrosis is a major contributor to postoperative morbidity after ILND. Our initial experience with a modified surgical approach of River flow incision, with no learning curve, has been most successful in eliminating flap necrosis. **Material and Methods:** A modified skin incision was used to perform ILND in 77 prospective patients. Irrespective of primary histology or timing of inguinal dissection, same technique was used in all cases. Two curvilinear parallel skin incisions (5-7cm long) were made; each sited about 4 cm above and below inguinal ligament. Flaps were carefully raised below Scarpa's fascia. Lymph node dissection was performed in both inguinal and iliac basin with a standard technique. All Patients were followed up prospectively for 30 days after surgery and complications if any, were recorded according to the Clavein-Dindo System of reporting surgical complications. **Result:** A total of 77 patients underwent 109 ILND from July 2012 till Nov 2015. Unilateral dissection was performed in 45 patients and 32 underwent bilateral ILND. Majority of patients had genital or lower limb malignancies. Carcinoma Penis (15), Vulvar Cancer (05), Inguinal metastasis of CUP (10), Primary cutaneous malignancy (Melanoma lower limb -13; SCC lower limb -21), Cervical cancer (02), Soft tissue sarcoma lower limb (05), Relapsed Anorectal cancer (03), & NSGCT (03). There were no instances of flap necrosis/loss. Complications recorded were Seroma (11.0%), Lymphedema (17.4%), Surgical site infection (11.9%), Deep vein thrombosis(2.7%), all corresponding to Clavein –Dindo Grade 1 & 2 . Surgical intervention corresponding to Clavein- Dindo grade 3A (Intervention not requiring GA) were required in 9.2%. **Conclusion:** 'River Flow' Incision is a simple but effective surgical modification which has enabled us to perform therapeutic ILND safely. Avoidance of flap necrosis, significantly decreased morbidity and almost no learning curve are highlights of this modification of surgical technique.

In silico profiling for identification of hypermethylated genes as potential biomarkers of Prostate Cancer

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Introduction: Prostate Cancer (PCa), a multifocal clinically heterogeneous disease accounts for being the most commonly diagnosed non-cutaneous neoplasm in men worldwide. Histone modifications and DNA methylation have emerged as new hallmarks of cancer owing to their contribution in modulation of tumor initiation and metastasis related gene expressions. The epigenome of Prostate cancer is a typical representation of catastrophic model of epigenetic alterations during tumorigenesis and progression. Alterations in methylation patterns in tumor suppressors, cell cycle, oncogenes and metabolism related genes are the most commonly observed epigenetic alterations in Prostate cancer. **Objectives:** In this study,we have developed an *in silico* strategy to identify methylated biomarker gene signature panels as potential targets of PCa. **Material and Methods:** A thorough literature survey was carried out to prepare a comprehensive list of hypermethylated genes in Prostate Cancer. This was followed by their epigenetic methylation profiling and gene enrichment analysis using online tools and databases to identify their potential contribution in tumor progression. **Results:** In the current study, using an *in silico* based approach we have evaluated a panel of five aberrantly methylated genes (GSTP1, CDH1, HIC1, CAV1, MGMT) for their methylation frequencies, CpG islands prediction, positions of methylated cytosines, transcription start sites and also their biological and functional annotations along with their phylogenetic analysis. **Conclusions:** The genes identified have critical roles in cell cycle, growth, metabolism, DNA repair, migration, differentiation, adhesion and metastasis. Using this approach we have tried to establish a strong association of these hypermethylated genes with PCa progression and to provide new insights into employing such panels of hypermethylated genes as potential therapeutic and diagnostic targets for PCa in near future. Further validation of these hypermethylation profiles clinically may lead to identification of novel molecular markers for the prognosis of early as well as advanced Prostate Cancer.

Simultaneous Whole-body ^{18}F-FDG PET/MRI in primary breast cancer staging

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Purpose: Accurate initial whole-body staging in breast carcinoma is important for planning treatment and prognostication. Dedicated dynamic contrast-enhanced breast MRI (DCE-MRI) has become an important tool in accurate pre-operative local evaluation of breast cancer. Whole body staging using ^{18}F FDG PET/CT is being predominantly used in distant metastatic staging of patients with locally advanced breast carcinoma with several reports of increasing utility in staging early breast cancer. With the advent of integrated PET/MRI, total comprehensive whole body evaluation is now feasible. With this study, we aimed at assessing the utility of whole body simultaneous ^{18}F FDG PET/MRI in initial staging of breast carcinoma. **Methods:** 99 patients with histologically confirmed breast carcinoma underwent simultaneous whole body ^{18}F FDG PET/MRI on integrated 3T PET/MR scanner (Siemens Biograph mMR) for primary staging. Primary lesion, nodes and metastases were evaluated on PET, MRI and PET-MRI for lesion count and diagnostic confidence (DC). Histopathology, clinical/imaging follow-up served as the reference standard. **Results**: A retrospectively study of 99 patients with 101 histopathologically proven index breast cancers of which 64 patients underwent surgery and 35 patients received systemic therapy. All index cancers were seen on PET and MRI. PET/MRI showed highest diagnostic confidence score of 5 compared to PET and MRI alone. 3/99 (3%) patients had unsuspected contralateral synchronous cancer detected on MR. On DCE MRI, 109 (76 FDG avid) satellite lesions with multifocality and multicentricity in 45(45.45%) patients were detected. For axillary lymph node detection, a sensitivity/specificity/false negative rate of 65.11/95.45/37.2% and 88.37/91/11.62% on PET and MRI respectively. Combined PET/MRI increased diagnostic confidence for nodal involvement (median DC 5, $p<0.05$). At the time of diagnosis, Distant metastases found in 20/99 (20.20%) patients with a total of 215 metastatic lesions on PET ($DC\geq4$) and 262 on MRI ($DC\geq4$), the difference being statistically significant ($P=0.001$). Overall PET/MRI led to a change in management in 33 (33.3%) patients with improved T staging in 14 (42.42%) patients and N staging in 4 (12.12%) and M staging in 15 (45.46%) patients. **Conclusion:** Simultaneous ^{18}F FDG PET/MRI has been found to be useful

for initial whole body staging of breast cancer resulting in significant change in management in one-third of patients.

Is more aggressive treatment needed for young breast cancer patients?

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Introduction: Breast cancer is the commonest malignancy among the Sri Lankan females. It counts to almost 1/3rd of total cancers. Though the risk is lesser than the west, still it carries 1:40 life time risk. Immunochemistry is a main component in the histological assessment of patients with breast cancer as this provides both prognostic as well as predictive factors of the disease. **Objectives:** Our aim was to compare the age of the prevalence of accepted prognostic factors of breast carcinoma patients in a single surgical oncology unit over a period of 3 months. **Material and Methods:** This was a retrospective descriptive study. The immunohistochemical reports of patients who underwent surgery as primary treatment for breast carcinoma at an Oncosurgical unit, were obtained and analyzed with SPSS 17. **Results:** Study included 62 female patients, mean age 57 years (SD ± 13.18). Oestrogen Receptor (ER), Progesterone Receptor (PR) and Her-2 Receptor were positive in 35(56.5%), 28(45%) and 18(29%) respectively. Students' t-test was applied to analyze the ages of specific receptor status. ER and PR positive patients were significantly older (61 versus 51, and 61 versus 53) and this was statistically significant (p=0.003 and p=0.026). Her-2 receptor was positive in younger age groups (50 versus 59.75) and this too was statistically significant. (p=0.01) The Ki67 proliferation index failed to show any relationship with the age of the patient (p=0.21). To confirm these findings, the molecular classification was analyzed with age. The mean age of Luminal type A and B (good prognostics) was 60.8. Her-2 positive disease and triple negative disease combined had a mean age of 52.11. This was statistically significant (p=0.009). **Conclusions:** ER and PR expression in the current study is very much lower than the western women, but compatible with some regional studies. According to the receptor profiling, unfavourable prognostic features are seen in younger individuals. This entails more aggressive treatment.

Slnb (sentinel lymph node biopsy) in carcionma cervix

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Introduction: Sentinel Lymph node study is established technique to identify occult lymph node metastasis in carcinoma breast & melanomas. But its role in Gynec-malignancy is not well established, and at present is not standard of care.The purpose of this study is to evaluate the feasibility, usefulness and clinical impact of this technique in twenty consecutive patients with early cervical cancer. **Method:** Between January 2010 and January 2012, twenty patients with biopsy proven early stage cervical cancer (FIGO Stage IB1 and IB2) were taken up for study at Manipal Comprehensive Cancer Centre. A combination of Methylene blue dye and radioactive 99 Tc-Sulphur nano-colloid was used. **Result:** The SLN was detected in all cases (Identification rate—100 %). The mean number of sentinel nodes was 2.7. Methylene blue dye could detect sentinel node (blue node) in 90 % cases (n=18). Gamma probe could detect SLN (hot node) in 95 % of cases (n=19). In one patient, only blue dye identified the SLN which was a parametrial node. In 6 patients (30 %) the SLNs were positive for metastasis, of these two had stage IB1 and remaining four had stage IB2 disease. In 33.3 %(n=2) cases the Sentinel node was the only positive node. The mean size of positive sentinel node was 0.8 mm. **Conclusion:** SLNB in early stages of cervical cancers is a promising surgical technique to confirm nodal status and minimise post-operative morbidity avoiding unnecessary lymphadenectomy in presence of negative SLN. However ours is a small study and for the clinical validity of this technique large randomized multi institutional trials are required.

Key words: Carcinoma cervix, sentinel lymph node biopsy, SLNB

Extensive Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (Extensive CRS + HIPEC) for advanced ovarian carcinomas - Single institute Indian study

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Background: Cytoreductive surgery combined with hyperthermicintraperitoneal chemotherapy (CRS + HIPEC) has been proposed as treatment for advanced ovarian carcinoma. We conducted this study to analyse perioperative outcomes of extensive CRS & HIPEC in Indian patients with advanced ovarian carcinoma. We also aimed to analyze short term oncological outcome of the HIPEC procedure**. Methods:** We included 38 patients from February 2013 to June 2015 with advanced EOC and pseudomyxomaperitonii treated by dedicated peritoneal malignant disease treatment team. All patients underwent extensive CRS + HIPEC. The post operative morbidity and mortality were analysed. All patients followed up with existing guidelines and oncological outcomes were analysed. **Results:** Our patients were grouped into frontline 21.1% (n=8), interval cytoreduction50% (n=19), and secondary cytoreduction28.9% (n=11) based on the timeline at presentation. Mean peritoneal carcinomatosis Index was 8.5 ± 7.45 (Range 3-36). Average surgery duration was 9 ± 2.7 hours (Range 5.5 – 19). Mean perfusion temperature used was (42±0.49°C). Patients with PCI score ≥15 had prolonged gastrointestinal recovery (p=0.043), post operative ventilator need (p=0.011), ARDS (p=0.014) and dyspnea (p=0.002) with trend towards adverse events. Closed method HIPEC was associated with prolonged hospital stay (p=0.011), wound related complications (p=0.006) and ARDS (p<0.001). Multivisceral resections associated with increased ventilator need (p<0.001), ARDS (p=0.010) and adverse events (p=0.044). The recurrent ovarian carcinomas were associated with more wound related complications (p=0.016). More adverse events with Cisplatin 100 mg /m^2 (p=0.03) like dyselectrolytemia, acute renal failure, and fall in hemoglobin. No 30 days mortality. After a median follow-up of 18 (2-29) months 15.8% (n=6) had recurrences and 5.3% (n=2) patients succumbed to disease. **Conclusions:** Ovarian peritoneal malignancies known for peritoneal recurrences are amenable to extensive cytoreduction and HIPEC in carefully selected patients with acceptable morbidity. The benefit of HIPEC in our study was limited to platinum sensitive recurrent cases only and not to platinum resistant cases.

Key words: Cytoreductive surgery, advanced ovarian carcinoma, ovarian peritoneal malignancy, HIPEC, hyperthermicintraperitoneal chemotherapy.

Identification of potential biomarker for early diagnosis of ovarian cancer

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Introduction: Ovarian cancer is a lethal gynecological malignancy. The high mortality of the disease is due to late diagnosis and 5 years survival rate is decreased to 30 % when the disease is diagnosed in advanced stage. Survival rates are over 90 % when it is diagnosed at an early stage thus highlighting the need for new biomarkers for early detection. **Methodology:** Plasma samples were collected from 89 serous ovarian adenocarcinoma patients and 199 healthy volunteers, which were subjected to immune-depletion followed by prefractionation with HIC8, WCX and IMAC-Cu magnetic beads to enrich the low abundant proteins. The proteins/peptides profile was acquired using MALDI-TOF mass spectrometer in linear mode. Statistical software tool ClinProt was applied to compare the mass spectrum profile of ovarian cancer against healthy controls to identify the discriminating peaks. **Results and Discussions:** Differentially expressed mass ranges showing 1.5–2-fold change in expression from HIC8 fraction (30 peptide peaks), WCX fraction (12 peptide peaks) and IMAC-Cu fraction (6 peptide peaks) were identified. **Conclusions:** We identified differentially expressed proteins using MALDI-ToF mass spectrometry in serous ovarian adenocarcinoma. We have to validate the plasma levels of differentially expressed proteins to prove blood based markers for ovarian cancer.

Influence Of Histological Type On Clinicopathological Behaviour And Survival In Surgically Treated Carcinoma Cervix

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Introduction: According to GLOBOCAN 2012, cervical cancer is the fourth most common cancer among women worldwide with more than 20% of all cancer cases being diagnosed in India. Present study was aimed at assessing difference in biological behavior as well as recurrence and survival pattern in different histopathologies in cervical cancer patients treated by radical hysterectomy as primary modality or as adjuvant or salvage procedure after radiotherapy/ chemo radiotherapy. **Material and Methods:** 124 cervical cancer patients who underwent radical hysterectomy at our center during 2006 to 2012 were enrolled in this study. The medical records of the patients were examined retrospectively for clinical and histopathologic details, surgical parameters, details of adjuvant treatment and disease status on follow up. Patients were followed up till minimum of 3 yrs. **Observation and Results:** The median age was 49 years of the study patients, with most patients in age group 41-50 years (40.3%). Of 124 patients studied, 85 (68.5%) were squamous, 34 (27.4%) were adenocarcinoma and 5 (4.0) were adenosquamous. Stage wise distribution among squamous and adenocarcinoma was found to be similar with majority belonging to stage Ib (67.6% and 68.6 respectively).The lymph node involvement was 8.2% in squamous cell carcinoma versus 17.94% respectively in adenocarcinoma and adenosquamous carcinoma (p=0.056). Locoregional recurrence was found to be 8.2% and 10.2% in squamous and adeno-adenosquamous carcinoma respectively. Overall survival was better in squamous but statistically non-inferior in both adeno and adenosquamous carcinoma (p=0.074). **Conclusion:** The study suggests that non squamous histologies of uterine cervix carries higher risk of lymphnodal metastasis and risk of local recurrence compared to squamous cell carcinoma. Although these histologies are less common in cancer cervix they need more aggressive adjuvant treatment.

Key words: Carcinoma cervix, Squamous cell carcinoma, adenocarcinoma

Evaluation of demography and response to chemotherapy in recurrent or metastatic cervical carcinoma : Experience of a tertiary cancer centre in southern india

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Introduction: Cervical Carcinoma is the most common malignancy in Indian women, many of which present in advanced stages with high recurrence rates and poor outcomes. **Objectives:** We tried to evaluate demographic parameters of patients presenting with recurrent or metastatic cervical carcinoma and assessed their response to chemotherapy. **Material and Methods:** We retrospectively analysed data from our hospital registry of patients presented with recurrent or metastatic cervical carcinoma between Jan 2013 to Dec 2014 who were planned for palliative chemotherapy. We analysed demographic parameters of these patients and assessed response after Paclitaxel 175 mg/m2 and Carboplatin AUC 5 3 weekly for 6 cycles using SPSS software. **Results:** 150 patients with Recurrent or metastatic cervical carcinoma were evaluated. Mean age at presentation was 48 years. Most common symptoms at presentation were bleeding per vagina (PV) (71%), White discharge PV (64%) and lower abdominal pain (45%). 95% of the patients were multiparous while 21% of them were grand multiparous. Histologically Squamous cell carcinoma was found most commonly, majority being grade 2 disease (59.1%) followed by grade 3 (21.7%) and grade 1 disease (10.4%). 4.3% and 3.5% of patients had adenocarcinoma and adenosquamous carcinoma respectively. 22.6% of patients were upfront metastatic while rest were recurrent disease. Amongst the patients with recurrent disease, 80% had recieved prior Radiation Therapy, while 20% had undergone surgery for their disease. Median time to progression was 18 months. 45% of recurrences were localised. The most common sites of metastasis were retroperitoneal lymphnodes (20.1%) followed by liver (13%), lung (8.9%), bone (7.9%) and supraclavicular lymphnodes (7.9%). After a median of 6 cycles of chemotherapy Overall Response Rate [ORR] was 43% with 15% Complete Remission. **Conclusions:** Recurrent or metastatic cervical carcinoma is an aggressive disease occurring in females with poor outcomes. We report our experience in these patients with their demographic profile. Our patients showed an ORR of 43% to Paclitaxel and Carboplatin combination chemotherapy. Further research is required for improving outcomes of this aggressive entity.

Fallopian tube carcinoma; A case series

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Primary fallopian tube carcinoma (PFTC) is an uncommon tumor accounting for approximately 0.14–1.8% of female genital malignancies. It resembles epithelial ovarian cancer both clinically and histologically. Approximately 30% of PFTC have been described in association with germ-line BRCA-1 and BRCA-2 mutations. The diagnosis of PFTC is rarely considered preoperatively and most patients undergo laparotomy for the presence of an adnexal mass with the presumed diagnosis of ovarian carcinoma. Management at present follows the concepts used in epithelial ovarian cancer, with no significant differences in survival. The most important prognostic variables are stage and residual tumor post cytoreduction. Recent research has suggested that serous tubal intraepithelial carcinomas (STIC) are a precursor lesion for PFTC, primary peritoneal (PPC) and ovarian carcinoma (OC), suggesting a common tubal origin. Future research should be directed towards incorporating the presence of STIC for classification of the serous pelvic cancers, which may change the epidemiological picture of these rare PFTCs. Further, identification of PFTC as an entity distinct from OC may help in better understanding the molecular pathways of pathogenesis and in developing distinct treatment protocols based on them. We hereby present a series of four cases of fallopian tube carcinoma over a period of June 2014 to June 2015. The mean age of presentation was 58.9 years. All cases were post menopausal. Most of them presented as adnexal mass. Three out of four patients underwent comprehensive surgical staging and two patients underwent chemotherapy. Grossly, dilatation of fallopian tube was noted and ovaries were normal. Histopathological evaluation reported serous carcinoma. A second primary malignancy was detected in two patients.

Follow up of eight months was uneventful. The clinical presentation, diagnostic methods used and management of these cases is described here.

Keywords: Fallopian tube carcinoma, gynaecological cancer

Carcinosarcoma of Uterus in post irradiation carcinoma cervix patients- Case series

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Introduction: Uterine Carcinosarcoma is a rare tumor.The carcinosarcoma of uterus after pelvic irradiation has been reported in very few cases. **Objectives:** To study the cases of Carcinosarcoma of the uterus for their presentation, unique features and management .

Material and Methods: In regional cancer center experience the carcinosarcoma of uterus was presenting in 3-4% of cases with uterine cancer. The irradiation induced carcino sarcoma were three cases in two years. They presented with the same clinical features – white discharge and post menopausal bleeding. Endometrial biopsy in these patients were not feasible due to stenosed cervical os. Intra operatively they had fibrosed pelvis posing problem in performing total hysterectomy.Underwent subtotal hysterectomy. Histopathological examination and immunohistochemistry confirmed carcinosarcoma of uterus.Pathients received adjuvant chemotherapy and are on follow up. **Results:** Carcinosarcoma of uterus in patients who received irradiation is seen rarely, and these patients pose problems in evaluation and management due to post irradiation changes. **Conclusions:** Carcinosarcoma of uterus a rare tumor of uterus in post irradiation patients, with difficulty in evaluation and management.

Interplay between miR-34a expressions and HPV in the progression of cervical carcinogenesis.

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Introduction: MicroRNAs are short sequence of nucleotides (18 to 25) non-coding RNA that regulate gene expression. Mature miRNAs post-transcriptionally regulate its target gene expression by messenger RNA (mRNA) degradation or translational repression depending upon the complementarity between miRNAs and 'seed sequence' of mRNA of gene. Differential miRNAs has been reported in many cancers including HPV mediated cervical cancer. **Objectives:** The aim of the study is the detection of differentially expressed miRNAs in HPV associated cervical pre-cancer, cancer in compare to controls samples for microRNA expression signature for cervical cancer prognosis. **Material and Methods**: We studied the expression profile miRNAs in cervical pre-cancer (n=10), cancer (n=20) and normal controls (n=20) by miRNA isolation, cDNA preparation followed by quantative real time polymerase chain reaction (qRT-PCR). **Results:** Study demonstrate an aberrant expression pattern of different miRNAs in cervical pre-cancer and cancerous cases when compared with normal controls. The majority of aberrant expressed miRNAs were belonged to miR-34a family which is found to be down regulated in cervical pre-cancer and cancer when compared with normal controls. In addition, we also observed a differential expression pattern of this miR-34a in different grades of cervical pre-cancer and cancer cases along with HPV infection. **Conclusions:** Therefore, the study demonstrated a crucial role of microRNA particularly of miR-34a family and could be a promising starting point for developing future miRNA-based cervical cancer biomarker.

Oral metronomic cyclophosphamide in heavily treated recurrent epithelial ovarian cancer: An old drug with a new concept.

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Introduction: Metronomic therapy comprising of continuous administration of low dose in oral form has recently gained attention due toits modest activity ,convenience and use in outpatient setting withfewer hospital visits.Freedom from iv infusion with minimum adverse effects are an addedprivilege. Metronomic therapy exerts its antitumour activity mainly due to it antiangiogenic effects,antitumour immunity and apoptosis; hence it is also described as mutitargetd therapy. **Objectives**: To evaluate safety and efficacy of oral metronomic cyclophosphamide in heavily treated recurrent ovarian cancer. Primary objective was to assess the progresson free survival and objective response rateORR(CR+PR), and clinical benefit rate CBR (CR+PR+SD). Secondary objective wasadverse events of therapy and compliance. **Material and Methods:** Retrospective analysis of patients receiving oral Cyclophosphamide 50mg/day. The therapy was continued till disease progression or unacceptable toxicity; whichever was earlier. The data was collected from Jan2014 to Oct 2015. Only patients previously treated with one or more platinum,Paclitaxel drug regimen and having radiological evidence ofrecurrence were included. All patients had ECOG Performance status <2,adequate bone marrow reserve, ANC>1500,platelet count 1lakh and bilirubin, liver enzymes and creatinine <1.5 times of their upper normal limits. Response evaluation was done at 3 months or as advised by the treating physician if indicated early. Response to treatment was assessed by RESIST1.0 criteria and toxicity was graded according to CTCAE version 4.0. PFS was calculated from date of starting the therapy till the first documentation of disease progression. **Results:** Total 24 patients were studied out of which 15 (62%) were Platin sensitive (unwilling for parenteral CT) and 9 (37.5%) were platin refractory. Median age of cohort was 52years and5, 16 and3 patients hadreceived 2,3 and 4 lines of therapy respectively. About 66% of patients were pre-treated with 3 lines of therapy. ORR of total patients was 4/24(16%) with CBR of8/24(37%). Totally, 12/24(50%) had PD,5/24(20%) SD,3/24(12%)PR and 1/24(4%)had CR. Median PFS was equal, 5 months in platinum sensitive andrefractory sub group,and 10/24(41%) had PFS of >6mths.Among Platin sensitive,6/15(40%)patients had PDand4/15(26%), 2/15(13%),1/15(6%) had SD , PR,CR, with ORR, CBR of 3/15(20%)and6/15(40%) respectively. In Platin refractory, 6/9(66%) had PD and1/9(11%),1/9(11%),0 had SD, PR,CR, with ORR, CBR of 8/9(22%) respectively. All patients tolerated therapy well while 1 patient developed grade III neutropenia and 1 had grade II hepatic dysfunction.None of the patients had grade IV toxicity. **Conclusions:** Metronomic oral Cyclophosphamide is well tolerated and has modest efficacy in heavily pre-treated ovarian cancer. Similar PFS in Platin sensitive and Platin refractory disease could be due to less number of Platin refractory patients. None the less it seems a promising optionwarranting further studies.

Dynamics of Putative Oxidative Stress Markers in Patients with Cervical Cancer Undergoing Therapy

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Background: The present study was undertaken in patients of carcinoma cervix to evaluate the Implication of chemo radiotherapy on status of oxidative stress biomarker such as protein carbonyl, lipid hydro peroxide and antioxidants defence mechanism of melatonin and total thiol levels. Methodology: Patient was delivered radiotherapy by external beam radiotherapy (EBRT) followed by brachytherapy.All patients will be given chemotherapy in the form of injection cisplatin.Blood samples were collected from patients as well as control before treatment and within 24 hours and six months after chemo radiotherapy. Newly diagnosed women with cervical cancer [N=192], 30-65 years of age and age- matched clinically healthy women [N=192] were included in this study. Result &Conclusion: The mean LOOH and PC levels in all three groups of cases were comparatively higher than controls. Further, the mean LOOH and PC levels increased in cases after the chemo-radiotherapy as compared to pre chemoradiotherapy (P<0.001). Study also found that the mean Melatonin level and total thiol level in all three groups of cases lowered comparatively than controls. Further, the mean Melatonin and total thiol in cases decreased after the chemo-radiotherapy as compared to pre chemoradiotherapy. We suggest that plasma PC, LOOH, PC, Melatonin and T-SH may serve as biomarkers for oxidative stress in patients with gynecological malignancy. A highly structured study with a larger sample size is required to establish the precise role of oxidative stress in pathobiology of cancer. Such oxidative biomarker can be used for diagnosis and prognosis of diseases in future.

Keywords: Chemotherapy, Oxidative stress, Radiotherapy, Cervical cancer.

Early Clinical experience of Sandwich Therapy in Endometrial Cancer

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Background: Concurrent chemotherapy and whole abdominal irradiation was initially used as adjuvant in endometrial cancer. Concomitant therapy was associated with greater toxicity. In order to alleviate toxicity, sequential adjuvant chemo- radiotherapy popularly known as "sandwich therapy" is recommended. **Objective:** The purpose of this retrospective study was to assess the tolerability and efficacy of sequential chemotherapy and radiotherapy for the treatment of high risk endometrial cancer. **Material and Methods:** We conducted a retrospective study of previously untreated high risk endometrial cancer patients who received sequential chemotherapy and radiotherapy in accordance with the sandwich approach from March 2012 until Dec 2014. High risk endometrial cancer patients underwent complete surgical staging followed by adjuvant therapy encompassing sequential chemotherapy, radiation therapy and consolidation chemotherapy. **Results:** The study analysis comprised 10 endometrial cancer patients. Mean age of the study group was 60.2 year (range 50-70 years). All subjects were initially treated with carboplatin and paclitaxel chemotherapy. For one patient, paclitaxel was substituted with liposomal doxorubicin after 3 cycles in view of grade3 peripheral neuropathy. And for another patient, only 3 cycles were administered in view of grade 4 toxicity. Total of94 cycles have been administered. Grade 4 neutropenia developed in 1 (10%) patient. Moreover, we observed grade 3 thrombocytopenia in two (20%) patients.Two patients exhibited progressive disease, one of whom has since expired. At a median follow up period of 3 years, median PFS has not reached and 3 years PFS is 64.3 ± 2.1%. **Conclusion:** Sequential adjuvant chemo- radiation is efficacious in endometrial cancer with tolerable toxicity profile.

Role of cytology in the follow-up of women treated for benign and malignant conditions of uterine cervix

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Objective: To assess the utility of cervico-vaginal/ vault cytology in the follow-up of women treated for cervical cancer and benign gynaecological disorders. **Material and Methods:** 3523 cervico-vaginal / vault smears from 2658 women who underwent hysterectomy and/or radiotherapy or chemotherapy, over a 10 year period were retrieved. Data was collected on type of treatment received, indication for hysterectomy, age of patient, presenting symptoms, stage of tumor, interval since treatment, cytology and biopsy results. The results of cytology versus other parameters were analyzed separately for women treated for cervical cancer and those hysterectomized for benign indications. **Observations:** Malignant cells were detected in 141/1949 (7.2%) follow-up smears from treated cervical cancer cases (140 recurrences and 1 vaginal intraepithelial neoplasia [VAIN]). Around 92% of recurrences of cervical cancer were detected with in 2 years of follow-up and 75% of these women were symptomatic. Cytology first alerted the clinicians to a recurrence in a quarter of cases. On the other hand, VAIN was detected in only 5/1079 (0.46%) vault smears from 997 women hysterectomized for benign gynaecologic disease. All these women were asymptomatic and majority (80%) were detected on follow-up smears performed between 3-10 years. **Conclusions:** Vault / cervico-vaginal cytology is an efficacious tool to detect local recurrences in women treated for cervical cancer. It may even first alert the clinicians to a possibility of recurrence in otherwise asymptomatic women. However, due to extremely low prevalence of VAIN / vaginal cancer, it seems unwarranted in women hysterectomized for benign indications, especially in resource constrained settings.

Key Words: Cervical carcinoma, vault smear, vaginal intraepithelial neoplasia (VAIN), cytology, hysterectomy

Role of cytology in the follow-up of women treated for benign and malignant conditions of uterine cervix

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possibility of recurrence in otherwise asymptomatic women. However, due to extremely low prevalence of VAIN / vaginal cancer, it seems unwarranted in women hysterectomized for benign indications.

Malignant pericardial effusion at initial presentation in a patient with metastatic carcinoma of the uterine cervix.

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Background: Involvement of heart and pericardium is an extremely rare occurrence in a patient with gynecologic malignancies. Pericardial metastasis from cervical cancer is an extremely rare event. Till date, only a few such cases have been reported in theEnglish Literature. In this case report a 26-year-old Afghan female patient with clear cell adenocarcinoma of the cervix was diagnosed to have malignant pericardial effusion at initial presentation. The patient was treated with palliative pelvic radiotherapy and pericardial effusion was managed with repeatedpericardiocentesis and chemotherapy. A brief review of the literature on the management of this type of metastatic presentation in patientswith canceris also presented in this presentation. **Materials and Methods:** A 26 year-old Afghan womanreferred to our institute in the month of November 2014, with complaints of post coital bleeding of 2 months duration and shortness of breath and heaviness in chest. Her past medical history was insignificant. Clinically, she was afebrile, pulse rate was 84/minute and regular, Blood pressure 106/70 mm of mercury, heart sounds were faintly audible on auscultation, jugular venous pressure was slightly raised. Pelvic examination revealed a growth measuring about 4x4 cm in size at the cervix with involvement of upper half of vagina and both parametrial infiltration upto the lateral pelvic walls.She was also found to have edema of the left upper limb and cervicaladenopathy. X-ray chest showed enlarged cardiac silhouette. Her routine blood counts, urine examinations etc. were normal. Ultrasonography of the abdomen and pelvic region, CT scan of the neck, chest, abdomen and MRI of the pelvis were done. MRI revealed 6x4x4 cm size lesion at cervix with multiple pelvic and para-aortic and inguinal nodes. CT scan showed extensive lymphadenopathy in the neck, mediastinum, abdomen and pelvis and inguinal region with moderate pericardial effusion. Bilateral hydro-nephrosis also noted. Doppler's study of the left upper arm showed thrombus in internal jugular vein and leftsubclavian vein. Echocardiography confirmed pericardial effusion. Left ventricular ejection fraction was 55%. Her cardiac markers were normal.Electrocardiogram (ECG) showed sinus tachycardia and low voltage QRS complex consistent with findings of pericardial effusion. .Biopsy from the cervical lesion was reported as adenocarcinoma. The patient underwent therapeutic pericardiocentesis and fluid cytology was reported as metastatic carcinoma.The patient was treated with a short course of palliative external beam radiotherapy to pelvic region. She received 4 cycles of carboplatin and paclitaxel based chemotherapy and also underwent repeated pericardiocentesis. The patient died due to her progressive disease in April 2015. **Conclusions:** Metastatic carcinoma of the cervix can present with malignant pericardial effusion or even with cardiac temponade. Therefore, gynecologists and gynecological oncologists and radiation oncologists need to be familiar with the diagnosis and management of this disease process.

Key words: Cervical cancer,Malignant pericardial effusion.

Comparison of the outcomes between locally advanced cervical adenocarcinoma and squamous cell carcinoma patients treated with definitive chemoradiation

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Background: Squamous cell carcinoma and adenocarcinoma are the two most common histology of carcinoma carvix. We aim to present comparison of survival outcomes between locally advanced adenocarcinoma and squamous cell carcinoma patients treated with definitive chemoradiation. **Materials and Methods:** It is a retrospective analysis and direct comparison between adenocarcinoma and squamous cell carcinoma cervix treated from January 2011 to December 2015. Of 73 patients analyzed 61 had squamous carcinoma histology and remaining 12 had adenocarcinoma. Inclusion criteria were patients with locally advanced stage (IIA) who have completed definitive chemoradiation and were available for response evaluation at 3 months of completion of treatment. Endpoints for the study were disease response evaluation at 3 months, progression rate, median progression free survival, median recurrence free survival, median loco-regional control, median distant metastasis free survival, median overall survival. **Results:** There was no significant difference between the two histology groups with respect to rate of achieving complete response (78.6 vs 75 %, p = 0.718) and rate of disease progression (36% vs 50%, p = 0.517). There was no significant difference between median PFS (57.75 vs 17.74 months; p = 0.964), median RFS (not reached {NR}vs 66.03 months; p = 0.876), median loco-regional control (not reached for both; p = 0.315), median DMFS (NR vs 66.03 months; p = 0.438) and median OS (NR vs 66.13 months; p = 0.884). **Conclusions:** Locally advanced squamous cell carcinoma and adenocarcinoma treated with definitive chemoradiation have similar outcomes. Small sample size is the limitation of this study.

Relationship between hormone receptor status, reproductive factorsand clinicopathological profile inBreast Cancer

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Background: The survivalin carcinoma breasthas been linked to a variety of clinical, pathologic and molecular features which includes histologic type, grade, tumor size, lymph node metastases and hormone receptor status. **Material and methods:** Aprospective study was conducted on 72 cases of histologically proven carcinoma breast treated between January 2014 to November 2015. Data was collected regarding clinical profile including parity, histological type, grade and hormone receptor status of tumors. **Results:** Majority of patients(59.7 %) were between 31-50 years of age. The disease was most common in multiparous(91.7%) as well as in post menopausal women (54.8%). Majority of patients had LABCi.e., Stage III disease (55.6%)out of which maximum (30. 6%) were in stage IIIB followed by stage IIIA (25%).Infiltrating/invasive ductal carcinomas not otherwise specified were the most common type of tumor (88.8%). Triple negative tumors were the most common subtype (37.50%), followed by Luminal A (36.11%) and Luminal type B (13.88%). Higher ER positivity was observed in the in patients≥50 years (p=0.014). No association was found between age and PRpositivity (p=0.326) or HER-2/neu receptor status (p=0.949). No significant association was observed between parity (p=0.595), menopausal status (p=0.881)and hormone receptor based subtypes of carcinoma breast. No significant association was found betweenhistological type(p=0.565) or gradeof tumor (p>0.05). A significantly higher frequency of ER/PR negativity being noted in subjects having advanced stage (III) breast carcinoma (p=0.040).Subjects with lymph node metastasis had the highest frequency of ER/PR negativity (65.9%) which was found to be statistically significant(p=0.006). The frequency of HER-2/neu positivity was higher in subjects with involvement of lymph nodes, however, the association was not found to be statistically significant (p=0.098). **Conclusion:** Breast cancer was found to be common in multiparous women. Higher incidence of lymph node metastasis was found in patients having HER-2/neu overexpression.A

significantly higher frequency of ER/PR negativity being noted in subjects having advanced stage (III) breast carcinoma (p=0.040).

A retrospective cohort study of cancer cervix patients registered in a tertiary care centre

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Cancer cervix is a major healthcare problem amongst females especially in developing countries. This is a retrospective cohort study of all the cancer cervix patients registered in the year 2012 in the department of radiotherapy of a tertiary care hospital. **Aims & Objectives:** The study was performed to document the epidemiological parameters, find out the compliance to the standard treatment, adequacy of the infrastructure available, outcome and follow-up of all the patients registered during this period. **Material & Method:** A total of 158 cases of carcinoma cervix were registered. Data was collated by a retrospective review of clinical notes. Vigorous efforts were made to find out the status of the patients who were lost to follow up. **Results:** Cervix cancer constitutes 7 % of all cancer cases registered. It is still the commonest amongst females in this part of the country followed by Breast & Head and Neck. The age ranged from 18 years to 65 (median 45). Commonest histopathology was squamous cell carcinoma (90%), adenoma carcinoma 8%, and others 2%. Out of total 158 patients 51(32%) cases reported only once in Out Patient department & then did not turn up for any further treatment. 40(25%) cases were registered as post operative cases. 62(40%) cases presented as de-novo and were registered for definitive CRT. 5 patients (3%) presented with distant mets. 62 patients (40%) who presented de novo were further analyzed for various other parameters. 35(56%) cases of the 62 patients took standard treatment of care in the form of concurrent CRT, however 16(26%) cases received NACT followed by concurrent CRT and 11(18%) cases received NACT followed by RT alone. To analyze the adequacy of resources available in the institution we calculated the time for initiation of RT since registration. Only 48 % cases could receive RT within one month of registration. All the patients were given EBRT dose 50 Gy in 25 & ICRT dose was 7 Gy in 3#. 48(77%) patients had CR one month after completion of treatment. **Conclusion:** The study concludes that cancer cervix is still probably the commonest malignancy in the state of Uttar Pradesh. Single OPD attendance of 30% of the patients reflects the status of highly inadequate infrastructure. The remaining patients who came for further treatment had to wait for minimum one month for initiation of RT, 52% had to wait for longer period and therefore NACT was given which is not the standard of care. Intermittent nonavailability of brachysource is a major issue because of which 18% patients were sent to other centers to receive ICRT.

Stage	No of Patients	Response		Status				
		CR	PR	LFU with disease	LFU without disease	Alive without disease	Alive with disease	Death
IB	04	3	1	1	2			1
IIA	10	6	4	2	3	2		1 2
IIB	31	26	05	7	11 2	3	1	4 3

Association of IL-10 (-592 A/C) genetic variants and serum IL-10 level in ovarian cancer patients in north Indian population

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Introduction: Interleukin-10 (*IL-10*) is a multifunctional cytokine with immunosuppressive and anti-angiogenic functions and have both tumor-promoting and tumor-inhibiting properties. Local and systemic secretion of immunosuppressive cytokines plays an important role in the impaired antitumor immune function. A large number of polymorphisms, primarily single nucleotide polymorphisms (SNPs) have been identified in the *IL-10* gene promoter. Variation in DNA sequence in gene promoter may lead to altered IL-10 production and/or activity, and hence can modulate an individual's susceptibility to ovarian cancer (OC). **Objectives:** We investigated the relationship ofIL-10 gene promoter -592 A/C polymorphism with the risk of OC in north Indian population. **Material and Methods:**Atotal number of 300 subjects were enrolled in the study after approval of the Institutional ethics committee. Out of 300 subjects, 150 were biopsy proven OC patients as a case and age, ethnicity matched independent 150 healthy subjects as controls were recruited withthe age range of 20-60 years. Polymorphisms in the *IL-10* gene were analyzed by using restriction fragment length polymorphism-polymerase chain reaction (PCR-RFLP) method. The concentrations of IL-10 in serum were determined by enzyme-linked immunosorbent assay **(**ELISA). **Results:** ASignificant association was foundwith IL-10 (−592) A/C heterozygous genotype (AC) with 1.62 fold risk of OC as well as C allele carrier and variant C allele having 1.57 fold and 1.52 fold risk for OC respectively. Serum IL-10 levels were significantly higher in OC patients as compared to healthy subjects (p=0.001). Serum IL-10 levels were also significantly associated with IL-10 (-592A/C) in heterozygous genotype of (AC) (p=0.001). **Conclusions:** Our results suggest that IL-10 gene polymorphism contributes to ovarian cancer risk.A relation between IL10 (−592) A/C in heterozygous genotype with elevated IL-10 serum level and ovarian cancer risk has been observed in the present study.

Keywords: IL-10, Ovarian cancer, Polymorphism, ELISA

MRI versus clinical staging and response assessment in locally advanced cervix cancer patients treated with concurrent chemoradiation in a tertiary cancer centre- A prospective study

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Background It is observed that FIGO stage may under or over stage the disease burden when correlated with imageology. MRI is a good modality in defining the soft tissue extent of the disease. Prospective trials comparing clinical and MRI in staging and treatment response is sparse. **Aims and objectives** Objective of this study is to compare the MRI versus clinical staging and response assessment in locally advanced cervix cancer patients. **Materials and Methods:** This is a prospective study conducted in our institution from 1st January 2014 to 1st January 2016. Pathologically proven locally advanced cervical cancer suitable for treatment with chemo radiation. Pretreatment investigations included complete haemogram, RFT, LFT, RUE, CXR & MRI pelvis. Patients were treated with external beam radiation (EBRT) 45Gy/23 # for 4.5 weeks followed by HDR brachytherapy 7Gy as single fraction weekly for a total 3 fractions and chemotherapy with Cisplatin 40mg/m2 weekly once during radiation. Treatment response was assessed clinically and radiologically with MRI as per RECIST criteria after 3-4 months of treatment completion. Toxicity evaluation was done with CTCAE3. Data analysis was done with the help of Excel 2010 and SSPS 16 statistical software. **Observations and Results:** Of the total 69 patients enrolled, 58 were available for assessment. All were staged clinically as per FIGO. Most common stage in this set of patients was stage 11B (26.6%)

followed by stage 111B & 111A which was 20.3% & 18.8% respectively. MRI was done after FIGO staging and there was change in the FIGO stage after this. 8 were down staged while 12 were upstaged. The agreement between MRI and clinical stage was evaluated by calculating the kappa value which is a measure of agreement & it was 0.18. It signifies that there is only low agreement in stage by stage between the clinical and MRI evaluation.32 had complete response, 23 had partial response and 3 had stable disease as per MRI. Clinically it was found that 46 had complete response, 11 had partial response and 1had stable disease. While comparing clinical response assessment to MRI assessment the kappa value obtained was 0.08 signifying poor agreement. The relation between response assessed by MRI and recurrence rate was evaluated .It was found that the hazard ratio of recurrence was 8.667 times between non-responders and responders. The p value was found to be 0.001. When assessing the response clinically, the hazard ratio was found to be 1.667 between non responders and responders but this was not statistically significant (p=0.438).The mean recurrence free survival was 17.4 months. Kaplan Meir survival analysis for recurrence free survival was 69.6% at the end of the study. Median survival was not reached. Only 10.7% percent of the responders as per MRI developed recurrence while 50 % of the non-responders had recurrence. 27.9% of clinical responders and 38.5 % of clinical non-responders had recurrence. Thus MRI has significant correlation between response and survival assessment whereas clinical assessment definitely is inferior. **Conclusions:** There is poor agreement between clinical and MRI with regard to staging and treatment response. MRI is a better tool than clinical assessment in treatment response evaluation.

Keywords Cancer cervix, MRI, clinical, response

"A PROFILE OF ENDOMETRIOID ADENOCARCINOMA OF UTERUS IN A TERTIARY CENTRE"

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Introduction: The incidence of endometrial carcinoma(EC) is around 4.2 to 4.3 per 10,000 in India. Management of EC almost worldwide is surgery. Current practice is to perform removal of enlarged pelvic lymphmodes. Complete PLND is done in patients with high risk features. Women with early stage disease has a favourable prognosis overall, hence adjuvant treatment recommendations are challenging. Women with advanced disease receive adjuvant radiotherapy with or without chemotherapy depending upon the stage and high risk features. **Objectives:** 1. Assessment of clinic-pathological variables .2. Correlation of pre and post-operatives tumor grades. 3. Lymphnode metastases with tumor grade and myometrial invasion (MI). **Material and Methods:** A retrospective analysis of 40 endometrioid cases were done. Primary line of treatment was surgery. Radiotherapy chemotherapy was administered as adjuvant treatment. Continuous variables were reported using mean +/- SD. Categorical variables were reported using number and percentages. Pre and Post Grades were compared using Wilcoxon Sign Rank Test. All the analysis were done using SPSS version 18.0. **Results:** The mean age was 58.65 years, 29were post menopausal and 28 patients presented with post menopausal bleeding. 28 patients had endometrioid variant, 8 were complex hyperplasia, 2 had endometrial intraepithelial neoplasia, 1 had atrophic endometrium. 28 had complete surgical staging. Five out of 10 who were preoperatively diagnosed as grade 1 tumors were upgraded to grade 2 tumors, 2 out of 11 who were grade 2 tumors were downgraded to grade 1 tumors and 2 out of 7 who were grade 3 tumors were downgraded to grade 2 tumors in post operative specimen.Out of 5 patients with LN metastases, 3 had <50% MI, 2 had >50% MI, 2 had grade 1 tumor, 2 had grade 2 tumor and 1 had grade 3 tumor. **Conclusions:** Complete surgical staging is the most precise way of determining stage and requirement of adjuvant treatment and it defines the prognosis and survival in a better way.

Granulosa cell tumour of ovary: a clinicopathological evaluation

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Introduction: Granulosa cell tumours of the ovary are very rare malignancies, represent around 2-3% of all malignant ovarian tumours. **Objective:** To evaluate the clinical characteristics and management of granulosa cell tumour of ovary. **Material and Methods:** The medical records of nine women diagnosed with granulosa cell tumour of ovary from June 2005 to October 2015 in the Department of Gynecologic Oncology of our institution were retrospectively evaluated. **Results:** The mean age of the women was 41.56 years (range –18-78 years). They presented with various symptoms: menorrhagia (44.45%), post-menoausal bleeding (22.23%), abdominal distension (33.34%) and pain abdomen (44.45%). One patient presented with abdominal pain and distension with breathlessness (chest X-ray showed multiple lung lesion? metastasis) and received neoadjuvant chemotherapy. Eight patients underwent primary surgery with complete staging in seven patients. Out of all, two patients underwent emergency laparotomy in view of massive haemoperitoneum. Four patients had ascites ranging from 100-3000 ml. Mean ovarian tumour size was 14cms (range 4-30cms). Fertility sparing surgery was done in one patient. The number of patients in various stages were I -4(IA-3, IC2-1); IIA-1; IIIC-1; IV-1 and unknown -2 according to the International Federation of Gynecology and Obstetrics (FIGO) -2014 criteria. The follow up duration ranged from 0-5 years. Two patients (one stage IA and other stage IIIC) recurred after three years. **Conclusion:** Granulosa cell tumour of the ovary occur in all ages. Symptoms related to hypere-strogenism occur in all age groups. Because of the high vascularity, tumour rupture is commonly seen. The primary management of these tumours is through surgery. The role of adjuvant therapy in early stages is controversial.

Role of Simultaneous ^{18}F-FDGPET/MRI in Staging Non-small cell Lung Cancer

Purpose: Therapeutic decisions in non-small cell lung cancer (NSCLC) patients depend on the tumor stage. Whole body Staging based using ^{18}F-FDG PET/CT has been widely accepted as the diagnostic standard of care. With the advent of integrated simultaneous PET/MRI, nodal and metastatic staging is expected to become more robust, especially when CNS and oligometastasis are considered. The purpose of this study was to evaluate the role of a whole body simultaneous^{18}F-FDG PET/MRI imaging in primary lung carcinoma staging in regards to primary tumor assessment, locoregional lymph nodal and metastatic evaluation using histopathology and/or clinico-radiological follow up asstandard ofreference. **Methods**: 30Patients (20 Males, 10 Females; Age±SD: 61.58±11.9 Yrs, range: 32-79 Yrs)with biopsy proven NSCLCunderwent simultaneous whole body^{18}F-FDG PET/MRI on an integrated 3T PET/MRI scanner (Siemens Biograph mMR) and an additional HRCT PET/CT chest forprimary staging. The mean and maximum standardized uptake value (SUVmean and SUVmax, respectively) and maximum diameter of the primary tumor was measured and compared in ^{18}F-FDG PET/CT and PET/MR imaging.T, N and M staging was performed by 3 readers in separate sessions for PET, MR and PET/MR image sets forlesion count and diagnostic confidence (DC). Results from histopathology or clinico-radiological follow up served as standard of reference. **Results**: Both PET/MRI and PET/CT agreed on T staging (DC≥4) in all of 30 patients (100%) with no statistically significant difference for lymph node metastases (P = 0.52).Size measurements showed excellent correlation between two imaging modalities. In PET/MRI evaluation, allindex cancers were seen on PET and MRI with PET/MRI showing highest DC score of 5 compared to PET and MRI alone for nodal and metastatic staging. Further, 24/30 patients presented with metastatic disease yielding 192 metastatic lesions while remaining 06 had

localized thoracic disease limited to lung and mediastinal lymph nodes.50% (12) patients with metastasis showed discordant findings on PET and MRI with MRI identifying 22 (11.45%) more suspicious lesions showing minimal to absent FDG uptake. These were mostly small enhancing brain lesions (15) followed by liver (5) which demonstrated increased size on follow up imaging. Furthermore, MRI characterized several benign lesions such as infarcts (1), liver cysts (2) and hemangiomas (3). **Conclusion:** In our preliminary experience,^{18}F FDG PET/MRI adequately addressed thoracic staging in patients with NSCLC. Furthermore, MRI identified more metastatic lesions than FDG PET suggesting simultaneous ^{18}F-FDG PET/MRIto be useful in comprehensive wholebodyinitial staging of NSCLC patients.

Outcome of breast conservation with Oncoplastic Techniques in small to medium sized breasts; Sri Lankan experience.

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Introduction: The breast cancer treatment has changed dramatically over the past few decades. The management of early breast cancer has diverted from mastectomy to Breast Conservation Therapy. Breast Conservation Surgery(BCS) combined with adjuvant Radiotherapy(RT). This provides aesthetic results without compromising the oncological safety. In Sri Lanka since many women have small to medium size breasts, BCS is always challenging. **Objectives:** Assess the outcome of BCS in small to medium sized breasts. **Material and Methods:** Patients presented with early breast cancer to National Cancer Institute, Maharagama, Sri Lanka from July 2013 were prospectively analyzed. They were offered Mastectomy(If patient insists) or BCS followed by RT. All patients were followed up for 2 years with standard surveillance protocol. The pre-operative evaluation, detailed surgical data, histopathological information and surveillance were recorded and analyzed. **Results:** Out of total 205 patients (mean age 59 years) who underwent BCS, 64% and 32% was in clinically T2 and T1 disease, respectively. 98(47.8%) had primary closure while 90(44%) had volume displacements and 17(8%) had volume replacements. Out of volume displacements, radial segmentectomy ± Tennis Racket extension was 34(37.8%), Segmentectomy with rotation flap 29(32%), Batwing mastopexy 10(11%) and Grisotti pattern 7(7.8%). Latissmus dorsi rotational flap 12(70%) was the commonest replacement type in this study group. 25 patients underwent re-surgery due to margin inadequacy and 16 out of them ended up with mastectomy. None of them presented with local recurrence during the follow up period (mean-14 months). **Conclusions:** In early breast cancer, BCS and RT has lead non inferior oncological outcome compared to traditional treatment, mastectomy. In small breast women, taking a wider margin in the primary surgery with volume displacement is reasonable, since conversion to mastectomy is higher in re-surgery.

Incidence of submental lymph node involvement in oral cavity cancers

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Introduction: The cancer of the buccal mucosa and lower alveolus together called the gingivobuccal complex cancer is the most commonly affected oral subsite in India.Treatment strategy for oral cavity cancers is mainly surgery. After complete resection of lesion, we need to reconstruct the defect. A variety of regional flaps and free flaps are available for reconstruction. Submental flap is a regional myocutaneous flap supplied by submental artery (2mm), a branch of facial artery. When this flap is harvested, submental lymph nodes are taken along with skin and subcutaneous tissue. Hence it is vital to know the status of submental lymph nodes in relation to T or N stage. The flap is oncologically safe, only if submental lymph nodes are histopathologically negative for metastasis. The purpose of present study is to assess the status of submental lymph nodes in oral cavity cancers, in relation to T and N stage. If the oncological safety of this flap is proven, it will be a good alternative to the radial forearm free flap for reconstruction small to medium defects after surgery of oral cavity cancers. **Objectives:** To study the histopathological status of Submental lymph nodes in oral cavity cancers in relation to T and N stage, as a surrogate marker of oncological safety of submental flap. **Material and Methods:** This retrospective and prospective study included 100 oral cavity cancer patients over a period of two years of June 2013- May 2015, who underwent neck dissection after written informed consentwas obtained. Subjects satisfying all the inclusion criteria and none of the exclusion criteria were enrolled in the study. All patients were operated for simultaneous tumor resection and neck dissection. Submental lymph nodes specimen sent separately from Neck dissection for histopathological examination. **Results:** Majority of patients i.e. 93% were negative and only 7% patient were positive for submental lymph nodes. Submental lymph node positivity found in clinical and pathological T &N stage as follows: cT1 (0%), cT2 (2.6%), cT3 (13.3%), cT4a (10.8%); cN0 (0%), cN1 (13.8%), cN2 (25%), cN3 (0%); pT1 (0%), pT2 (2.4%), pT3 (33.3%), cT4a (12.5%) and pN0 (0%), pN1 (18.2%), pN2 (17.2%), cN3 (0%), which werestatistically significant. **Conclusions:** We found that submental flap can be safely done in early stage and cautiously in late stage oral cavity lesions on basis of histopathological status of submental lymph nodes.

Key words: Submental lymph nodes, submental flap, oral cavity cancer

Aggressiveness of human oral cancer and the role of glycogen synthase kinase 3isoforms α/β signaling

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Introduction: Glycogen synthase kinase (GSK3) is a novel tumor suppressor, and emerging evidence has suggested its active role in oral cancer pathogenesis. **Objectives:** The study aims to evaluate the role, regulation and consequences of glycogen synthase kinase 3 isoforms α/β (GSK3α/β) in human oral cancer progression and invasion. **Material and Methods:** The expression and activity of GSK3 α/β as well as the cell cycle, cell survival, cell death and cell invasion regulators like cyclin D1, β-catenin, p53, c-myc and reversion-inducing cysteine-rich protein with Kazal motifs(RECK) were assessed in human oral cancer tissue samples, apparently normal adjacent tissues, benign tumor samples, premalignant lesions and healthy normal tissues were studied by using various biochemical methods, such as immunohistochemistry, western blot assays, immunoprecipitation, RT-PCR and bisulphate modification-PCR. **Results:** Oral cancer tissue samples showed elevated expression and inactivation of GSK3α/β, compared to normal oral mucosa. The overexpression of GSK3β is significantly higher in SCC than inthe other types non-SCClike Adamantinoma, Adenocystic carcinoma, Basal cell carcinoma, Acinic cell carcinoma and Mucoepidermoid carcinoma. Overall, the increased expression of pS9GSK3β was compared with the expression of cyclin D1,p53, c-myc, nuclear β-catenin, RECK and promoter hypermethylation of RECKat various stages of oral tumor progression. This study provided insight on the GSK3 pathway and the overall aggressiveness of human oral tumor. **Conclusions:** Collectively, our results demonstrated the deregulation of the GSK3β pathway, is an important event in oral cancer progression and invasion and hence used as a marker for assessing disease severity or may be exploited for therapeutic interventions.

Keywords: GSK3α/β, cyclin D1, β-catenin, p53, c-myc and RECK

Robot-assisted thyroidectomy using a gasless, transaxillary approach for the management of thyroid disorders – Novel technique

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INTRODUCTION: Recent advances in surgical techniques have led to the development of various minimally invasive approaches, with the main aim of improving cosmetic outcomes at no additional morbidity. Robot-assisted transaxillary thyroidectomy is an emerging surgical technique that needs to be evaluated. **Material and Methods:** From August 2011 to December 2014, a prospective study was performed in Manipal Comprehensive Cancer centre. 25 patients with thyroid nodule underwent robot-assisted thyroid surgery using a gasless transaxillary approach. All patients were selected using predetermined inclusion criteria after considering surgical risk, and all procedures were completed successfully using the da Vinci S surgical system (Intuitive Surgical, Sunnyvale, CA). Serum TSH , Ultrasound of the neck and Fine-needle aspiration cytology (FNAC) was performed pre operatively for all patients. **Results:** The median age of the cohort was 28.6 years (range, 16–47 years), and 21 (84.0%) of the patients were women. The median size of the largest nodule was 3.2 cm (range, 1.0–4.0 cm). eighteen patients underwent less than total and 7 patients underwent total thyroidectomy with central compartment neck dissection in three patients. The mean operating time for hemithyroidectomy was 96 minutes and for total thyroidectomy was 129 minutes. The mean number of dissected central lymph nodes was 4. No case was converted to conventional open surgery.The mean postoperative hospital stay was 2.5 days. Post-operative complications 2 patients had transient brachial nerve palsy, 2 had hematoma, 3 had temporary hypocalcemia, 1 patient had seroma. The cosmetic results were good. **Conclusion:** With the advent of minimally invasive techniques in thyroid surgery, robot-assisted transaxillary thyroid surgery has emerged as one of the most promising approaches. Minimal access surgery of the head and neck using a robotically assisted approach is feasible and safe. Our experience with the transaxillary gasless robotic thyroidectomy described herein suggests that patient satisfaction in India will be high.

Key Words: Robotic thyroidectomy, minimally invasive thyroidectomy, transaxillary gassless thyroidectomy

Comparison of chemotherapy (cisplatin) enhanced radiotherapy and biotherapy (cetuximab) enhanced radiotherapy in locally advanced head and neck cancer – first retrospective study in Asian population

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Aim: To present a direct comparison between Chemotherapyenhanced Radiotherapy (CERT) and Biotherapy enhanced Radiotherapy (BERT) in locally advanced head and neck cancer (LAHNC). **Methods:** It is a retrospective analysis of 53 patients of LAHNC treated from August 2006 to December 2008. For CERT, patients received weekly cisplatin dose of 40mg/m^{2}and for BERT loading dose of 400mg/m^2 of cetuximab was given one week prior to radiotherapy treatment and dose of 250mg/m^2 was given weekly along with radiotherapy. Disease free survival (DFS) and overall survival (OS) was computed with Kaplan-Meier curve with log-rank test for comparison between the two groups. Univariate and multivariate Cox proportional hazards regression analysis were performed to estimate the impact of relevant prognostic factors. **Results:** CERT group was found to have better median DFS (50.82 vs. 11.66 months, p=0.021), median OS (53.61 vs. 32.55 months, p=0.044), 3 years DFS (60.0% vs. 13.4%;p=0.026) and 3 years OS (74.0% vs. 42.1%;p=0.032). There were no significant differences in acute toxicities of all grade and grade ≥3 such as mucositis, dysphagia, radiation dermatitis and acneiform rash between the two groups. The compliance to treatment and assisted feeding (percutaneous endoscopic gastrostomy or ryle's tube) dependency for more than 6 months duration were also not significantly different. **Conclusion:** CERT is associated with better outcome with no significantly increased toxicities than BERT.

Key Words: Cetuximab, cisplatin, head and neck cancer

Medullary thyroid cancer: a retrospective analysis of a cohort treated at a single tertiary care centre between 2008 to 2012.

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Introduction: Medullary thyroid carcinomas (MTC) constitute about 5 to 7 % of thyroid neoplasms. **Aim and Objective:** The aim of this study is to examine clinical aspects, surgical management and long term survival of patients with medullary thyroid carcinoma. **Materials and Methods:** This is a retrospective analysis of the cases diagnosed as Medullary Thyroid Carcinoma (MTC) in Regional Cancer Centre, Trivandrum,Kerala, India over a period of 5 years (2008-2012). A total of 22 cases were accrued. The demographic data, clinical details and the treatment modalities were studied. The period of follow-up ranged from 1.8 year to 5.6 years. **Results and discussion:** In this study out of total 22 patients male to female ratio was 12:10. None had family history. Type of surgery weretotal thyroidectomy(TT) with neck dissection(ND) in 13 patients; completion thyroidectomy with ND in 4 patients and TT alone in 5 patients. External Beam Radiotherapy (EBRT) was given in 4\22 (18%) because of extra thyroidal spread or extra capsular spread.6 (27.2 %) patients had subsequent nodal recurrence, all six patients had raised calcitonin level after initial surgery in spite of no macroscopic or radiologic disease, they all had salvage surgery and all of them were advised EBRT but one refused. Three (13.6 %) patients had distant metastases of which one patient died after 18 months. The 5 year overall survivalprobability was 85.5% and disease free survival probabilitywas 76.7%. **Conclusion:** Our Survival outcome is comparable to other international studies.

Persistent elevated serum calcitonin levels correlated with loco regional and distant metastases.

Reconstruction of extensive scalp and neck defects with lower vertical trapezius myocutaneous flap – our experience

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INTRODUCTION: Radical resections for head and neck tumours can lead to devastating cosmetic and functional morbidities causing a major impact on the quality of life of the survivors. **Material and Methods**: We report our experience in a low resource tertiary referral centre with Vertical lower trapezius myocutaneous flap as a safe and reliable option for reconstructing defects in the posterior neck, occipital region and parotid region with minimal morbidity and good cosmetic outcome**. Material and Methods:** Reach and survival of the lower trapezius myocutaneous flap used for reconstructing major defects in the posterior aspect of neck, occipital and parotid region, cosmesis, functional outcome and donor site morbidities were assessed. Retrospective study from December 2006 to January 2015 comprising thirteen patients. **Results:** There were eight men and five women with age ranging from 23 years to 64 years (Mean 54.9 +/- S.D of 6.1). All the flaps survived. The only morbidity observed was prolonged serous drainage through the drain in a patient. All donor sites were closed primarily. The upper fibres of trapezius were preserved in all the patients. All of them had good cosmetic and functional outcome. **Conclusions:** The vertical lower trapezius myocutaneous flap is a useful adjunct in the

reconstruction armamentarium of head and neck surgeons. The flap has its greatest utility in closure of lateral skull base and posterior scalp defects. It is safe and reliable with a donor site that can be closed primarily .It can also serve as a backup for parotid, oral and oropharyngeal defects.

Carcinoma of oral tongue: a case series analysis of clinical presentation, prognostic factors & surgical outcomes

Nadimul Hoda

Background: Carcinoma tongue is relatively common in India, second only to buccal mucosa cancer among all head and neck malignancies. Although lesion is mostly either ulcerative or proliferative on an easily visible organ, it is a sad fact that many patients presents in late stages. Both radiation and surgery have their advocates and the modality of treatment vary according to type of lesion & stage of disease. **Objective:** To analyse the clinical presentation & prognostic factors determining the outcome of oral tongue cancer. **Material and Method:** This is a retrospective study of cases of oral tongue cancer from a regional cancer institute in south India over a period of five years from 2008 to 2013. **Results:** Out of two hundred four patients treated over the period of five years, 128 were male &74 female, having median age of 48 years. About two-third of oral tongue tumors were diagnosed at early stage with localized discomfort being the most common complaint. Surgical treatment was given to 56% of patients while 32% treated with radiotherapy. Tumor thickness greater than 6 mm was the only independent prognostic factor indicating a poor prognosis in overall survival(P=0.049). Presence of involved lymph nodes indicated a tendency toward a poorer prognosis in relapse free survival(P=0.043). **Conclusion:** Most of the patients of oral tongue carcinoma presents in early stage and increased tumor thickness and number of metastatic lymph nodes are poor prognostic indicators.

Keywords: Tongue carcinoma; depth of invasion; lymph node metastasis

A clinicopathological study of neoplastic and non neoplastic lesions of salivary glands

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Salivary glands are the site of origin of different types of pathological processes constituting a variety of lesions ranging from inflammatory lesions to neoplasms.The present study was conducted over a period of 7 years. Chronic sialadenitis being the commonest non neoplastic lesion(53.8%). Pleomorphic adenoma(85.7%) was the most common benign tumour and constituting 64.8% of all neoplastic tumors of the salivary glands. Mucoepidermoid carcinoma was the commonest malignant tumor (55.5%) out of 9 cases of the malignant tumors and 13.5% of all salivary gland tumors. A female preponderance was seen in almost all tumors except Warthintumor and a peak age incidence of 2nd to 6th decade. The commonest site being the parotid gland in 67.5% of all tumors followed by minor salivary glands and submandibular glands in 29.7% and 2.7% respectively. The most common clinical presentation was in the form of mass alone(62%) followed by mass associated with pain(16%), with the duration being mostly less than 1 year.

Predictivity of HPV positivity in advanced oral cancer

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Background and Objective:HPV is a known prognostic factor world over in patients of carcinoma oropharynx. Role of HPV in oral cancers has not been investigated adequately. We tried to identify standard clinicopathological features in oral cancer which would predict HPV positivity. **Methods:** This was a retrospective analysis of 124 cases of T4 oral cancer patients at our centre. HPV positive was defined in accordance with positive p16 IHC done on pretreatment local tumor site biopsy. Age, sex, habits (smoking history and oral tobacco),ECOG PS, T stage , N stage, grade and site were selected, for testing of prediction for HPV positivity. The analysis was performed by R studio version 3.1.1. Two-sample test for equality of proportions with continuity correction was used to identify factors predicting for HPV positivity. p value of 0.05 was taken as significant. **Results:** Out of 124 patients, 16 patients(12.9%) were HPV positive.The median age of the whole cohort was 43 years (IQR 37-52 years) with 15 females.(12.1%) All had squamous cell carcinoma. (100%). The grade of the tumor was well differentiated in 9 patients (7.2%), moderately differentiated in 98 patients (79.1%) and poorly differentiated in 17 patients (13.7%). The ECOG performance status 0 in 19 patients(15.3%), 1 in 104 patients (83.9%) and 2 in 1 patient (0.8%). The subsite of tumor was buccal mucosa in 74 patients (59.7%), anterior two third of tongue in 33 patients (26.6%) and others in 17 patients(13.7%).None of the tested factors except use of oral tobacco were statistically significantly associated with HPV positivity. History of tobacco usage had statistical trend towards ability to predict HPV positivity. The proportion of patients with HPV positive oral cancer in patients without history usage of oral tobacco was 31.3% while it was 10.2% in patients with previous history of tobacco use. (p=0.03). **Conclusion:** Standardclinicopathological variables could not predict for HPV positivity.Negative history of tobacco (smokeless) usage showed statistical trends towards ability to predict HPV positivity in oral cancer patients.

Post laryngectomy Pharyngocutaneous fistulas - On the rise?

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Introduction: Pharyngocutaneous fistula is a common complication after total laryngectomy. It not only increases length of hospital stay and financial burden on the patient but also delays adjuvant therapy, increases morbidity, and may rarely end with a fatal outcome. **Objectives:** The objective of our study was to determine the frequency and predisposing factors of pharyngocutaneous fistula in postlaryngectomy patients. **Material and Methods:** Patients who were treated with total laryngectomy with or with reconstruction or gastric pull up for laryngeal or laryngopharyngeal carcinoma in our department ,from August 2014 to December 2015, were prospectively studied. 52 patients were included in the study. The variables studied for the development of pharyngocutaneous fistula (PCF) after total laryngectomy were: age and gender, diabetes mellitus, post-operative hemoglobin, ischemic heart disease, chronic obstructive pulmonary disease, tumor characteristics including tumor site, stage, differentiation and extension into pyriform sinus, pre-operative radiotherapy, pre-operative chemotherapy, pre-operative tracheostomy and positive surgical margins, closure layers, technique, suture material and authenticity of leak test intraoperatively. **Results:** Univariate analysis showed diabetes, pre-operative radiotherapy and pre-operative tracheostomy to be significantly associated with the formation of PCF. However, multivariate regression revealed that only pre-operative radiotherapy was highly associated with the formation of PCF. **Conclusions:** 36 patients developed pharyngocutaneous fistula, of which 2 were managed surgically. It is possible that > 50% of patients in our study developed PCF, because of the current concept of organ preservation. Herein, most patient receive radiotherapy with or without chemotherapy as primary treatment for laryngeal cancers. This rising trend of organ

preservation protocol will have to be re examined so as to establish stringent indications to reduce post operative complications.

Parathormone in predicting long term post operative hypocalcemia

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Introduction: Transient hypocalcemia is one of the postoperative complications of thyroidectomy (either total or completion), and Preoperative and postoperative intact parathyroid hormone (iPTH) assays are used to predict postoperative hypocalcemia especially long term ones lasting more than 6 weeks, requiring supplementation. **Objectives:** The current study was conducted prospectively over a period of 6months, after ethical committee clearance and institutional funding. The objective was to correlate clinical features of hypocalcemia with biochemical fall in serum calcium, with corresponding fall in pre and post op parathormone levels on postoperative day 1 (POD 1) so as to predict hypocalcemia (both transient and longterm) occurrence after total or completion thyroidectomy. **Methods:** 70 patients who underwent total or completion thyroidectomy (with or without lymphnode dissection) for thyroid malignancies at our centre during a period of 6 months (from Mar 2014) were studied.Pre op and post op calcium and PTH levels were correlated with clinical signs and symptoms of hypocalcemia.. The patients' serum PTH level was measured on POD 1, and their serum calcium level was measured on POD 1 and on POD2 while they were still inpatients and compared with their pre op values. **Results:** Hypoparathyroidism after cT or TT with or without LN dissection was ultimately diagnosed in 13 of 70 patients. Among them hypocalcemia was diagnosed on POD 1 in 9 and POD-2 in 4 patients. All those diagnosed with hypocalcemia received calcium and vitamin D supplementation therapy. The fall in serum iPTH level was around 80% on POD 1, and corresponded to fall in serum calcium to levels less than 7.5g/dl. Permanent hypoparathyroidism developed in 3 patients. **Conclusions:** Except for the cost issues, iPTH measurement on POD 1 with respect to pre op value is useful to determine whether or not to start calcium and vitamin D supplementation in order to maintain normocalcemia after surgery. It also helps to avoid repeated calcium estimation with regard to tapering the treatment dosage by predicting permanent hypocalcemia.

Novel variation in IL-10 promoter polymorphism in oral Squamous Cell Carcinoma by Denaturing High-Performance Liquid Chromatography

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Introduction: Oral cancer is the most common malignancy in India especially among tobacco users. Chronic inflammation coupled with alcohol, betel quid, and cigarette consumption is associated with OSCC. Among the genetic factors Interleukin-10 is a critical mediator of chronic inflammation and implicated in many cancers. **Objectives:** To identify the novel SNP in IL10 gene in OSCC in Indian Population. **Material and Methods:** To find out the novel SNPs in IL-10 gene in oral squamous cell carcinoma in this population, we screened the whole gene, using short fragment of gene at a time with overlapping primers was amplified by Polymerase chain reaction (PCR) followed by screening through high throughput method dHPLC (denaturing high-performance liquid chromatography) and further confirmed by direct sequencing. **Results:** We have screened the short fragment of IL-10 gene with 60 samples of oral cancer cases and equal number of controls. By using dHPLC, segments containing genetic variants were identified and subsequently sequenced. Thus we found one novel SNP in IL-10 promoter region and apart from this SNP we also found previously reported SNP in IL-10 promoter region also confirmed by direct sequencing. This novel SNP submitted to the gene bank and we got the accession number (KT153594). **Conclusion:** This is the novel approach to find a new SNP in IL-10 gene, in an ethnic population like India that may be associated with oral squamous cell carcinoma. Once we find the association with this disease pathology, this novel SNP may be utilized for personalized medicine for the treatment of Oral squamous cell carcinoma (OSCC) in future.

Ultra Structural Analysis Of Oral Exfoliated Epithelial Cells Of Tobacco Smokers And Betel Nut Chewers- A Scanning Electron Microscope Study

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Objectives: The study was undertaken to correlate epithelial surface pattern changes of oral exfoliated cells of tobacco smokers and betel nut chewers and also to compare them with patients of oral squamous cell carcinoma and healthy individuals). **Materials and Methods:** A total of 50 persons were included in the study out of which 30 formed the study group (15 each Tobacco smokers and Betel nut chewers) and 20 control group (10 each of OSCC patients-positive control and 10 normal buccal mucosa- negative control). Their oral exfoliated cells were scraped, fixed and studied under Scanning Electron Microscopy. The statistical analysis was determined using ANOVA, Tukey HSD, chi-square (χ^2) test and statistical package SPSS. **Results**: Oral squamous cell carcinoma, tobacco smokers and betel nut chewer's cells displayed modified surface characteristics which have been tabulated as compared to normal oral mucosa. **Conclusion**: In normal oral mucosa cell surface morphology is dependent on the state of keratinisation of the tissue. Thus, these ultra structural characteristics maybe of value to detect any carcinomatous changes at its incipient change by SEM and also provided us an insight into the ultra structure of oral exfoliated cells.

Differential effects of anti-angiogenesis treatments on bete-nuts related head and neck squamous cell carcinoma in Taiwan

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Background: The treatment of head and neck squamous cell carcinoma (HNSCC) in Taiwan is very challenging and might be related to bête-nuts use. Betel-nuts chewing might contribute to (1)strong inflammation, invasion, and angiogenesis; (2)easy recurrence or metastasis; (3)poor response to chemotherapy, radiation, and epidermal growth factor(EGFR) inhibitors. **Purpose:** We try to prove different kinds of anti-angiogenesis treatments will lead to different response on betel-nuts related HNSCC in Taiwan. **Methods:** Different anti-angiogenesis treatments, such as axitinib(VEGFR2 inhibitor),nintedanib(VEGFR2/FGFR/PDGFR triple inhibitor), foretinib (VEGFR2/Axl/c-MET triple inhibitor), and regorafenib(VEGFR2/FGFR/ more othersignals inhibitor) were first used to treat (1)HUVEC; (2)HNSCC cell lines(SCC4, SCC9, SCC15, SCC25, FaDu, SAS, KB, Cal27, and TW2.6, betel-nuts related) to evaluate (a)invasion capacity by wound healing; (b) drug sensitivity by MTT assay; (c)synergistic effect with chemotherapy, EGFR inhibitor, and polo-like kinase inhibitor. Western blotting was also used to test signal change by treatments. TW2.6 had already been proved to possess defective p53, p16 loss, and increased Bcl2. **Results:** In our previous

study, TW2.6 was resistant to chemotherapy, radiation, EGFR inhibitors, and anti-angiogenesis treatments, such as axitinib andsunitinib. Axitinib, pure VEGFR2 inhibitor, was found to suppress HUVEC more prominently than the other three drugs did. Invasion capacity of all HNSCC cell lines was well blocked by the four drugs but foretinib did mostly well. However, axitinib had no effect on TW2.6; nintedanib and regorafenib had moderate response on TW2.6; however, foretinib had promising response on TW2.6. Besides, nintedanib, regorafenib, and foretinib all would resensitize TW2.6 to respond to chemotherapy, EGFR inhibitor, and polo-like kinase inhibitor again.Western blotting showed mesenchymal differentiation markers(slug, Twist, snail, Axl, c-MET, Vimentin) decreased after nintedanib, regorafenib, and foretinib use, too. **Conclusion:** TW2.6 might reflect treatment refractoriness of betel-nuts related HNSCC in Taiwan. In addition to PI3K/mTOR dual inhibition and polo-like kinase inhibitor with radiation(our studies shown in AACR and ESMO2015), VEGFR2/FGFR/PDGFR(like nintedanib and regorafenib) orVEGFR2/Axl/c-MET(like foretinib) triple blockage might be effective on TW2.6 and resensitize TW2.6 to EGFR inhibitor, polo-like kinase inhibitor, & chemotherapy, maybe through the inhibition of mesenchymal transformation. These two combinations will be future treatment backbones of betel-nuts related HNSCC.

Early diagnosis and treatment: How does it affect treatment modality and prognosis of oral squamous cell carcinoma ?

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Introduction: Squamous cell carcinoma accounts for 90% of all oral cancers. Detecting oral cancer at an early stage is believed to be the most effective means of reducing rates of death, morbidity and disfigurement from this disease. The aim of the present study was to investigate the role of early diagnosis in determining the treatment modality and prognosis of the disease. **Method:** Seven patients with oral squamous cell carcinoma (T_1 and T_2) operated at different private centres of Bangladesh was studied over a period of two years. They were studied preoperatively for stage of disease, preoperatively for surgical treatment, postoperatively for histopathological assessment of the postoperative specimen for marginal clearance, nodal metastasis. They were followed up in every 3 months and no adjuvant treatment was started until there is sign of recurrence. **Results:** Among the 7 patients 3 were male and 4 were female and 3 of them presented with T_1 lesion whereas the other 4 presented with T_2 lesion. None of the patients presented with palpable lymphnode. Surgery in the form of wide excision of the lesion, marginal mandibulectomy or maxillectomy and supra-omohyoid neck dissection was done within 2 weeks of diagnosis. In postoperative biopsy none of them has shown lymphnode metastasis and positive margin. Postoperatively no patient has yet received radiotherapy or chemotherapy and not shown any recurrence. **Conclusion:** Early diagnosis and treatment of oral squamous cell carcinoma is key to success and if treated early single modality treatment can give a disease free life. Avoidance of multimodality treatment can improve quality of life reducing mortality and morbidity. Continuing education in oral squamous cell carcinoma and precancerous lesions is important to reduce the personal and professional delay.

Assessment of expression of survivin in oral squamous cell carcinoma and oral dysplastic lesions

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Background: Biological markers are instrumental in identifying the aggressive phenotypes of malignancies reflecting their prognosis and treatment planning. Survivin is one such recently introduced tumor marker regulated in human cancers.Survivinis a bifunctional protein and a prognostic marker that belongs to the Inhibitor of apoptosis(IAP) gene family and is expressed in most solid and hematological malignancies. Recent research has shifted focus towards survivin as a target of cancer therapy and hence there is a significant interest in the role of survivin in various types of cancer. The aim of the study is to assess the expression of survivin in oral squamous cell carcinoma (OSCC) and oral dysplastic lesions. **Material and Method:** The biopsy samples were obtained from the patients undergoing surgical exicision for OSCC, oral dysplastic lesions and healthy samples from the patients undergoing routine dental surgical procedures. Samples were also collected from archival tissue (embedded paraffin blocks) of OSCC, dysplastic oral lesions and healthy mucosa.The data was divided into 3 main groups as:Group 1 with OSCC (n=30),Group 2 as Oral dysplastic lesions (n=30)and Group 3 as Control group (normal oral mucosa) (n=30). Serial sections (4μm) from formalin-fixed, paraffin-embedded blocks were cut for each case, and one section stained with H&E was used to confirm the histopathological diagnosis. Only sections containing sufficient epithelium to assess the antibody reactivity with 1000 cells were considered for this study. Informed consent was obtained from all the cases. **Results/ Conclusion:** The survivin expression was calculated, and it was noted that there was an increased expression of survivin in OSCC, with the increase in the aggressiveness of the phenotype. There is no significant expression of survivin in oral dysplastic lesions and normal oral mucosa, however this marker helps determining the behaviour of the tumor biology.

De-regulated balance and clinical relevance of Th1, Th2, Th17 and Treg cytokines in oral cancer patients

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Background: Immune dysfunction aroused due to altered cytokine levels in cancer patients leads to poor prognosis. Hence, we investigated the cytokine balance in oral squamous cell carcinoma (OSCC) patients and their diagnostic relevance to provide new therapeutic insights. **Materials and Methods:** The quantification of different Th17 (IL17A), Treg (TGFβ1), Th1 (IL2, IFNγ) and Th2 (IL4, IL10) cytokines in the sera of 78 cases and 39 controls was done by ELISA. Also, the intracellular expression of these cytokines was analyzed by flow cytometry in representative 10 subjects from each group. Statistical tests explored the diagnostic significance and risk associated with these markers. Results: Serum levels of IL17A, TGFβ1, IL4 and IL10 were significantly higher while IL2 and IFNγ were relatively lower in patients as compared to controls. TGFβ1 (r=0.55), IL4 (r=0.75) and IL10 (r=0.80) significantly ($P<0.0001$) correlated with disease progression and their elevated levels showed increased odd ratios of approximately 18, 14 and 37 respectively. IL17A appeared as a risk factor (OR=2.21, 95% CI=0.89-5.42) although statistically insignificant. The levels neither correlated with disease progression nor with TGFβ1, IL4 and IL10 but showed positive association with IL2 (r=0.51, $P<0.0001$) and IFNγ (r=0.24). Flow cytometry showed concordantly similar trend. **Conclusions:** We found a distinct TGFβ1 and Th2 (IL4, IL10) polarization with a borderline elevation of IL17A while, a suppression of Th1 (IL2, IFNγ) cytokines in OSCC patients. IL4, IL10 and TGF β1 can be used as a complementary diagnostic factor for oral cancer.

Giant hemangioendotheliomaof the face: surgical management and challenges for reconstruction.

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Background: Giant hemangioendothelioma of the face is very rare skin vascular tumor, which measures 10 cm or greater in diameter. Very few studies have reported on the incidence, resection and reconstruction of the lesion. **Methods:** In total, 10 patients with giant hemangioendothelioma

of the head and neck region underwent surgical excision and reconstruction at surgical department, Tashkent medical academy. Medical charts were retrospectively reviewed and analysed. **Results:** The lesion was usually in the forehead, eyelid, lips or nasal-cheek region. The greatest diameter ranged from 10 to 15 cm, with 15 cm being the most common size at the time of presentation. All patients had their tumour resected and reconstructed in a single-stage procedure, mostly with a localadvancement flapor free flap, and with no post-operative flap failure. **Conclusion:** Giant hemangioendothelioma of the head and neck can be successfully treated with a local flap or free flap in a single-stage approach.

Neo-adjuvant Chemotherapy (Preoperative chemotherapy) or Induction chemotherapy (sequential chemo radiotherapy) in very locallyadvanced unresectable primary or second primary head and neck cancers:

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Introduction: Theoptimal sequence of chemotherapy, radiationand surgery remains a subject of debate in the management of locally advanced head and neck squamous cell carcinoma. Multiplephase III trials including multiplemeta-analyseshave failed to show consistent survival or local control benefit from induction chemotherapy(sequential chemo radiation) approach. HoweverNeo-adjuvant chemotherapy (Preoperative chemotherapy) in unresectable advanced primaries followed by surgery for responding patients has shown to improve overall survival in few published reports. We report our experience of neoadjuvant chemotherapy/Induction chemotherapy(sequential chemoradiotherapy) in this study. Overall response rate (CR+PR+SD) seen is 64%, with progressive disease and treatment related mortality of 17%. Progressive disease patients continued palliative chemotherapy for local and distant lesion. Conclusion: 1)Preoperative Chemotherapy/Induction chemotherapy with doublet/Triplet Taxane and cisplatin based combination is useful in very locally advanced technically unresectable primary head and neck squamous cell carcinoma as compared to second primary head and neck cancers. 2) Good response patients (CR & PR) have the opportunity for curative surgery as well as sequential chemo radiation if surgery is not contemplated by patient refusal. 3) Also induction chemotherapy helps in selecting patients who have biologically aggressive or refractory disease to ANY treatment. Finally care should be taken to select appropriate patients and supportive care during preoperative or induction chemotherapy to avoid treatment related morbidity and mortality.

Brain metastases: Sociodemographic profile of patients treated in a medical college of western Rajasthan.

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Background: Today, it is estimated that 10% to 30% of patients with solid tumors are diagnosed with CNS metastasis. Several reports place the incidence of Brain metastases found during autopsy between 20% and 40%. This study was conducted with the aim to understand the sociodemographic profile of patients treated for brain metastases with Whole Brain Radiotherapy (WBRT). **Materials and Methods**: In this retrospective study, the radiotherapy records of patients treated in the Department of Radiotherapy between 2004 and 2014 with Whole Brain Radiotherapy (WBRT) for Brain Metastases were collected and analysed. The socio-demographic parameters including patient details, primary diagnosis and histopathological diagnosis, history, clinical examination, imaging findings and WBRT details were collected. The statistical analysis was done using Microsoft Excel. **Results:** In all 192 patients with brain metastases were treated with WBRT between 2004 and 2014. The median age of the patients was found to be 55 years (range 12-82 years). 58.85% of them were found to be male. 33% of the patients were in their 6th decade. Carcinoma of Lung was the most common diagnosis of primary (47.4%) and the most common histopathological diagnosis was non-small cell carcinoma (35.41%). 26.56 % of the patients were found to be defaulters and did not complete the planned WBRT schedule amongst whom, the most common primary was found to be carcinoma of lung (47.48%). Only 6.25 % of the patient had received multimodality treatment for brain metastases (Surgery and WBRT) and majority (93.75%) received WBRT only.

Patient characteristic	Number (percentage)
Median age in years	55
Sex	
Male	113 (58.85)
Female	73 (41.15)
Occupation	
Agriculture	95 (49.48)
Private sector	61 (31.77)
Housewife	21 (10.94)
Others	15 (7.81)
Primary cancer site	
Lung	91 (47.40)
Breast	49 (25.52)
Unknown Primary	25 (13.02)
Sarcoma	7 (3.65)
Others	20 (10.41)
Histopathology	
Non-small cell carcinoma	68 (35.41)
Infiltrative duct carcinoma	49 (25.52)
Small cell carcinoma	23 (11.98)
Unknown	23 (11.98)
Others	29 (15.11)
Site of Brain metastases	
Bilateral	185 (62.29)
Left	35 (11.78)
Right	27 (9.09)

Conclusion: Our study concurs with previously published studies in most of the socio-demographic, epidemiological and clinical parameters. With increasing incidence, better treatment options and longer survival, it will continue to be a challenge to provide a better quality of life for patients with brain metastases. More robust data and results of newer treatment approaches will help us a long way in meeting this challenge.

Keywords: Brain metastases, WBRT, sociodemographic profile

Prognostication of Head & Neck cancer recurrence and re-recurrence by clinico-pathological phenotypes correlation with Life style factors

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Objective: To study the HNC (Head and Neck Cancer) risk phenotypes by correlating all clinical phenotypes with the life style related risk factors which

can give new insight toward cancer recurrence management. First time we tried to identify the facts of multiple recurrence phenotypes occurrence of HNC (Head and Neck Cancer). **Introduction:** Head and neck squamous cell carcinoma (HNSCC) recurrence and therapy resistance is a worldwide issue that need research's new insight for better cancer management. Tumors deriving from residual disease reflect recurrence, while independent origin accounts for a Second primary cancer (SPC). Epidemiological studies have shown that 70-90% of all cancers are environmental. Lifestyle related factors are the most important and preventable among the environmental exposures. Tobacco consumptions either as chewing tobacco or smoking tobacco accounts for 50% of all cancers in men. Dietary practices, reproductive and sexual practices will account for 20-30% of cancers. And 10-15% is due to genetically predisposition genes. Changes in lifestyle can improve the relative survival of HNC patients. **Methods:** In this study we included 117 numbers of HNC recurrent patients who get recur or re-recur and second primary malignancy. All the patients sample and clinical data were collected with the patient's consent and prior permission from HCG-Panda Cancer Curie Centre, Cuttack, Odisha, India from 2013 to 2016. Then all the recurrent cases categorised with different clinical parameters by univariate analysis correlated with recurrent time, post-treatment addiction status and co-morbidity factors by multivariate analysis using GraphPad prism 6.0 and MedCalc software. **Results:** Age group of 56-65 years of Male HNC patients observed recurrences and re-recurrences specifically in the site of mucosa, tongue and retromolar area in oral cavity of a moderate to highly undifferentiated grade during primary onset of cancer. The entire re-recurred patient's incidence is higher in metachronous state. All recurred cases showed therapy resistance which are in a moderate to highly undifferentiated form during primary onset of cancer. The tumor tissue extension (invasion and metastasis) status also regulated the HNC recurrence/re-recurrence of histology majorly squamous cell and verrucous type. Hence, for first time we have found life-style risk phenotypes such are recurrent time, post-treatment addiction status and co-morbidity factors that induced HNC recurrence/re-recurrence. **Conclusion:** Head and neck cancer recurrence or re-recurrences is a major problem that affected relative survival. We indentified some new risk factors and found new insight toward cancer recurrence/re-recurrence. By correlating the phenotypes-genotypes risk factors, HNC recurrence/re-recurrence can be managed successfully.

Awareness of Oral Cancer in Out Door Patients in VSPMSDental College Research Centre

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Introduction: Oral cavity has the most predominant location in the head and neck region for primary malignant tumors[1]. The incidence of oral cancer is rising in most countries, especially in developing countries. Oral carcinoma is the sixth most common malignancy worldwide.[2] In India, the extremely popular use of the smokeless tobacco product called gutkha, along with betel quid especially among the youth lead to a greater risk of developing oral submucous fibrosis, a premalignant disease resulting in increased incidence of oral cancer in younger patients.[3]The higher rate of oral cancer in India is due to life style, habits, poverty, lack of education and awareness and less access to medical services.[1,4,5,6] With early detection of cancer the treatment becomes less complicated and better functional and esthetic results can be obtained. Thus, the objective of the present study is to determine the level of awareness of oral cancer, knowledge about it early signs and the associated risk factors. An attempt will also be made through the questionnaire to increase the awareness of the participants as regards to oral cancer. **Objectives:** To study the awareness of oral cancer amongst Patients visiting OPD. **Material and Methods:** The study was conducted in the outpatient unit of department of oral medicine and radiology, VSPMDental College Research Centre. The patientsreceived the questionnaire after agreeing to participate and giving verbal consent. Questionnaire consisted of 11 questions regarding knowledge, causes and signs of cancer. Sample size & Sampling - All the patients attending Oral medicine OPD from 25/11/2015 to 15/1/2016(1000 patients).were included in study.Inclusion criteria – Patients between 16-80years of age who visited OPD in Department of oral medicine Exclusion criteria – Persons related to Medical profession. **Results:** Results will be analysed by doing statistical analysis. Data will be entered MS excel and analysed by EPIINFO.

Correlation among modulators of Angiogenesis FGF-2, FGFR-2, FGFR-3, Decorin and CD-34 in Oral precancer and Cancer and their expression in response to treatment

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Background: Oral cancer is major public health problem in India because of the habit of tobacco consumption in various forms like bêtel quid, khaini, pan masala and gutkhaand it is well known that angiogenesis is involved in early as well as in late carcinogenic processes and finally contributes to metastases. The process of angiogenesis is a result of changes in the equilibrium between positive and negative angiogenic factors. Among them Fibroblast growth factor (FGF-2) and its receptors FGFR-2 and FGFR-3 and Decorin are some of the modulators of angiogenesis. The aim of this study is to find the correlation among angiogenesis modulators in oral precancer and cancer and evaluate their expression in response to treatment. **Material and Methods**: Formalin Fixed tissue biopsies from 70 Oral precancer (40 Leukoplakia and 30 Oral submucous fibrosis), 100 Oral cancer and 50 healthy controls were subjected to immunohistochemistryby using antibody against FGF-2, FGFR-2, FGFR-3, Decorin and CD-34((Santa Cruz Biotechnology Inc., Santa Cruz, CA). **Results:** In cases of oral precancer FGF-2 was positively correlated with FGFR-2 and FGFR-3, FGFR-2 was positively correlated with FGFR-3 and Decorin, FGFR-3 was positively correlated with Decorin only. In cases of oral cancer FGF-2 was positively correlated with FGFR-2 and FGFR-3, FGFR-2 was positively correlated with FGFR-3 and CD-34, Decorin was positively correlated with CD-34.No association was found between FGF-2, FGFR-2, FGFR-3 with CD-34 in oral precancer and cancer.Among all these modulators of angiogenesis only FGFR-3 and Decorin was significantly associated with response to treatment. **Conclusions:** The positive correlation among the markers FGF-2, FGFR-2, FGFR-3 and Decorin shows their combined role in oral precancer and cancer angiogenesis and FGFR-3 and Decorin may be used as biomarker in response to treatment.

Keywords: Oral cancer, Precancer, Angiogenesis.

End Binding 1 (EB1): A potential biomarker for tumor progression and poor prognosis in oral cancer

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Introduction: Oral squamous cell carcinoma (OSCC) patients are at high risk of loco-regional recurrence and despite the improvement in treatment strategy, 5-year survival rates are about 50%. Identifying patients at high risk of recurrence may enable rigorous personalized post-treatment management. Earlier high throughput proteomics study revealed EB1 over expression in OSCC.The aim of the present study was to investigate the diagnostic and prognostic significance of alterations in expression of EB1 in oral cancer. **Methods:** In this retrospective study, the expression of EB1 protein was evaluated in 259 OSCCs, 41 dysplasia, 166 hyperplasia and 126 normal tissues using immunohistochemistry and correlated with clinical-pathological parameters and prognosis of OSCC patients over a follow-up period of up to 91 months. **Results:** A significant cytoplasmic overexpression of EB1 was observed in hyperplasia [$p < 0.001$, Odds ratio OR) = 7.2, 95% Confidence Interval (CI) = 4.1-12.8], dysplasia ($p < 0.001$, OR =

21.8, CI = 8.8-50.2) and OSCCs ($p < 0.001$, OR = 10.1, CI = 5.8-17.4) in comparison with the normal mucosa. Furthermore, univariate analysis also revealed the association of cytoplasmic EB1 over expression with tumor grade, size and recurrence of the disease ($p < 0.004$). Kaplan Meier survival analysis in EB1 overexpressing OSCC patients showed significantly reduced disease free survival (DFS) ($p=0.003$). Notably, Cox-multivariate-regression analysis also exhibited the association of EB1 overexpression with reduced DFS in OSCCs patients ($p=0.004$, Hazard ratio = 2.1). **Conclusion:** In the present study we demonstrate that EB1 over expression is an early event in oral cancer progression and cytoplasmic EB1 accumulation is associated with poor prognosis and tumour recurrence in OSCC patients.

Association of Cancer Metabolism Related Proteins in Oral Submucous Fibrosis: Potential Biomarkers?

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Background: Population with oral submucous fibrosis (OSF) has a high malignant potential for conversion to oral squamous cell carcinoma (OSCC) where tumor metabolism is a crucial factor. OSF is considered as integrated metabolic ecosystem which includes several pathways towards carcinogenesis. The molecules involved in metabolic pathways of the fibrotic process appeared to be either down- or up regulated at different stages of the disease. Metabolites related to glucose, fatty acid and protein metabolism along with etiological factors has been proposed as important factors.This study aims to explore the transcript (mRNA) profiles in OSF for understanding tumor progression, and identifying the primarily affected metabolic pathway that may be responsible for conversion to progressive stages of OSCC. **Materials and Methods:** Expression of 7 selected genes: GLUT-1, GLUT-3, Hexokinase 2, Alpha Enolase 1, Fatty acid synthase, Glutamine, Glutamate dehydrogenase 1 were analysed in normal oral mucosa (n=10), and OSF tissue specimens (n=10) by real-time polymerase chain reaction (qPCR) analysis using SYBR green protocol. **Results:**Expression of GLUT1, hexokinase 2 and alpha enolase 1 were significantly increased in the carcinogenesis of OSCC. The study provides the first evidence of significantly altered expression of mRNA transcript of GLUT1, Hexokinase 2 and Alpha Enolase 1 in OSF patients as compared to controls. On the other hand, expression profile of Fatty acid synthase, Glutamine, Glutamate dehydrogenase 1 and GLUT3 mRNA level were comparable between the 2 groups. **Conclusions:** Our findings indicate two-fold increase in RNA expression of GLUT1, hexokinase 2 and alpha enolase1 in comparison to OSF and healthy tissues. Over expression of glycolysisrelated proteins might play an oncogenic role in the proliferative processes and disease progression to malignancy. However, in order to establish them as potential biomarker of OSF, further confirmation is required at post translational level both in tissue and peripheral circulations.

Keywords: Oral submucous fibrosis, Metabolites, Biomarker, Real time PCR.

PMMC with single stage DeltoPectoral (DP) Composite Flap in huge defects after head and neck surgery:- A innovative solution

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Introduction: Carcinomas of Oral cavity are the most common malignancy in our country. Its not very uncommon for cancer to present at advanced stage. Resection of such lesion may result in large complex defects. Reconstruction of such defects could be done by loco Regional Flaps or combination offlaps or alone by free flaps. We describe the technique of composite PMMC –DeltoPectoral(DP) Flap reconstruction for reconstruction of such defects . This is a single stage procedure. Also the technique of DP has been modified so as to avoid detachment of flap later on so as minimize in hospital patient stay. **Methods:** The patients with locally advanced oral cavity cancerfrom the period of September 2015 to December 2015 were operated & reconstructed using this technique in our institute.Standard Techniques used for resection & neck dissection. DP flaps were raised first with the usual technique after which PMMC flaps were raised.PMMC Flaps were used for coverage on the mucosal side of the defect and DP flap was used to cover the skin loss and both flaps sutured to each other at the junction. Donor site was covered with spilt thickness graft taken form thigh. Postoperative outcome and final cosmesis was evaluated. **Results:** 10 patients were reconstructed using this technique. 9 were males and one was female. 4 patients were with central arch mandible lesion with involvement of chin skin, 5 were RMT and alveolus skin lesions with involvement of cheek skin. One patient was parotid malignancy with skin involvement .Only one patients suffered major Flap necrosis.. But patient recovered and reconstructed using the same flap. Two patients developed minor orocutaneous fistula which recovered on conservative management.The cosmesis of the patients was good. **Discussion**: Large complex defects involving both oral cavity and skin posses a unique reconstructive challenge . Although a single free flap or combinations of free flap may represent a better solution, in country like ours such facilities may not be always available .This technique represents an innovative solution in reconstruction oral cavity defects with large skin loss . This flaps provide inner PMMC in oral lesion & DP provides outer skin coverage. We believe such technique resection has not been described in previously in literature. There has been a case where oral cavity defect was covered with PMMC and skin involvement in neck was covered by DP flap. But to use both the flaps which are sutured at the junction represents a new answer to difficult question of reconstruction of large defects. Also that solution does not require complex micro vessel anastomosis or significant donor site morbidity.Other options for reconstruction for such defects are bipaddle PMMC or forehead flap.Bipaddle PMMC is cumbersome in patient with fatty chests or females. Whereas forehead flap are esthetically not suitable for large defects they may also require second stage for division of flapDeltopectoral flaps also require second stage surgery for delay / divison of flap. We have modified the technique of flap in such a way that edge of flap is sutured to neck dissection wound. This avoids the need for second stage for divison of defect. Resulting in shortening of traditionally long hospital stay required for standard deltopectoral flaps.With continuing use of such composite flaps we plan to refine better technique & modifications to improve outcomes and cosmesis in patients requiring large reconstructions.

Keywords : PMMC, Deltopectoral , Composite , single stage

Table 1: Relative mRNA expression, fold increase ($2^{-\Delta\Delta}$ CTmethod) real time PCR

Target Gene	GLUT1	HK2	ENO1	FASN	SLC1A5	GLUD	GLUT3
OSF	1.90±0.43	1.33±0.08	1.69±0.50	0.95±0.00	1.36±0.30	1.28±0.31	0.63±0.10
Control	1.23±0.03	1.11±0.47	1.18±0.54	1.04±0.50	1.26±0.24	1.11±0.11	0.66±0.21

Profile of malignant Hypercalcemia in Head and Neck Cancer Patients:Review of 16 cases from tertiary Cancer Institute in North India.

Robert Louis.A*,Rajat Bajaj,Mohit Agarwal*, Sunil Kumar Gupta*, Manish****

Rajat Bajaj

**Consultants ,Medical Oncology Unit II,Rajiv Gandhi Cancer Institute & Research Center,New Delhi ** DNB Residents ,Medical Oncology ,Rajiv Gandhi Cancer Institute & Research Center,New Delhi Introduction:Malignant hypercalcemia is rarely seen in Head and neck squamous cell cancers.Here we report the profile of 16 cases of malignant hypercalcemia in head and neck cancer patients along with outcome details.*

Methods : We retrospectively reviewed our case of Head and neck cancer patients who presented with or developed malignant hypercalcemia during the course of disease from 2012 to 2015 referred to unit II Medical Oncology ,at Rajiv Gandhi Cancer Institute .16 cases of malignant hypercalcemia were analysed out of total 110 Head and neck cancer patients treated during this period. **Results:** The incidence of malignant hypercalcemia in our head and neck cancer patients is 14.5% (16/110). Median age of presentation is 50 years and all were males.The sites were distributed as Buccal Mucosa(n=6),BOT (n=2),oral Tongue(n=5),NPX(n=1),second primary(n=1).Malignant Hypercalcemia developed synchronously at presentation in six patients and during course of disease in 10 patients.Two patients had recurrent hypercalcemia episodes and admitted for emergency care.The median ionised calcium level in Hypercalcemia is 1.6 and it ranged from 1.38 to 1.9.Four patients were symptomatic with altered sensorium requiring intensive care during hypercalcemia and n=12 were non-symptomatic(normal sensorium but sick) .Five patients had bone metastatic disease during hypercalcemia while n=11 had no bone disease during hypercalcemia.Most of the symptomatic patients had bone disease(four out of five patients with bone disease).All patients were treated with adequate hydration and steroids. Most of them received Zoledronic acid(n=15) and Calcitonin(n=14) for hypercalcemia control.Median duration to control hypercalcemia is 4 days and it ranged from 2 to 6 days.Four patients died and seven patients were lost to follow up for more than 1 to 2 yr which can be sensored to death status.one patient is alive and is on palliative chemotherapy. **Conclusion:** Malignant hypercalcemia should be looked for in head and neck cancer patients even though the incidence may be undermined or underreported as it portends poor outcome and should be screened for associated bone metastasis in symptomatic patients. Calcium level should be routinely checked in all locally advanced or recurrent head and neck cancer patients during the course of their treatment.

Maxillary sinus t-cell lymphoma: a rare case presentation.

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Gandhi Medical College

Non-Hodgkin's Lymphoma (NHL) are a group of neoplasms that originate from the cells of the lymphoreticular system. Forty percent of Non-Hodgkin's lymphoma arises from extranodal sites. The nasal cavities and paranasal sinuses are rarely affected by primary NHL. Most patients present with rapidly enlarging masses, often with symptoms both locally and systemically (fever, recurrent night sweats, or weight loss). The presentation of unusual lymphoma are different from the usual cases. Nasal T-cell/natural killer cell lymphoma is often a locally destructive (stage 3 and stage 4), disease typically presenting with the obliteration of the nasal passages and maxillary sinuses. Involvement of the alveolar bone, hard palate, orbit and nasopharynx is found in more than 50 % cases and is associated with extensive soft tissue masses. Presence of bone erosion is suggestive but not diagnostic of the disease. We present a case of T-cell lymphoma involving the right maxillary sinus. The patient was treated with systemic chemotherapy and responded partially. Initially patient presented with nasal stuffiness and diagnosed as a case of nasopharyngeal carcinoma on clinical grounds but it later came out to be a presentation of lymphoma of maxillary sinus.

Key words: NasalT-cell lymphoma, maxillary sinus, chemotherapy

Evaluation of surgical options in reconstruction of defects following post wide excision of oral cavity cancer

Harish Kumar H

Kidwai memorial institute of oncology

Introduction: Incidence of oral cavity cancer has been increasing over years. The real challenge faced by an oral oncologist is not in removing the tumor, rather in reconstructing the surgical defect,various flaps have been evaluated over the period of one year ranging from local flaps to free flaps. Versatality of each flap have been evaluated. The reliability of local flap over free flap have also been evaluated..Different flaps like masseter flap, pmmc flap,trapezius flap, nasolabial flap, forehead flap, temporalis flap, transverse cervical artery flap, free flaps like radial free forearm flap have been done,postoperative complications have been evaluated.Cosmesis in case of regional flaps were comparable to free flaps. **Methods:** Over a period of one year , around 86 reconstructions of oral cavity defects have been done.Of which, 57 pmmc flap, 18 nasolabial flaps, 2 radial free forearm flaps, 4 forehead flaps, 3 temporalis flaps, 2 transverse cervical artery flap, 2 trapezius flap, 2 deltopectoral flaps have been done. Regular mouth opening excercises are advised in postoperative period using heisters caliper and ice cream sticks and shoulder excercises are also advised. **Results:** Complications in relation to flap was noted in 4 cases.1 Case, there was necrois of distal aspect of nasolabial flap.2 Patients had problem with pmmc flap , where skin paddle was necrosed, which had to be excised and grafted. In 2 patients, there was seroma formation between 2 paddles of pmmc flap.Microstomia was noted in 3 cases , where the defect at angle of lip. **Conclusions:** When it comes to treating oral cancer surgically, it goes without saying , that one has to be well versed with different flaps .We hereby present different available options to reconstruct oral cavity defects, its reliability and versatality.

Versatality of nasolabial flap in surgical defects following oral cancer surgery

Harish Kumar H

Kidwai memorial institute of oncology

Introduction: nasolabial flap was designed long ago by sushrutha,its use has been evualuated over a period of time.We hereby present a data on versatality of nasolabial flap in reconstruction of buccal mucosa defects in post wide excision status of oral carcinoma.It has been used to reconstruct tongue, floor of mouth, to cover exposed mandible following marginal mandibulectomy, buccal mucosa defects, as an island nasolabial flap in reconstructing togue and floor of mouth.Technicaaly being not of much difficult procedure, comes as a very useful technique when it comes to reconstructing oral defects. **Methods:** 18 Nasolabial flaps have been done, its reliability and versatality have been evaluated. **Results and Conclusions:** Only in one case, we had necrosis of distal 2 cm of flap was seen.Otherwise, it's a highly reliable and versatile flap in reconstructing buccal mucosa defects.

Interaction between the developmental genes and the telomeric shelterin complex-its prognostic implication in Head and neck squamous cell carcinoma

Swatishree Padhi*, Arka Saha*, Madhabananda Kar, Chinmoy Ghosh, Amit Adhya, Manas Baisakh, Nachiketa Mohapatra, Shriram Venkatesan, Manoor Prakash Hande ,Safeena Kulsum, Amritha Suresh, Arkasubhro Ghosh and Birendranath Banerjee*

KIIT School Of Biotechnology,KIIT University

Introduction: HNSCC is highly prevalent in Eastern India and is associated with low prognosis and high mortality rates mainly due to lack of suitable marker for early detection. Dysregulated developemental genes in association with the telomeric shelterin complex play an important role in genome instability and process of tumorigenesis. **Objectives:** We designed a multiparametric molecular pathological approach to relate the dynamics of β -catenin and telomere Rap1 in conferring chemoresistance and its implication in patient prognosis in HNSCC. **Material and Methods:** Patient sample collection (102), HNSCC cell lines Cal 27 and Hep 2, MDR cell line, Rap1 Silencing, western blot analysis, IHC for grade specific protein localization, qRT PCR for grade specific gene expression, analysis of genome instability markers, Cell viability Assay, Immunoprecipitation. **Results:** Stable β-catenin expression was observed in tumor as compared to stroma (72/102). MDSCC cases showed nuclear β-catenin localization and higher genome instability and decrease in telomere length. Association of the developemental pathway and shelterin complex is observed. Telomeric Rap1 silencing sensitised the Cal-27 cell line to Cisplatin. Patients who recurred on follow up showed high Rap1 as compared to the patients without recurrence. Gene expression confirmed a significant correlationship of stable β-catenin and Rap1 with poor clinical and pathological outcome. **Conclusions:** The Stabilisation and accumulation of β-catenin was significant in the cohort of patient under study. The interaction of β-catenin and the telomeric shelterin component Rap1 initiates the process of tumorigenesis and correlates with prognosis and therapy outcome of the patients in the cohort.

Interaction between the developmental genes and the telomeric shelterin complex-its prognostic implication in Head and neck squamous cell carcinoma.

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Prevalence of high risk Human papilloma virus in squamous cell carcinoma of oral cavity

NaseemAkhtar: Assistant Professor Department of Surgical Oncology King George's Medical University Arun Chaturvedi: Professor & Head

Dept of Surgical Oncology king George's Medical University, SanjeevMisra :Director & CEO, All India Institute of Medical Sciences , Jodhpur Professor Dept of Surgical Oncology King George's Medical University Vijay Kumar :Additional Professor Dept of Surgical Oncology King George's Medical University Sameer Gupta: Assosiate Professor Dept of Surgical OncologyKing George's Medical University Husain Nuzhat :Head & Professor Dept of Pathology Director, Ram ManoharLohia Institute , Lucknow

Background: Oral squamous cell carcinoma (OSCC) is one of the most prevalent malignancy in India. It ranks number one in terms of incidence among men and third among women.An increased involvement of Human papilloma virus (HPV) in the HNSCC has been reported in past 10 years but its presence is not as consistent in it as in cervical cancers and therefore its actual prevalence is still vague in HNSCC and need the more solemn attention of researchersin this direction. **Aims:** Present study aims to explore the prevalence of HPV in OSCC, and its correlation with other risk factors in North Indian population. **Materialand Methods:** Study Population: A total of 250 clinically and histological proven cases of OSCC were included prospectively in the study between Oct 2013 to Jan 2015. Tissue biopsies were collected in 10% buffered formalin and in 1X phosphate buffer saline (PBS, pH 7.4) and stored at -80°C for molecular analysis. The demographic and clinical details of the patients were recorded on standard questionnaire. HPV detection was performed by using Real Time PCR & Conventional PCR.The Chi-square test was used to compare the dichotomous/categorical variables and unpaired t-test was used to compare the continuous variables. The p-value<0.05 was considered significant. All the analysis was carried out by using SPSS 16.0 version (Chicago, Inc., USA). **Results:** The study encompasses 250 cases of OSCC. Out of these HPV presence was confirmed in 23(9.2%) cases.The mean age of HPV positive patients was 47.17 while HPV negative cases had mean age 47.69, but this difference was statistically insignificant. HPV presence associated significantly with female gender. Buccal Mucosa was the most frequent site (52.2%) in patients. Most of HPV positive cases were well differentiated SCC (60.9%), eight cases were moderately differentiated or keratinized while only 4.3% cases showed a basaloid morphology. According to Log rank test median survival of HPV positive patients was better (16.5) compared to HPV negative patients (12.9) but the difference was not significant (p=0.62). **Conclusion:** Our findings illustrate that 9.2% OSCC cases harbor HPV in North Indian population which is slightly lower than that observed in previous studies and we report tobacco as a major risk factor in both HPV negative as well as positive cases. Therefore the independent role of HPV in the causation of oral cancer is difficult to evaluate in our case series due to the strong confounding influence of tobacco.

Prevalence of high risk Human papilloma virus in squamous cell carcinoma of oral cavity

Naseem Akhtar

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Marginal mandibulectomy in oral squamous cell carcinoma :5 years of institutional experience.

Naseem Akhtar

King George Medical University

Background: We are living in an era when treatment is not only guided by oncological safety but also by quality of life. Sacrificing whole of mandible merely to take adequate margin or for minimal erosion is not advisable. Leaving behind some part of mandible is best way to achieve optimal functional and psychological outcome. **Methods:** We have analysed the outcome of 66 patients who underwent marginal mandibulectomy during 2011 to 2015 at King George's Medical University for squamous cell carcinoma of oral cavity. **Results:** A total of 66 marginal mandibulectomies were done for SCC in gingival buccal complex and 24 for floor of mouth SCC. The mean age of patients was 47years, (range,25–73 years). All patients had histopathologically confirmed squamous cell carcinoma. The primary site was in buccal mucosa in 28 patients , gingivobuccal sulcus in 20 patients , lower lip in 6 patients , tongue in 5 patients, floor of mouth in 4 patients, and retromolartrigone in 3 patients. Out of 66 marginal mandibulectomies,56 were alveolar ridge marginalmandibulectomies, 5 were inner table marginalmandibulectomies, 3 were reverse marginalmandibulectomies and 2 were combined alveolar ridge and inner table marginal mandibulectomies. Bone was microscopically involved in 5 (7.6%) patients. Only one patient developed osteoradionecrosis after treatment. **Conclusion:** In carefully selected patients, marginal mandibulectomy in oral squamous cell carcinoma achieves good local control and survival.

Spectrum of Fungal Infection in Patients of Head and Neck Malignancies on Chemoradiotherapy. Role ff Antifungal Prophylaxis??

Dr Gunjesh Kumar Singh, Dr Jaspreet Kaur, Dr Malini R Capoor, Dr Deepthi Nair, Dr K. T Bhowmik

VMMC & Safdarjung Hospital

Background: Radiotherapy given for the treatment of head and neck malignancies causes alteration of oral mucosal barrier predisposing to oral mucosal colonization and infection. Such infections give rise to pain and burning sensation thus contributing to major morbidity.

Objective:

1. To identify the fungi isolated from the patients undergoing radiotherapy for head and neck malignancies.
2. To determine their antifungal susceptibility and week of colonization of these isolates.
3. To find out association between oral fungal infection and severity of oral mucositis.

Materials and methods: Study was done on 45 patients of head and neck malignancies who were advised concurrent chemoradiotherapy. Three samples (throat, urine, blood) were collected for fungal culture and sensitivity. These samples were collected before the start of radiotherapy, during radiotherapy (2nd and 6th week) and post radiotherapy (8th week). These were processed as per standard procedure. Clinical examination for response and toxicities were done weekly during the treatment. **Results**: Fungal infection was found in 23/45 patients (51.11%) out of which *Candida albicans* was isolated in 9/45 (20%) andamongst non-*albicans candida* species 7/45 (15.55%)were *Candida parapsilosis*, 4/45(8.88%) were *Candida tropicalis*, 2/45(4.44%) were *Candida kruzi*, 1 was *Candida guillermondii*intheir throat swabs.About 70% (16/23) isolates were sensitive to fluconazole (p=0.061). Maximum isolation of yeast was in 6th week of radiotherapy. All grade 4 (2/2) and 75% (9/13) of grade 3 oral mucositis were found in patients who were positive for fungal infection. Radiotherapy interruption was found in 2 patients during the treatment. Incidentally, complete remission (CR) rates were found to be better in patients with throat swab negative for fungal culture (10/15) compared to those who were positive (5/15). **Conclusion**: Higher rate of oral fungal colonization and infection was found in patients with grade 3/4 oral mucositis. Prophylactic fluconazole in head and neck cancer patients on concurrent chemoradiotherapy has the potential to reduce the associated morbidity. However, further studies are needed to confirm this finding.

An Audit And Analysis of Different Cuses of Defaults in Head and Neck Irradiation Patients and - A Tertiary Regional Cancer Center Experience

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Department of Radiation Oncology,AHRCC, Cuttack

Introduction: Adherence to treatment is defined as the extent to which a person's behaviour corresponds with agreed recommendationsfrom a health care provider by WHO(1).Strict adherence and timely completion of the EBRT schedule is one of the most important prognostic factors in survival of head and neck cancer patients(2). However many patients do not complete the radiation treatment due to various reasons resulting in a poor outcome. **Qbjectives:**To study the pattern of defaults and it to identify various possible causes for possible intervention. **Methods and materials**: We did a retrospective epidemiological analysis of the patient data available in the treatment record of the patients in department of radiotherapy, AHRCC, Cuttack. We enrolled patients who had started taking EBRT for head and neck cancers with curative intent from January 2014 to December 2014and did not receive the prescribed dose. Unplanned treatment breaks in the treatment was not taken into consideration. Only completion of the treatment after receiving the desired dose and fractions was taken into consideration. All data were analysed by SPSS Version 21. **Results**: Total 92 out of 458 (20.08%) patients didn't complete the EBRT. 63 out of 347(18.15%) male and 29 out of 111 (26.1%) (p=0.06) female patients defaulted in treatment. 56 out of total 92 patients (60.9%) who defaulted stopped taking treatment within 15#s i.e. halfway in the treatment. 12 out of total 92 patients (13%) stopped taking treatment just at the 22nd/23rd #.defaulter rates in patients from nearby districts and faraway places are in the range of 12.8 – 33.0% but was statistically not significant(p=0.224).

There was no particular age (p=0.966), disease site (p=0.354)preponderance among defaulters .There was no statistically significant difference among various treatment modalities prior to radiotherapy(p=0.597) or intent of treatment even with use of concurrent chemo-radiation in radical or adjuvant settings(p=0.406). **Conclusions**: Radiation induced acute toxicity is not the only cause of patients not completing the treatment. Socioeconomicstatus and distance plays minimal role as a cause of patients stopping taking EBRT. Female patients are more likely to discontinue their treatment as compared to their male counterparts. There no particular relation between age, disease site, treatment received prior to radiotherapy or intent of treatment in patients receiving radiotherapy. Use of concurrent chemo-radiation hardly makes any significant difference in defaults among patients receiving radiotherapy. There may be some causes unique to that particular radiotherapy center which needs to be explored and addressed. Proper counselling of the patients while starting radiotherapy treatment and timely management of any radiation toxicityand individualised personal care to the patient can immensely improve the compliance and so as treatment outcome.

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Bipaddle pectoralis major myocutaneous flap: In Indian context.

Mahendra Singh Hada

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Background: Despite the free flap is a first choice in reconstruction of head neck oncologic defect, Pectoralis major myocutaneous pedicle flap (PMMC) has its own utility and become first choice in certain circumstances. Most of tertiary carecentresin developing countries like India are facing long surgery waiting list because of time, money and resource constrains. **Materials And Methods:** Analysis of prospective collected data from June 2013 to sept 2015. Over **47** PMMC till now **23** bipaddle PMMC were used to reconstruct oral cavity full thickness defect.Other PMMC were excluded from study. Financial burden, surgical time, uptake rate, donor morbidity, flap morbidity (OCF, outer paddle necrosis), monitoring (ICU/close) required, delay in adjuvant Rx, requirement of special training etc. **Results:** Flap 21x8 to 15x6cm. Max outer paddle 9x10cm. Less financial burden compared to free flap 30-40K INR, less surgical time (145- 180 min, 160.6mean), uptake rate almost 100%, donor morbidity (suture gap 17%, seroma 8.7%, rib/chondral pain 12.9%) flap morbidity (ocf 4.3%, outer paddle minor necrosis 4.3%), no ICU/close monitoring required as in free flap, no patient delayed in adjuvant radiation, patient discharged 7-15 days mean 7days, compared to free flap learning curve is short. No patient required salvage of flap. Suitable for post radiated (recurrent/residual). **Conclusion:** Bipaddle PMMC has advantage over free flap asrequirements of surgical time and money were less. fewflap morbidity, suitable in resource constrain settings and no close monitoring required. However it does not mean that it replace free flap in oral cavity full thickness defect but to some extent it becomes preferred flap in low resource setting like in developing countries.

Keywords: Bipaddle, Free flap; myocutaneous; pectoralis; reconstruction

Toxicity analysis of TPF neoadjuvant chemotherapy in patients with head and neck cancers

Anant Ramaswamy

Background: There are lack of data systematically addressing the issue of toxicity with TPF/DCF regimen in routine care. Hence we planned this study with the aim of detection, profiling and quantifying the toxicity of TPF used in Indian head and neck cancer patients receiving neoadjuvant TPF chemotherapy in routine clinical practice (non-trial setting). **Methods:** Patients of locally advanced head and neck cancer receiving TPF chemotherapy were selected for this analysis. The patients received 2 cycles of TPF chemotherapy three weekly. Patients were monitored for the occurrence of adverse drug reactions in accordance with CTCAE version 4.03 during the indoor stay daily (at least until day 8 post start of chemotherapy), then at day 15 & at day 20. Descriptive statistics have been performed. Predictive markers for toxicity were sought. **Results:** The cumulative rate of grade >3 anemia, neutropenia and thrombocytopenia were 12.1%, 56.9% and 5.2 % respectively. The cumulative incidence of febrile neutropenia was 20.7% (12 patients, n=58). None of the selected factors predicted for the development of febrile neutropenia. The cumulative incidences of mucositis and diarrhea were 67.2% and 74.1% respectively. There was no mortality associated with induction chemotherapy and 100% patients completed the planned 2 cycles of TPF. **Conclusion:** The toxicity of TPF in Indian patients in routine practice differs substantially from that in the western population in the trial setting. Strict selection criteria for TPF regimen can ensure high compliance to completion of TPF induction and low mortality.

Keywords: Toxicity; profiling; TPF; NACT; Induction; Head and neck cancers.

Follicular Variant of Papillary Thyroid Carcinoma a Unique Clinical Entity: A retrospective study

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Introduction: Well differentiated carcinomas (papillary and follicular) constitue majority of the thyroid malignancy.Among Papillary thyroid carcinoma(PTC) , Follicular variant of papillary thyroid carcinoma (FV-PTC) has been increasingly diagnosed in recent years. However, little is known about its clinical behaviour. The purpose of this study was to determine the disease characteristics of FV-PTC, and to compare it with classical papillary thyroid carcinoma (C-PTC) and follicular thyroid carcinoma (FTC). **Methods:** All cases of C-PTC, FV-PTC, andFTC fromAugust 2013 to December 2015 were identified. Tumourbehaviour and patient survival were compared among these three groups. **Results**: 355 surgical cases were identified, including 202 C-PTCs,47 FV-PTCs, and 17FTCs. Extrathyroidal extension and lymph-node metastases were more common in FV-PTC than in FTC, but significantly less common than in C-PTC (p< 0.0001). Distant metastasis rates were present in 2% of patients with FV-PTC, in 1% with C-PTC, and in 4% with FTC (p< 0.0001). The presence of extrathyroidal extension and distant metastases were stronger predictors of disease-specific mortality in FV-PTC than in C-PTC. **Conclusions:** FV-PTC is a common variant of PTC. Its clinical behaviour is unique and represents an intermediate entity with clinical features that are between C-PTC and FTC.

DPD mutation in Neoadjuvant chemotherapy in head and neck cancers. Myth or reality?

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Purpose: The TPF regimen in India is associated with high percentages of grade 3-4 toxicity. This analysis was planned to evaluate the incidence of DPD mutation in patients with severe GI toxicity, to assess whether the mutation could be predicted by a set of clinical criteria and whether it has any impact on post NACT response. **Methods:** All consecutive patients who received TPF regimen in head and neck cancers between January 2015 to April 2015 were selected. Patients who had predefined set of toxicities in Cycle 1 were selected for DPD mutation testing. Depending upon the results, C2 doses were modified. Post completion of 2 cycles, patients underwent radiological response assessment.Descriptive statistics has been performed.The normally distributed continuous variables were compared by

unpaired student t test while variables which were not normally distributed by wilcoxon sum rank test. For non continuous variables, comparison was performed by fisher's exact test. **Results:** Out of thirty four patients who received TPF, 12 were selected for DPD testing and 11(32.4%, 95% CI 19.1%-49.3%) had DPD mutation. The predictive accuracy of the criteria for the tested DPD mutations was 81.3% (95% CI 62.1-100%).Of the 11 DPD mutation positive patients,except for one patient, all others received second cycle of TPF.The dose adjustments done in 5 FU were 50% dose reduction in 09 patients and no dose reduction in 1 patient. The response rate in DPD mutated patients was 27.3% (3/11) and that in DPD nonmutated/ non tested was 39.1% (9/23) (p=0.70). **Conclusion:** Nearly 1/3rd of patients with Head and neck cancers in India have DPD mutation. Clinical toxicity criteria can accurately predict for DPD mutation. Post dose adjustments of 5 FU from C2 onwards, TPF can safely be delivered in majority of patients with DPD heterozygous mutations without decrement in efficacy.

Philadelphia chromosome positive Acute Lymphoblastic Leukemia: 8 years' experience from a tertiary care centre in India

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Introduction: The Philadelphia chromosome (Ph) is the most common cytogenetic abnormality associated with adult acute lymphoblastic leukemia (ALL), occurring in 20% to 40% of patients.[1-4] It is also detected in 2% to 5% of children with ALL.[5]The Ph chromosome results from a reciprocal translocation (t) between chromosomes 9 and 22 (t[9,22][q34;q11])[6,7] and produces a fusion gene on chromosome 22, namely, the breakpoint cluster region-Abelson leukemia viral proto-oncogene (*BCR-ABL*). BCR-ABL fusion proteins are constitutively active tyrosine kinases that can alter multiple signaling pathways, contributing to tumor growth and proliferation. The p190 *BCR-ABL* fusion gene occurs in about 90% of children with Ph-positive ALL and between 50% and 80% of adults with Ph-positive ALL. The p210 *BCR-ABL* gene constitutes the rest of the Ph-positive ALL population.[8,9]Historically, patients with Ph-positive ALL carried a dismal prognosis, with poor response to most chemotherapy combinations, short remission durations and long-term disease free survival (DFS) rates of 10% to 20%.[11-13]The advent of tyrosine kinase inhibitors (TKIs) has revolutionized therapy of Ph-positive ALL. Synergistic effects have been observed in vitro when Imatinib has been combined with commonly used chemotherapy agents,[14] and a number of studies have investigated the benefit of concurrent or sequential administration of Imatinib with chemotherapy. Results from these trials suggest that the incorporation of Imatinib into standard ALL therapy results in complete remission (CR) rates that approach 95%, and 3-year overall survival (OS) rates exceeding 50%.[15-21]The benefit of the TKIs also extends to instances where consolidation with allogeneic stem-cell transplant (SCT) in first CR, which is the standard of care for Ph-positive ALL, is prohibited by older age, significant comorbidities, or lack of a suitable donor. Several trials have examined various strategies to spare these subsets of patients from the morbidity or mortality associated with intensive treatment regimens and Allogeneic SCT, including a chemotherapy-free treatment based only on a TKI and steroids.[18]Despite these advances, the emergence of resistance to Imatinib attributed to *BCR-ABL*-dependent and *BCR-ABL*-independent mechanisms has presented new therapeutic challenges. The development of second- (e.g., Dasatinib, Nilotinib) and later-generation TKIs with enhanced inhibitory potency against wild-type and mutated ABL (in some cases with inhibitory effects against other relevant targets such as Src kinases) may potentially improve upon the encouraging results observed with Imatinib.[22,23]We performed a retrospective analysis of patients with Ph-positive ALL during the period 2007 to 2014 at Nizams' Institute of Medical Sciences, Hyderabad, Telangana, India. **Materials and Methods: Patients** This retrospective and descriptive single centre study was carried out based on data retrieved of 508 patients treated for ALL from 2007 to 2014. Of these30 (5.9%) patients were Ph-positive ALL and were available for analysis, and these patients were included in the study. **Methodology Diagnosis:** Ph-positive ALL was defined as ALL carrying the t(9;22) translocation on standard karyotype and/or fluorescent in situ hybridization (FISH) analysis and/or positivity for *BCR-ABL* fusion transcript detection by real-time quantitative polymerase chain reaction (RQ-PCR) analysis. Patients with antecedent myeloproliferative disorders including chronic myeloid leukemia (CML) were not included. Immunophenotyping of ALL cells was systematically performed on bone marrow and/or on peripheral blood samples using monoclonal antibodies against the CD2, cytoplasmic CD3, CD5, CD7; CD19, CD10, cytoplasmic CD22 or CD79a, cytoplasmic immunoglobulin μ, κ, and λ chains; CD34, CD33, CD13, CD65, HLA-DR antigens, and surface immunoglobulins. In addition, anti-CD20, anti-CD22, anti-CD3, anti-CD1a, anti-CD4, anti-CD8, monoclonal antibodies were used to confirm the B-lineage or T-lineage origin of the leukemic cell population. **Treatment protocol:** The regimens were chosen based on age, performance status, comorbidities and financial status as the majority were completely dependent on state sponsored health schemes which had a capping of the amount that could be sanctioned for the entire course of therapy. The regimen adopted was one of either a course of hyperfractionated cyclophosphamide, vincristine, doxorubicin, and dexamethasone (Hyper-CVAD),[24] MCP 841,[25] BFM-95[26] or Siebel protocol.[27]Patients received TKIs based on the results of BCR-ABL and subject to availability of the drug as part of a patient support program for eligible patients. **Response evaluation:** Routine hematology, liver and renal function tests, and serum electrolytes were measured prior to each treatment cycle, and at follow-up visits. Responses were classified as either CR defined by the absence of circulating blasts and less than 5% marrow blasts on a bone marrow examination done at the end of induction chemotherapy or failure, including persistent disease and early death. **Statistics:** Data were analysed using SPSS 16 for Windows. Categorical variables were denoted and frequency distribution was performed using the chi square test. Cox regression analysis (or proportional hazards regression) using the backward elimination method was used to assess the effect of risk factors on response at the end of induction therapy. The probability of survival was estimated with the use of the product limit method of Kaplan and Meier and compared by the log-rank test. **Results:** Data from 30 patients (5.9%) diagnosed with Ph-positive ALL were analysed out of a total of 508 patients of ALL diagnosed and treated between 2007 and 2014 at Nizams' Institute of Medical Sciences, Hyderabad, Telangana, India. Patient baseline characteristics, cytogenetic and molecular data and treatment details are summarized in Tables 1, 2 and 3. **Treatment details:** The choice of first line TKI was Imatinib in 25 (83.3 %) patients and Dasatinib in 1 (3.3 %) patient. The dosages of Imatinib received was 260 mg/m2;300 mg in 3 (10 %), 400 mg in 5 (16.7 %) and 600 mg in 17 (56.7 %) patients.One patient received Dasatinib as the first line TKI at a dose of 100 mg which was escalated to 140 mg. Dose modifications of Imatinib were made in 7 (28 %) patients due to cytopenias, of these the majority 4 (57.1 %) were seen in those who received 600 mg. The choice of second line TKI after relapse while on Imatinib, was Dasatinib in 3 patients and Nilotinib in 1 patient. IRMA test detected a mutation in the P loop domain with hexanucleotide insertion GGG GGC at position 294 and 295 in one patient and a T315I mutation in another patient. **Response at the end of Induction therapy:** Response was analysed by doing a bone marrow aspiration and biopsy at the end of induction therapy. Fourteen patients (46.6 %) had a CR, 3 (10 %) had a partial response (PR), 8 (26.6 %) had persistence of disease. Of the 8 patients who had persistence of disease, 4 were on Hyper CVAD protocol and 4 were on MCP 841 protocol. 4 patients did not receive Imatinib during induction, two patients were on sequential strategy with Imatinib for a month followed by chemotherapy, one patient was a case of Ph-positive T-ALL. Cox regression analysis was done to assess the predictive factors for a complete response to induction therapy, with independent variables age, gender, initial hemoglobin, initial WBC count, initial platelet count, peripheral smear blast percentage, bone marrow blast percentage, presence of additional cytogenetic abnormalities, B or T lineage and aberrant of expression of myeloid markers. The only factor that influenced post induction marrow response was age (p = 0.006). **Complications during induction chemotherapy:** Bacteria were isolated in atleast one blood culture in two patients. The organisms isolated were E.Coli and Pseudomonas aeruginosa. One patient had a soft tissue infection of the forearm from which Rhizopus (a saprophytic fungi) was isolated. Three patients had evidence of possible invasive Aspergillosis. The non-infectious complications during induction chemotherapy were steroid related-diabetes (n = 3) and myopathy (n = 1), acute pancreatitis (n = 1), azotemia (n = 1), acute fulminant hepatic failure (n = 1) and lower limb deep venous

thrombosis (n = 1). One patient died of acute coronary syndrome 20 days after induction chemotherapy. **Induction deaths:** Of the 30 patients in whom induction therapy was initiated there were 3(10 %) induction deaths. Two patients succumbed to infectious complications,one was documented by culture positivity with E.Coli and the other was culture negative. One patient died of bacterial meningitis.The median time to induction death was 20 days (Range 10 to 34). **Survival analysis:** An additional 14 (51.8 %) patients died post induction during the period of study. Of these the majority 8 (57.1 %) of deaths were due to disease relapse and 2 were due to persistence of disease.Twopatients died in remission during subsequenttreatment due to neutropenia (infections), one patient died of ARDS and one patient died of acute coronary syndrome 20 days after induction.The overall survival in those who received sequential chemotherapy followed by TKI (n = 4) was 28.5 months (95% CI 10.78 to 46.21 months) compared with 13.98 months (95% CI 6.04 to 21.97 months) for patients who received concurrent chemotherapy and TKI (n = 20), 3 months (95% CI 1.04 to 4.96 months) for sequential TKI followed by chemotherapy (n = 2), and 2 months (95% CI 0.04 to 3.96 months) for patients who received chemotherapy alone (n = 4); log rank (Mantel Cox) X2 = 8.33, p = 0.040). Kaplan Meier curves for overall survival are shown in Fig 1. **Discussion:** Long-term survival rates in ALL approach 80% in children aged <5 years but decrease to approximately 50% to 60% in adolescents and young adults, to approximately 30% in adults ages 45 to 54 years, and rarely exceed 15% in older adults.[28-30]The introduction of a standard protocol (MCP 841) and improvements in supportive care in major cancer centres in India led to an increase in the EFS from less than 20% to 45-60% at 4 years. The challenges faced during treatment of ALL patients in India are manifold, and have been reported asmore extensive disease at presentation partly explained due to delayed diagnosis, higher toxic death rates, comorbidities (intercurrent infections), differences in the level of hygiene achievable in the average home, poor access to acute care, and more limited supportive care facilities in Indian hospitals.[31]There is a paucity of published data on outcomes in specific subgroups such as Ph-positive ALL from India.The incidence of Ph-positive ALL in the current study which included both pediatric and adult patients was 5.9 % (30 out of 508 patients). Sugapriya et al reported the incidence of BCR-ABL translocation detected by RT-PCR to be 8.3% (2/24 patients).[32] Bhutani et al detected Ph chromosome in 4/17 (24%) of childhood cases of ALL.[33]The median age of 27.5 years (range: 7-55) is strikingly different from that routinely reported in the literature from developed countries. This lower median age could be explained by the different population pyramid structure in India, where 87.5 % of the population is less than 55 years of age.[34]Combining Imatinib with conventional chemotherapy has improved outcomes of Ph-positive ALL. We found a CR in 14 out of 30 patients (46.6 %), and this did not correlate with results of published studies in the western population where CR rates now approach 95 %.[15-21]Imatinib was not systematically added from Day 1 of the first induction course due to logistic reasons, adding a TKI during induction was possible in only 11 (36.6 %) patients. This could be the explanation for the lower CR rates, due to a slow and partial reduction of the leukemic clone by initial chemotherapy.[35]The only factor that influenced post induction marrow response was age (p = 0.006) which is in line with published data from western nations. Outcomes in Ph-positive ALL with the advent of TKIs have improved dramatically and 3 year OS rates can exceed 50%.[15-21]The initial debates focusing on the optimal schedule, concurrent versus sequential imatinib, have been largely settled by several reports of good tolerability and improved efficacy of the concurrent treatment as demonstrated by significantly higher percentage of patients converted to PCR negativity and lesser relapse rates. The OS in the current study in those who received sequential chemotherapy followed by TKI (n = 4) was 28.5 months (95% CI 10.78 to 46.21 months) compared with 13.98 months (95% CI 6.04 to 21.97 months) for patients who received concurrent chemotherapy and TKI (n = 20). Of the 4 patients who received sequential chemotherapy followed by TKI, 2 were detected to be Ph-positive only after they relapsed while on the maintenance phase of chemotherapy; of them 1 patient received Imatinib (overall survival of 38 months), and 1 patient was started on Imatinib, later switched to Dasatinib, followed by Nilotinib, detected to have a T315I mutation and succumbed a month later (overall survival of 36 months). One patient was detected to be Ph-positive only after induction chemotherapy with Hyper CVAD and repeat induction with Mitoxantrone plus Etoposide failed to achieve remission, was started on Imatinib, detected to have a mutation in the P loop domain, switched to Dasatinib and is alive on follow up for 27 months. Consolidation with Allogeneic transplant in first CR is the standard of care in Ph-positive ALL.[36]In India, there are 11 centres currently reporting their data to CIBMTR (Center for International Blood and Marrow Transplant Research).[37]Until September 2005, data were collected from six transplant centres in India and a total of 1540 transplants were performed in India at these centres. Of these half were autologous transplants mainly for myeloma.[38]Centres which perform regular HSCT are low due to various reasons like lack of infrastructure and expertise and lack of knowledge of safety, efficacy and cost of the procedure both in the general population and in medical fraternity. The indication for allogeneic BMT was ALL in only 39 (7.9 %) patients out of 522 allogeneic BMT performed at Christian Medical College Hospital, Vellore between October 1986 to December 2006.[38] Given the limited utility of transplant as an option in the treatment of ALL, the optimal use of TKIs integrated with chemotherapy regimens assume significance, though their long term benefits require validation by more robust data. **Limitations:** A limitation of our study was the retrospective design. However, Ph-positive ALLs are rare in the general population, making a prospective study with an adequately sized sample extremely difficult. Our sample size was fairly small at 30 patients, which limited the number of patients in certain subgroup analysis of overall survival. **Options to improve treatment:** Limiting the variations in the design of Imatinib administration (time of onset, sequential versus continuous administration, daily dosage),adopting a definite protocol with regards to the number of days Imatinib is to be administered during intensive chemotherapy and assessment of early response to chemotherapy and TKIs with documentation of molecular response to risk stratify patients and intensify treatment strategy to consider the possibility of an Allogeneic SCT. **Conclusion:** Imatinib has revolutionized the outcome of patients with Ph-positive ALL and is at the forefront of treatment of Ph-positive ALL. Newer TKIs such as Dasatinib and Nilotinib, appear to be safe and efficacious in patients with Ph-positive ALL who have Imatinib resistance.The results of our study showed that treatment employing an integrative chemotherapeutic regimen using concurrent or sequential strategieswith TKIs improved response rates, and better long term outcomes compared to chemotherapy alone. However, we still have a long way to go to match outcomes of western published series, even when the same treatment protocol is used, probably due to the underutilization of Allogeneic SCT as an option in first CR.

Assessment of therapeutic response of Radioimmunotherapy with Yttrium-90-labelled Rituximab (chimeric anti-CD20 antibody)in patients with relapsed and refractory B cell NHL- a first prospective trial in India

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Aim: The aim of the study was to evaluate the safety and efficacy of Radioimmunotherapy (RIT) with a human chimeric anti-CD20 antibody labelled with Yttrium-90 (^{90}Y-Rituximab) in patients with B cell Non Hodgkins lymphoma (NHL). **Materials & Methods:** This was a prospectivestudy done in the department of Nuclear Medicine, AIIMS, New Delhi and was the first study in the country to assess the therapeutic response of RIT in B-cell NHL patients.Twenty patients with CD20+ B-cell lymphoma in progressive state after at least one line of therapy were included.The patients had undergone a median of 2 (range 2-5) prior standard chemotherapy ± immunotherapy regimens.^{90}Y-Rituximab was administered according to approved schedule: a first infusion of rituximab 250 mg/m^{2}on days 1 and 8, and either 14MBq/kg or 11MBq/kg of ^{90}Y-Rituximab on day 8 (maximum dose, 1120 MBq) depending upon their platelet count.Post therapy, patients were followed clinically, biochemically and radiologically.^{18}F-Fluorodeoxyglucose-Positron Emission Tomography/ Computed Tomography (^{18}F-FDG-PET/CT) was performed not more than 10 days before treatment and repeated at 1, 3 and 6 months after for response assessment.Hematological assessment was obtained at baseline

and weekly after the treatment for 6 weeks or until recovery from nadir. **Results**: Disease histologies of twenty patients included mainly Diffuse Large B-cell lymphomas (n=16), Follicular(n=2) and Mantle Cell Lymphoma (n=2). No acute adverse effects were observed after the administration of ^{90}Y-Rituximab. Toxicity was primarily haematological. The therapy was well tolerated with grade IV thrombocytopenia, neutropenia and anemia was observed in 3, 4 and 2 patients respectively. Overall response rate (ORR) was 55% of which complete response (CR) was observed in 2 patients, stable disease (SD) in 1 patient, partial response (PR) in 8 patients and progressive disease (PD) in 9 patients. The median overall survival of the responders was 8.2 months (2.2 - 17.9 months) and the parameters which attributed for higher response rates and higher survival rates were histology of follicular or MCL, KPS more than 60 and extranodal disease ≤ 95cc and. The major limitation of the present study was its small sample size which precludes generalisation of the results and that the Overall survival (OS) was shorter as compared to the existing literature which can be explained by the Karnofsky Performance Scale (KPS) of patients at time of recruitment confounding the results of survival. **Conclusion:** Toxicity with ^{90}Y-Rituximab wasprimarily hematologic, transient and reversible.^{90}Y-Rituximabtherapy was safe and well tolerated in high risk extensivelypretreated NHL patients.

Keywords: mAb, Rituximab, NHL, Radioimmunotherapy, Y-90

Study the efficacy and toxicity of low-dose cytarabine in aml patients not eligible or willing for standard induction

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Introduction: Acute myeloid leukemia (AML) is the most common type of leukemia inadults, yet it continues to have the lowest survival rate of all leukemias.While the results of treatment have improved steadily in younger adultsover the past 20 years, there have been limited changes in survival amongindividuals of age >60 years. Despite the use of various treatment, curerate is <10% in elderly patients and those with co morbidities. Treatment of AML in elderly and those not fit or willing for standardtreatment has always been a challenge. Treatment decisions in these patients are difficult and remaincontroversial. Many studies have used less intensive agents (low dose cytosar) orinvestigational agents like azacitidine, decitabine, clofaribine orgemtuzumab etc. in these patients but the long term outcome remainspoor overall. **Objectives:** So the intent of this study is to provide lessintensive treatment to these patients with co-morbidity, those in whomremission is unlikely or those who do not wish to take standard treatmentdue to financial constraint or social issues and thus give them betterquality of life at the same expected survival. **Material and Methods:** Present study was a prospective observational study and in this study patients of acute myeloid leukemia (except APML) presenting to our Institution between Dec.2012 to Dec. 2014; who were not eligible or willing for standard induction therapy were evaluated and included.Exclusion criteria were poor performance status(ECOG >2), patient previously on treatment, had cns disease and renal or hepatic impairment.There were two groups in this study, group A treated with low dose cytosar and group B with 6-Thioguanine. Both the groups were wellstandardized in demographic factors and distribution of disease.Patient was monitored with CBC with manual differential and toxicity at thebeginning of each cycle and followed up till death or last follow uptill study end date.Bone marrow examination was done once complete blood countswere normalised i.e. (Hb>8g/dl, WBC > 4000 and platelet >1,00,000).Quality of life was assessed in terms of days of hospitalization, numberof PCV transfused, no. of Platelet transfusions required and improvementin symptoms. **Results:** Total 24 patients were included in this study and median age in group A was 57 years and in group B 58 years. In group A, three patients had co-morbidities; two werediabetic and one was hypothyroid. In group B, two patients were comorbid(Hypertension and IHD in one each).Response evaluation was done in each group at the time of morphologicalresponse in peripheral smear. In group A, 2(16.6%) patients and in group B, 1(8.3%) patient was in complete remission. Partial remission in group A was seen in 2(16.6%) patients and one(8.3%) patient in group B.Two deaths were seen in both groups, one was due to febrile neutropeniaand other was due to bleeding in group A while in group B, one was due to disease and other was due to bleeding.Group A patients took one to five number of cycleswhile group B patients took one to four number of cycles. Median number of cycle inGroup A was 2 and in Group B was 1.Common toxicities due to disease and chemotherapy were nausea, vomiting, mucositis and cytopenia. In group A, 2 patients had mucositis, while in group B, 1 hadmucositis. In group A, 2 had infection and in group B 1. In both group Aand B , one patient each had bleeding. The mean PCV transfused in group A was 2.1+1.2 while in group B was 1.83+0.83. The mean platelet transfused in group A was 3.08+3.58 while in group B 2.91+2.06. **Conclusion:** So, this study shows that those patients who are not eligible and affordable for intensive treatment can be considered for less intensive therepy in form of low dose cytosar. Response rate is higher in lowdose cytosar arm as compared to 6-TG while maintaining Quality of life.

Efficacy of Curcumin and TRAIL (TNF related apoptosis inducing ligand) as a chemopreventive agent in Myeloid Leukemic Cell Lines

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Introduction: Curcumin, traditionally utilized as a flavoring zest as a part of Indian cooking, has been accounted to decrease the proliferation potential of most cancer cells. . Apoptosis, a mechanism by which most anticancer therapies including chemotherapy, radiation, and antihormonal therapy kill tumor cells.Novel agents that may sensitize drug-resistant tumor cells for induction of apoptosis by customary treatments could lead to the regression and improved prognosis of the refractory disease Indeed, chemotherapeutic agents have been shown to sensitize cancer cells to killing by death ligands such as tumor necrosis factor-α. **Objectives**: Toinvestigate curcumin as a chemopreventive agent and its ability to induce cytotoxicity and apoptosis in chronic myeloid leukemic cell line KCL-22. **Material and Methods:** Different doses of curcumin and tumor necrosis factor–related apoptosis-inducing ligand (TRAIL) alone and combine regimen were exposed to myeloid leukemic cell KCL-22. The cell viability was monitored by MTT assay, apoptotic activity by binding of Annexin V-FITC using fluorescence microscopy and cell cycle check points by flow cytometry**. Results:** Cytotoxic assay revealed that Curcumin and TRAIL induced a dose and a time-dependent decrease in cell viability. Significant cell cytotoxicity was seen in combine regimen of both Curcumin and TRAIL at 48 h of exposure.Cells treated with curcumin and TRAIL were arrested at the S phase, according to the flow cytometric analysis.Subtoxic concentrations of the curcumin-TRAIL combination induced strong apoptotic response in KCL-22 cells as demonstrated by the binding of Annexin V-FITC**. Conclusions:** Our study concludes that curcumin inhibits the cancer cell growth by inducing apoptosis and enhance the therapeutic potential of TRAIL which suggests that curcumin alone or in combination with TRAIL may be useful.

Management of Elderly Lymphoma : A Tertiary Cancer Center Experience

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Objective: Review the epidemiology,disease characteristics, frontline treatment outcomes of elderly patients with Lymphoma. **Methodology:** Electronic Medical Records (EMR) of 1955 consecutive adult lymphoma

patients [>17 years] from May2011 to Dec 2014 was reviewed. 692 patients greater than 60years (35%) were evaluated for demography,clinical features,staging,associated co-morbidities and first-line treatment response. 209 patients with no definite treatment or follow up prescribed at our center were considered as 2nd opinion seekers and were not included for management assessment. **Results:** The median age was 67 years, with 61% between 60 and 69 years, 31% between 70 and 79 years and 8% above 80 years. The gender ratio was 2.3 : 1. High Grade comprised 44%, Low grade 35% and Hodgkin Lymphoma 5%. The remaining 14 % was T cell and lymphomas not specified. Co- morbidities at presentation [45%] included Hypertension in the majority, followed by Diabetes, hypothyroidism, COPD and IHD. 5 patients had hepatitis markers and 2 in the cohort were HIV positive. Three hundred and fifty two patients (51%) were evaluated for their 1ST line treatment. The subtypes were Hodgkin Lymphoma [HL#20], chronic lymphatic leukemia/ small lymphatic leukemia [CLL/SLL # 61], follicular lymphoma [FL # 30], marginal zone [MZL # 24], mantle cell lymphoma [MCL # 16]and diffuse large B cell [DLBCL # 188], and others [13]. The common treatment regimens included ABVD for HL, Bendamustine Rituximab [B R] for low grade NHLs and CHOP like regimens for High grade NHL. The Overall response rates were similar to younger patients treated at our center. However the complete response rates were lower. The median progression free survival for our elderly cohort is 20 months [range 3 to 52 months]. Detailed results will be presented at the meeting. Thirty six (5%) were treated for Relapsed/ Refractory disease and 95 [14%] treated elsewhere are on follow up at our center. **Conclusions:** Adult lymphoma patients above 60years comprise 35% presenting to the clinic.More than half of these patients (55%) take treatment for their diseases.The common co-morbidities observed are Hypertension/ IHD. The CR rates were lower than that for younger patients. Treatment decisions and completion were dependent on social support available.

Analysis of 13 patients of Chronic myelomonocyticleukemia: A single centre study

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Background: Chronic myelomonocytic leukemia (CMML) is a rare hematological malignancy categorized as myelodysplastic/myeloproliferative (MDS/MPD) disorder.World Health Organisation (WHO) classification committee proposed CMML to differentiate CMML as a 'dysplastic' type (MDS-CMML) and 'proliferative' type (MP -CMML). On the basis of blast percentage CMML differentiated into 2 subtypes, CMML-1 and CMML-2. **Methods:** We evaluated total 13 patients diagnosed as CMML at RGCI RC fromJan 2011 to Feb 2015. We have used diagnostic criteria proposed by FAB (French-American-British) for CMML. **Results:** We have analyzed 13 CMML patients with different laboratory parameters and characteristics. Patients of age more than 65 years were found to have shorter survival. CMML patients with low hemoglobin level, low platelet count, high white blood cell count, high monocyte count showed shorter median survival. Presence of circulating immature cells (IMCs), high percentage of marrow blasts, low percentage of marrow erythroid cells were associated with poorer survival. Even though our study didn't correlate, abnormal cytogenetics and serum lactate dehydrogenase also considered as independent prognostic indicators. RBCS transfusion dependency, b2 microglobulin leveland Ferritin level has been mentioned as another independent prognostic variable. The distinction of CMML into MP- and MD- variants should be maintained in the diagnostic workup.WHO classification; CMML-1 and CMML-2 subtype provides independent prognostic information. Cytogenetic risk classification for CMML is used as independent prognostic capacity.There are different scoring systems andMayo prognostic model has been validated for assessment of CMML patients. **Conclusion:** In CMML patients independent covariates and different validated prognostic models can be used as predictive of disease behavior.

Univariate analysis of the effects of patient characteristics on survival

Patients Characteristics	No. of patients	No. of deaths	Median Survival (months)
Hemoglobin level			
Less than 12g/dl	11	3	9.66
12g/dl or higher	2	0	10.2
Platelet count			
No higher than 100 x109/L	7	3	9.66
100 x109/L or more	6	0	10.2
White blood cell count			
No higher than 10 x109/L	2	1	28.07
10 x109/L or more	11	2	9.04
Monocyte count			
No higher than 4x109/L	6	2	15.13
4x109/L or more	7	1	9.66
Peripheral blood IMCs			
No higher than 10%	1	1	34.91
10% or more	12	2	9.35
BM blasts			
Less than 5%	6	2	16.3
5% and more	7	1	6.34
BM Erythroid cells			
No more than 10%	6	1	7.2
More than 10%	7	2	12.06

Key words: Chronic myelomonocytic leukemia, prognostic variables

Promoter polymorphism (-909C/A) in platelet derived growth factorα receptor gene and Imatinib induced thrombocytopenia.

Pooja Singh

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Background: BCR/ABL chimeric oncogene is the underlying molecular cause responsible for the initial phase of chronic myelogenous leukemia (CML). This is effectively treated by the BCR-ABL inhibitor Imatinib. However over the course of time a significant number of patients become resistant to the treatment and progress to blast crisis, an event that is driven by additional genetic alterations like point mutations, chromosomal abnormalities and epigenetic aberrations. In this study we characterized the PDGFRα promoter polymorphism in CML patients in different stages. **Objective:** To characterize the role of -909C/A PDGFRα gene promoter polymorphism in CML patients. **Methodology:** -909C/A PDGFRα gene promoter polymorphism was studied in 50 CML patients and 50 age and sex matched healthy controls. DNA was extracted from peripheral blood from all subjects by Gene Aid, India, extraction kit according to the manufacturer's instructions. The -909C/A PDGFRα gene promoter polymorphism was studied by allele specific PCR (AS-PCR). A p-value of <0.05 was taken as significant. **Results:** Out of 50 CML patients 45 (90%) had CC genotype and 5(10%) had AA genotype compared to 43(86%) and 4 (8%) out of 50 healthy controls respectively. Heterozygosity (C/A genotype) was observed in 3 (6%) healthy controls whereas CML patients did not exhibit C/A genotype.

A nonsignificant association (p value = 0.20) of variation in genotypes of -909C/A PDGFRα gene promoter polymorphism was observed in CML patients with respect to healthy controls.In addition 28 (93%) out 30 CP patients, 8 (80%) out of 10 AP patients and 9 (90%) out of 10 BC patients showed CC genotype, whereas 2 (7%) out of 30 CP patients, 2 (20%) out of 10 AP patients and 1 (10%) out of 10 BC patients had AA genotype, but the difference was not significant. A statistically significant correlation (p value = 0.002) was found when -909C/A PDGFRα gene promoter polymorphism was compared with presence or absence of thrombocytopenia in CML patients. **Conclusion:** In this study we propose that AA genotype of -909C/A PDGFRα promoter polymorphism may be associated with thrombocytopenia in CML patients treated with imatinib.

Platelet Derived Growth Factor Receptorα (PDGFRα) gene expression is associated with Imatinib induced thrombocytopenia in chronic myeloid leukaemia.

Sameer Ahmad Guru

Maulana Azad Medical College and Associated Hospitals

Background: Chronic myeloid leukemia (CML) is a myeloproliferative disorder characterized by the expansion of a clone of hematopoietic cells that carry the Philadelphia chromosome (Ph). Ph chromosome results from reciprocal translocation between chromosomes 9 and 22 t(9;22) and results in *BCR-ABL* gene, encoding a constitutively active protein tyrosine kinase. Imatinib is the first line treatment for CML, which specifically targets BCR-ABL tyrosine kinase. However, a significant number of CML patients treated with Imatinib, develop drug resistance and/or some side effects like thrombocytopenia among others, the mechanisms of which in most cases are unknown. Platelet-derived growth factor receptor (PDGFR) is involved in the regulation of hematopoiesis. Imatinib mesylate, a platelet-derived growth factor receptor inhibitor, induces thrombocytopenia in a significant proportion of patients with chronic myeloid leukemia. **Objective:** To explore the role PDGFRα in imatinib induced thrombocytopenia in chronic myeloid leukaemia. **Methodolgy: Expression of PDGFRα gene** was characterized in 50 CML patients in different clinical stages, recruited from Lok Nayak Hospital, Maulana Azad Medical College, New Delhi, with respect to 50 age and sex matched healthy controls. RNA was isolated from all the subjects using Trizol RNA extraction method and then converted to cDNA. The expression study was performed using SYBR green based qRT-PCR and the results were expressed as median fold change. **Results:** In CML patients PDGFRα gene expression was found to be 1.26 fold higher in comparison to healthy controls. Patients in blast crises had a lower PDGFRα gene expression (median fold change 0.65) as compared to patients in chronic phase and accelerated phase (median fold change1.21 and 2.19 respectively). However, this difference did not reach statistical significance (p value = 0.43).Further, there was a significant difference in PDGFRα gene expression, between thrombocytopenic and non-thrombocytopenic CML patients (p value = 0.03). Patients having thrombocytopenia had lower expression of PDGFRα gene compared to patients who were non thrombocytopenic (median fold change 0.13 and 1.49 respectively). **Conclusion: PDGFR** α being a side target of imatinib may be down regulated in CML patients receiving Imatinib therapy which may be a cause of thrombocytopenia in these patients.

Promoter hypermethylation of RASSF1 gene increases in disease progression of chronic myeloid leukaemia and its association with drug response.

Musadiq Ahmad Bhat

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Background: Chronic Myeloid Leukaemia is a haematopoietic stem cell disorder resulting from a reciprocal translocation between chromosomes 9 and 22. The presence of a balanced translocation between the long arms of chromosomes 9 and 22, t(9;22) (q34;q11), known as the Philadelphia (ph) chromosome, is the basis of the diagnosis and a hallmark for treatment. The disease is heterogeneous in its presentation and clinical course, prognosis and therapy, which has changed during the last few years. The availability of more effective therapy with Imatinibmesylate has changed the natural history of the disease, and today represents the major success in the era of target-directed cancer chemotherapy. However, in addition to the presence of Ph chromosome, there are many genetic and epigenetic changes which are stated to be responsible for drug resistance and progression of the disease. RASSF1 gene methylation has been foundto have a role in many cancers. But, there is not enough literature about the role of RASSF1 gene promoter methylation in CML. The main of the study was to characterize the role of promoter hypermethylation in CML patients. **Objective:** To characterize the role of promoter hypermethylation of RASSF1 gene in disease progressionof Chronic Myeloid Leukaemia. **Materials and methods:** RASSF1 gene promoter hpermethylation was studied in 100 CML patients and 25 age and sex matched healthy controls. The CML patients were recruited from LokNayak Hospital to the Deapartment of Biochemistry, Maulana Azad Medical College, New Delhi. Promoter hypermethylation was studied by Allele Specific Polymerase Chain Reaction (AS-PCR). A p-value of <0.05 was taken as significant. **Results:** RASSF1 promoter hypermethylation was found to be positive in 16 (16%) CML patients and it was found negative in all control subjects and the association was found to be statistically significant (p = 0.0001). A statistically significant association was also found in clinic-opathological features like phases of the disease, molecular response and haematological response with p- value of 0.001, 0.002 and 0.002 respectively. **Conclusion:** RASSF1 promoter hypermethylation was found to be associated with the disease progression and drug response in Chronic Myeloid Leukaemia.

Immunomodulatory *Glu/Man*-directed *Dolichos lablab* lectinregressesangiogenes is dependent neoplastic malignancy through NF-κB signalling cascade

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Introduction: Immunomodulatory approach for cancer therapy is a recent trend in developing novel strategies for atarget specific action without triggering the deleterious effects. Lectins arehighly specific carbohydrate binding proteins, known for their immunomodulatory effects exhibiting wide range of anticancer properties particularly by modulating various signalling pathways. Identification of such lectins from dietary source which triggers mitogenicity in lymphocytes and activates cytokine signalling endogenously isa better concept in accepting "prevention is better than cure". **Objectives:** To investigate the impact of *Dolichos lablab*based lectin (DLL) in tumor angiogenesis by exploring its molecular targets by validating the immunomodulatory action. **Material and Methods:** Isolation and characterization of lectins:Ovalbumin-Sepharose 4B affinity chromatography, SDS-PAGE, HPLC, MALDI-TOF, Heam- and Leucoagglutination assay, Glycocode estimation, Thermal and pH stability.Mitogenicity assay: MTT, trypan blue against human & murine lymphocytes, FACS. Angiogenic assays-[Non-tumor models- *in-ovo*&*ex-ovo*CAM assay, Aortic ring assay, Rat corneal assay/micropocket method] and [tumor angiogenesis models- DLA peritoneal angiogenesis assay, Microvessel density (MVD) by H&E staining and CD31 immunostaining, A549-CAM Xenograft system].Antiproliferative and mechanism studies – murine ascites model and solid tumor. Gene expression studies: IB, IHC, ELISA, RT-PCR and gelatin zymography. **Results:** The dietary lectin DLL

has specific glucose/mannose binding activity, with apparent molecular weight of ~17-19 kDa and it exhibited a pan heamagglutinating characteristics without blood group specificity. DLL exerted a strong mitogenic activity against human lymphocytes and murine splenocytes & thymocytes*in-vitro on par with* Con A with a minimal concentration of 5μg/mL. DLL could inhibit neovessel formation in various angiogenesis models and regressed tumor growth in murine models and xenograft. Altered CD31 MVD counts on endothelial cells and change in invasive and migration pattern is a clear evidence for angiopreventive action of DLL. Mechanism of tumor inhibition *in-vivo* is due to the increased lymphocyte proliferation and secreted cytokines like IL-12. Altered transcription factor NFκB and it target genes MMP-2, MMP-9, and VEGF inferred an involvement of NFκB mediated signalling in immunomodultory effect. **Conclusions:** Dietary source derived lectin DLL isolated from *Dolichos lablab* presented a tumor angioinhibitory mechanism through immunomodulatory potential, thereby opening a new gateway for specifically targeting cancer without any side effects. This indicates that DLL would have a possible therapeutic intervention in cancer in near future.

Key words: Lectin, Immunomodulation, Tumor Angiogenesis

Gefitinib or Erlotinib in the management of patients with stage 4 non-small cell lung cancer (NSCLC) harbouring an EGFR driver mutation

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Background: Treatment with EGFRTKIs (Tyrosine Kinase Inhibitors) gefitinib, erlotinib and fatinib is the standard of care for patients with EGFR mutation positive non small cell lung cancer. However, there are no trials comparing gefitinib and erlotinib, the two most commonly used TKI. **Material and Methods:** Were trospectively analy zedour data of NSCLC patients with EGFR positive mutation diagnosed between January 2013 to October 2014. Patients treated with gefitiniborerlotinibeither up front or after chemotherapywere analyzed for responserate, progression free survival (PFS) and over all survival (OS). **Results:** Out of 194 patients EGFR mutations were detected in 64 patients (37.9%). 63 were adenocarcinoma and one large cell carcinoma. EGFR mutation detected were –deletion 19 in - 37 patients (57.8%), exon 21 in - 23 patients (35.9%), exon 18 in - 3 patients 4.7%) andex on 20 in 1 (1.6%). Thirty nine patient srceived gefitinib (19 up front, 20 after cyto toxicche motherapy), twenty two received erlotinib (7 up front, 15 after cyto toxicchemotherapy), one patient afatinib and one best supportive care only. Median number of cyto toxicche motherapy cycles given before EGFRTKI started were - 4 (minimum 3 and maximum 6). At amedi an follow up of 14.5 months % of patients progressi on free and survivingasa whole, in gefitinibanderlotinib group are 29.7%,25.6%,31.8% and59.4%,53.8%, 72.2%respectively.

Table 1. Over all responserate (ORR = complete + partialresponse), stablediseaserate, progressive disease rate, PFS and OS in whole EGFR mutation positive , gefitinib treated and erlotinib treated patients

Patients (n)	ORR (%)	Stable disease Rate (%)	Progressive diseaserate (%)	PFS (months)	OS (months)
EGFR positive (64)	73.43	14.1	12.5	10	NR
Gefitinib Treated (39)	71.8	15.4	12.8	9.5	NR
Erlotinibtreated (22)	77.3	13.6	9	10.4	NR

Conclusion: Inpatientswithstage 4 non - small celllung cancer (NSCLC) harbouring an EGFR drivermutation RR, PFS & OS were similar forge fitini banderlotinib.

Key words: NSCLC, gefitinib, erlotinib

Cancer and Opportunistic Infections among the People living with AIDS on ART in Eastern Nepal

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Background: Opportunistic infections (OIs) are more frequent and severe because of immune-suppression in HIV-infected persons, and are the major clinical manifestation of HIV patients. Cancer is a significant cause of mortality and morbidity in people infected with HIV; in fact 30% to 40% will develop a malignancy during their lifetime. The objective of this study was to find out the prevalence of Opportunistic Infections (OI) and Cancer among the PLWA on ART in eastern of Nepal. **Materials and Methods:** Descriptive cross-sectional research design was used to carry out the study. The PLWA receiving ART residing in eastern Nepal constitute the population of the study. Using convenient sampling technique 75 subjects were selected for study during the period of 15th June 2014 to 30th July 2014 of six weeks. **Results:** Majority of the PLWA (52.65%) were of age group of 35-45 years, Male (62.7%) and Hindu (81.3%). Among the PLWA about 13% were illiterate; 18.7% were farmer, 13.3% house wife, 10.7% were driver and 9.7% were labour. Most of the respondents (60%) were from Sunsari District and 61.3% belongs to rural areas. The common OIs found were Pulmonary Tuberculosis (33.3%), extra Pulmonary TB (14.7%), Oral Thrush (30.7%), fungal infection (22.7%), Herpes Zoster (14.7%) and Hepatitis-C (18.7%); whereas regarding Cancer it was found that 22.7% had Lymphandopathy, 18.7% had Skin Cancer and 2.7% had Kaposi-Sarcoma. **Conclusions:** It can conclude that the Opportunistic Infections among PLWA were Tuberculosis, Oral Thrush,Fungal infection, Hepatitis-C, and Herpes Zoster; whereas, cancer of Lymphnode, skin cancer and Kaposi-Sarcoma was found among the PLWA receiving ART in eastern Nepal.

Key Words: Cancer, Opportunistic Infections, People living with AIDS

Prospective observational study of thromboembolic events in patients of advanced stage Non-Small Cell Lung Cancer (NSCLC) treated with platinum based chemotherapy.

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Introduction: Cancer is a prothrombotic state and its treatment is frequently complicated by thromboembolism. It is associated with an increased risk in both venous and arterial thromboembolic events (TEs), including deep venous thrombosis (DVT), pulmonary embolus (PE), cerebrovascular accident, and unstable angina/myocardial infarction (MI). Based on many retrospective analyses in patients with lung cancer, thromboembolic complications are a common event with incidences ranging from 10-17 %. **Objectives:** To determine the incidence of both arterial and venous TE s in patients of lung cancer treated with platinum-based chemotherapy and to analyse the prognostic value of patients baseline and treatment characteristics in predicting occurrence of TEs. **Material and Methods:** All patients of advanced lung cancer (age >18 years) who were started on platinum based chemotherapy were included. Those patients who had prior TEs or inherited coagulopathy or those on therapeutic anticoagulation, regular NSAIDs / aspirin or those on bevacizumab were excluded. All patients were evaluated at the baseline prior to start of chemotherapy by a detailed history and physical examination. Baseline characteristics of the patients and their treatment were noted. During routine outpatient visits, patients were enquired for the

development of any venous /arterial TEs. Duration of follow up was 4 weeks from the last dose of chemotherapy. In the presence of a positive history relating to development of any TE , relevant diagnostic tests were performed for confirmation of the diagnosis at the discretion of treating physician. A thromboembolic event was considered associated with chemotherapy, if it occurred between the time of the first dose of chemotherapy and 4 weeks after the last dose. **Results:** A total 74 patients were enrolled in the study, out of which 64 patients completed treatment till the end of November 2015 and were included in the analysis .Out of these 64 patients, 2 patients were lost to follow up after the accrual. Of the 62 patients , 58.0% (36/62) received carboplatin with gemcitabine, 38.7% (24/62) received carboplatin with pemetrexed and 3.2 % (2/62) received cisplatin with pemetrexed. Median number of days on platinum were 96.5 (range 1-478). The median number of chemotherapy cycles administered was 5 (range 1 6). Thromboembolic events occurred in 6.3 % of patients (4 out of 62 patients) which were related to the platinum chemotherapy. Three patients had a pulmonary thromboembolism and one patient developed a cerebral infarction. All four patients were symptomatic and the patient with cerebral infarction died because of the infarction. The majority of events (75%) occurred within the first 100 days of starting platinum chemotherapy. Overall, the median time until occurrence was 57.5 days (range, 10 to 129days). None of the presumed risk factors associated with thrombosis were found be related to the occurrence of TEs on univariate analysis. **Conclusions:** This study suggests that patients of advanced Non- Small Cell Lung Cancer on platinum based chemotherapy are predisposed to development of thromboembolism due to many factors. It is imperative to analyse the results in higher number of patients to make a conclusion regarding the incidence of thromboembolism among these patients.

Autoimmune Hemolytic Anemia in a Patient of Adenocarcinoma Lung: Rare Case Report

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Background: Autoimmune hemolytic anemia is commonly associated with hematologic malignancies and association with solid tumours is uncommon. Lung cancer has rarely been reported as a cause. We are reporting a rare case of adenocarcinoma presenting simultaneously with autoimmune hemolytic anemia. **Case Report:** A 66 year old male with a smoking history of 40 pack years was investigated outside for a breathlessness of 2 months duration and was found to have massive right sided pleural effusion. Diagnostic pleural fluid tapping had revealed undifferentiated carcinoma. A PET-CT imaging showed right lung mass with widespread metastatic disease. Based on the above findings he was given two cycles of chemotherapy with albumin bound Paclitaxel and Carboplatin. The patient came to our institution with increasing weakness and fatigue. His general examination revealed severe pallor and respiratory examination showed diminished breath sound with dull percussion note in the right side of the chest. Laboratory investigation showed markedly low hemoglobin level with normocytic mormochromic anemia on peripheral smear. Liver function test showed mild hyperbilirubinemia with mildly elevated LDH levels. Blood transfusion was planned but the blood sample was positive for Directcoomb's test. Incidentally his blood was also found to have alloantibody to S-antigen. A review of patients history was negative for any previous blood transfusion. In view of above findings, the patient underwent blood transfusion under cover of steroid followed by intercostal drainage of pleural fluid. He then underwent core biopsy from the lung mass which showed moderately differentiated adenocarcinoma. With the improvement in general condition, the patient was started on Carboplatin and Pemetrexed combination therapy . **Discussion:** Autoimmune hemolyticanemia (AIHA) is a well knownparaneoplastic phenomenon in lymphoproliferative disorders but there are also a number of case reports of such an association with solid tumors.Joe Puthenparambil, Klaus Lechner and Gabriela Kornek from Viena university, in a critical analysis of 52 reported cases of AIHA in solid tumours, found AIHA was more common in renal cancer and Kaposi's sarcoma. Only 9 cases of AIHA in Lung cancer have been reported so far. They also concluded with the observation that the curative treatment of such cancers lead to the cure of AIHA. Paucity of literature in this respect commands reporting of such cases to enrich the scientific knowledge.

Keywords: Autoimmune hemolytic anemia, adenocarcinoma lung

EGFR positive lung cancer: The non trial scenario

Anant Ramaswamy

Purpose: The aim of this study was to report the median OS in EGFR mutation positive patients who were either not eligible for clinical trial or denied participation in them. **Methods:** Lung cancer patients have harboring activating EGFR mutation who were either ineligible for clinical trial enrolment or denied participation in it were selected for this analysis. The reason for non participation, the tumor characteristics, staging details, treatment details and outcome details were sought from a prospective lung cancer database. Overall Survival (OS) was calculated from the date of start of therapy to the date of death from any cause. The Kaplan Meier method was used to estimate survival. Log rank test was used for univariate analysis while COX proportion hazard model was used for multivariate analysis. **Results:** There were 225 patients subjected to the selection criteria. The median age of the cohort was 56 years (Range 29-85 years). The poor ECOG performance status of 3 or 4 was the major reason (83 patients, 36.9%) for ineligibility of patients for the study. The major reason provided by eligible patients for non participation in the study was long distance of travel (65 patients, 28.9%). The first line treatment received was TKI in 110 patients (48.89%) and chemotherapy in 115 patients (51.11%). The median OS in patients with PS0-2 was 18.17 months (95%CI 15.6-20.8 months) while it was 12.1 months (95%CI 9.0-15.2 months) in patients with PS 3-4. {HR-0.579 (95%CI 0.398-0.843) p=0.004}. **Conclusion:** Non trial patients who were ineligible for study due to poor PS had lower survivals however patients with good PS have similar OS to that reported in multiple clinical trials.

Keywords: EGFR mutation, Lung cancer, Palliative chemotherapy, Non trial

Efficacy of second line Erlotinib in patients post progression of first line chemotherapy in Head and neck cancers

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Background: Oral TKI (gefitinib and erlotinib) have been used in palliative treatment of head and neck cancers with limited success. In this report we aim to quantify the symptomatic benefit, progression free survival and overall survival when erlotinib is given as second line treatment in Head and neck cancers. **Methods:** This was a post hoc retrospective analysis of a randomized study comparing metronomic chemotherapy with cisplatin. Patient who progressed on chemotherapy and had a PS0-2 were offered second line chemotherapy. Patients who had received erlotinib (150 mg PO OD) as second line treatment were selected for this analysis. Erlotinib was discontinued in case of either progression of disease or if the patient had intolerable side effects. Patient were monitored 1 week after start of erlotinib and subsequently at monthly intervals. The toxicity was recorded in accordance with CTCAE version 4.02 and the response was graded in accordance with RECIST version 1.1. All of these patients were followed up till death. **Results:** Twenty three patients were identified. The median age of these patients at the start of second line was 47 years (IQR 40.5 to 51.75 years).The primary site of distribution was oral cavity primary in 17 patients (77.3%) and non oral cavity primary in 05 (22.7%) patients. The immediate

last chemotherapy regimen received was cisplatin in 9 patients (40.9%) and metronomic chemotherapy in 13 patients(59.1%).Symptomatic benefit post second line erlotinib was seen in 18 patients(81.8%). The most common adverse events (any grade) seen were anemia in 20 patients (90.9%), rash in 10 patients (45.5%) and diarrhea in 7 patients (31.8%) .The best radiological response documented were PR in 04 patients (19.2%). The median estimated PFS and OS were 110 days (95%CI 61-175 days) and 156 days (95%CI 126-185 days) respectively. **Conclusion:** Erlotinib single agent has promising activity in second line and needs to be explored in future studies.

Epidermal Growth Factor Receptor Mutation in Small Cell Lung Cancer Patients in an Indian Tertiary Care Oncology Hospital: Incidence and Clinical Outcome

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Background: Epidermal growth factor receptor (EGFR) mutation is uncommon, but reported in small cell lung cancer (SCLC). Our data add to this uncommon finding, which will have future therapeutic implications [1]. **Materials and Methods:** We present a retrospective study to evaluate EGFR mutation rate in SCLC with demographic correlation and clinical outcomes. Our study was approved by the institutional ethics committee and registered with the Clinical Trials Registry of India (reg. no. CTRI/2015/03/005648). Patients were selected from the department database with adequate tissue for EGFR mutation analysis, which was evaluated and confirmed by a thoracic pathologist. EGFR mutation analysis was carried out by real time polymerase chain reaction [2]. SPSS v17 software was used for the analysis. Descriptive statistics were used for demography. Survival was analysed using the Kaplan–Meier method with comparison carried out by Log-rank test between EGFR mutation positive and negative patients. **Results:** In total, 91 SCLC patients were selected for EGFR mutation testing. Four patients tested positive for EGFR mutation. Two were positive for exon 19 and two for L858R in exon 21. The median age of all patients was 56 years, compared with 50 years for the EGFR mutant SCLC patients (P = 0.093). 89% of all SCLC patients were men as compared with 50% of the EGFR mutant SCLC patients (P = 0.058). Never-smokers constituted 15% of all SCLC patients and 25% of the EGFR mutant SCLC patients (P = 0.494). At a median follow-up for surviving patients of 28 months (95% confidence interval 21.06–34.94 months), estimated progression-free survival for all patients was 8 months (95% confidence interval 7.1–8.9) and for EGFR mutant positive patients was 9 months (95% confidence interval 5.1–12.9); P = 0.84. Overall survival of EGFR mutation negative patients was 14 months (95% confidence interval 11.7–16.2) versus 9 months (95% confidence interval 5.08–12.92) for EGFR mutant positive patients; P = 0.11. **Conclusions:** Four per cent of our SCLC patients are EGFR mutation positive. This will help to plan informed personalised targeted therapy in these patients.

Incidentally Detected Superior Mediastinal Thymoma: An Interesting Case Report".

Virender Suhag

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We will be discussing an interesting case of thymoma which was detected on imaging for routine health check-up and was managed successfully by surgery and adjuvant radiotherapy. However, there is no section/topic category on mediastinal/thoracic tumors in the conference website. Please let me know if I can submit the abstract.

An Extremely Rare Case of Small Cell Undifferentiated Carcinoma of Submandibular Salivary Gland

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Introduction: We report on an extremely rare and interesting case of Small Cell Undifferentiated Carcinoma of submandibular salivary gland. To the best of our knowledge, only two such cases have been reported in world literature till date and our case may be the very first in India. These tumours constitute 1-2 % of all salivary gland tumours. Small Cell Undifferentiated Carcinomas are most frequently found in parotid glands and less commonly in submandibular and sublingual glands.Age distribution is fourth to sixth decade of life with a male predilection. Clinically it manifests as a fast growing mass with or without concomitant cervical lymphadenopathy. **Objectives**: The aim of presenting this case is to highlight an extremely rare case of Small Cell Undifferentiated Carcinoma of submandibular salivary gland as it was a diagnostic and therapeutic challenge for us due to its rarity and scarcity of relevant literature. We also feel duty bound to add to the existing scant case reports, our findings to help in very small way in formulation of guidelines for treatment of such cases in future. **Materials and Methods**: This is a prospective study of a case of Small Cell Undifferentiated Carcinoma of submandibular salivary gland. A thorough literature search was done and comparisons of all aspects of the disease in our patients was made, including the clinical presentation, evaluation, overall course, multimodality treatment given and the response to treatment. **Result**: A 29 years old male presented with 5x4 cm right neck swelling levels IB, II. Imaging showed right submandibular gland swelling and bilateral neck nodes. Bone scan and WBFDG-PET showed localized disease. FNAC submandibular gland showed Monomorphic Adenoma. Patient underwent excision of lesion and MRND. Post-operative histopathology revealed Small Cell Undifferentiated Carcinoma with CD 56 and S100 positivity on immunohistochemistry. He has been treated with adjuvant radiotherapy to face and neck and has shown significant response to therapy. **Conclusion**: Primary salivary gland small cell neoplasms are extremely rare and aggressive malignancy. These tumors have a tendency towards recurrence and increased likelihood of local and distant metastasis with an overall survival rate of 40-50%. However timely diagnosis and aggressive treatment may improve locoregional control and survival.

Keywords: Small Cell Undifferentiated Carcinoma, submandibular salivary gland, major salivary glands

Efficacy and toxicity profile of continuation maintenance pemetrexed in patients with PS 0-2 with stage IV adenocarcinoma lung in Indian population.

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Introduction: Lung cancer has been the most common cancer in the world for several decades. Pemetrexed is recommended as an option for the maintenance treatment in metastatic adenocarcinoma lung, if disease has not progressed immediately following platinum-based chemotherapy. **Objectives:** To study efficacy and toxicity profile of pemetrexed as a maintenance chemotherapeutic agent in patients with stage IV adenocarcinoma lung, not progressing after first line chemotherapy **Material and Methods:** This was an observational, prospective. We enrolled patients with stage IV adenocarcinoma lung who has not progressed on first line chemotherapy, from September 2013 to August 2014 at department of Medical Oncology at Rajiv Gandhi cancer Institute (RGCI), a tertiary care cancer institute in North India. In all, 108 patients with stage IV adenocarcinoma lung were started on induction pemetrexed/platinum chemotherapy. After 6 cycles, 60 patients with no disease progression & ECOG PS 0-2 were started on Pemetrexed maintenance. Best overall response (BOR) and progression free survival (PFS) and toxicity profile were recorded. **Results:** Median PFS (in days) for all the patients was 171.50 days. Median PFS for patients with PS 0, 1 was 176.5 days & for PS 2 was 136.5 days. Median PFS for patients with stable disease as BOR was 134 days &

for patients with partial & complete response as BOR was 267.5 days. 14 patients had grade III/IV adverse events with anemia being the most common in 3/60 patients (5%). **Conclusions:** Pemetrexed continuation maintenance chemotherapy is active and well tolerated. Pemetrexed maintenance should be considered in PS 0 to PS 2 patients with advanced adenocarcinoma lung patients who has not progressed on completion of induction chemotherapy.

Leucocytosis in a known case of adenocarcinoma Lung

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A 56 year old male presented with shortness of breath and generalized body ache for 2-3 months. CECT showed right lower lobe collapse with right pleura effusion. The haematological profile was normal. The video assisted thracoscopic biopsy from lung revealed adenocarcinoma. The patient was started on palliative chemotherapy. After receiving two cycles, a rising total leucocyte count was noted ranging from 27,000 to 28000. The sepsis work up was negative. Complete blood counts showed Hb of 9.1gm %, total leucocyte count 2.73x10 ^{9}/L and platelets 208x10 ^{9}/L. Differential count revealed 64 polymprphs, 23 lymphocytes, 08 monocytes, 02 eosinophils, 02 myelocytes and 01metamyelocyte. 03 nRBC per 100 WBC were also noted. Bone marrow aspirate and imprint smears showed tumor cells arranged in clusters and occasional gland formation. The trephine biopsy also showed infiltration by the tumor cells. Small areas of preserved marrow spaces were identified.Same chemotherapy was continued and leucocytosis responded to it. **Discussion:** Leucocytosis is one of the manifestations of the paraneoplastic syndrome seen in approximately 1.4 to 14.5% patients of lung cancer.Differential diagnosis for leucocytosis in lung cancer patients include infection, tumor necrosis, corticosteroid therapy and production of the growth factors (G-CSF, GM-CSF) by the tumor cells. **Conclusions:** Leucocytosis, as a paraneoplastic syndrome in lung cancer, is often unsuspected. It may also develop during the course of treatment. Once infection has been excluded, this entity should be kept in mind.Continuation of chemotherapy is usually the best treatment.

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Title: RELEVENCE OF LATERALITY IN LUNG CANCER: RESULTS FROMA TERTIARY CANCER CARE CENTER

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Background: Lung cancer is one of the commonest cancers and cause of cancer related deaths all over the world. It accounts for 13 per cent of all new cancer cases and 19 per cent of cancer related deaths worldwide. In India, lung cancer constitutes 6.9 per cent of all new cancer cases and 9.3 per cent of all cancer related deaths in both sexes; it is the commonest cancer and cause of cancer related mortality in men.The time trends of lung cancer show a significant rise in Delhi, India. The present study was conducted to access the relevance of laterality of lung cancer in tertiary cancer care centre. **Methods:** In this study, 7785 cancer patients who were registered in the year 2012 at Rajiv Gandhi Cancer Institute and Research Centre, Delhi were included in the analysis.Demographic, diagnostic, clinical details of the patients was extracted from the hospital medical records and analyzed. **Results:** A total of 7785 cancer cases were registered of which 628 were lung cancer cases, contributing to 8.06% of all the malignancies of which, 485 (77.2%) cases were males.Overall,majority of the lung cancers were reported after 40 years of age out of which right lung constituted of 47.4% cases, left lung 30.1% cases followed by bilateral 4.5.1%, 17.8% cases with unknown laterality. The most common metastatic site was bone withright lung constituting24.4% cases, left lung 22.8% cases and bilateral involvement 20.6%.Positive metastatic lymph node reported with 60.4%, 53.3% and 58.6% in right, left and bilateral cases respectively. Cancer incidence differed significantly by laterality at site studied; out of all lung cancers registered right lung contributes 47.4%, left lung 29.9, 4.6% were bilaterally involved and 17.9% cases were not specified in terms of laterality. Howeverbilateral lung cancers were found to have greatertendency to metastasize with 68.9% cases followed by 55.0% right lung cases and 50.5% left lung. Also, 75.8% cases of bilateral lung cancer reported at stage IV of the disease. **Conclusions:** Cancer incidence differed significantly by laterality; right lung is the more common lateral site. Bilateral lung cancers are more aggressive and usuallymetastasize hence should be treated with more stringent treatment protocols.

Clinical profile and treatment outcomes of patients with malignant thymoma in a tertiary care centre

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Background: Malignant thymomas are rare tumours with an incidence of about 0.15 case per 100000 population. But they are the most common tumours diagnosed in the anterior mediastinum. They can present with various systemic and autoimmune diseases. The tumour is both chemosensitive and radiosensitive. Surgery is the mainstay of treatment. Chemotherapy has a role in neoadjuvant, adjuvant and palliative settings. **Materials and methods:** A retrospective review of 16 case files of patients of thymoma diagnosed and treated at Kidwai memorial institute of oncology from January 2006 to December 2011. Details of patients, noted down were demographic data- age, gender, presenting symptoms and the duration, WHO and Masaoka stages, therapeutic factors and survival for 3 years after treatment. **Results:** Median age in the patients of malignant thymoma was 40 years. Of the 16 patients, 10(62.5%) patients were males and 6(37.5%) were females. The most common presenting symptom was breathlessness followed by non productive cough. 9 patients (56.25%) had superior vena caval obstruction at presentation. Median duration of symptoms was 3.5 months. 4(25%) patients had ocular symptomsand exertional fatigue and were later found to have myasthaenia gravis. Other systemic conditions found on further investigations were autoimmune cytopenia in 2 patients, thyroiditis and nephrotic syndrome in 1 patient and rheumatoid arthritis in another patient. Majority of the patients-8(50%) had locally advanced inoperable tumours at presentation. Masaoka Stage of tumour at presentation was stage I in 1(6.25%), II in 4(25%), III in 8(50%) and IV in 3(18.75%) of patients. WHO histological subtypes were Type A in 2(12.5%), AB in 5(31.25%), B1 in 2(12.5%), B2 in 3(18.75%) and B3 in 4(25%) patients. Among 4 patients of myasthenia gravis, 3 had stage II and 1 had stage III disease and WHO subtypes were AB in 2, B1 in 1 and B2 in 1 of the patients. 12 patients received neoadjuvant chemotherapy in stages II, III and IVa inoperable diseases with 3 to 6 cycles of chemotherapy with cyclophosphamide, doxorubicin and cisplatin. Among them, 5 patients (41.6%) had resectable disease after chemotherapy. Another 2 patients received chemotherapy in adjuvant and palliative settings. Only 2 patients had diseases resectable at presentation. Survival rates at 3 years were found to be 100%, 75%, 37.5% and 0% in Stage I,II,III and IV diseases. Thus, the survival rate at 3 years was found to be 43.75%. **Conclusion:** Malignant thymoma is a rare and slowly growing disease presenting as a mediastinal mass. It is both chemo and radiosensitive. It has a good survival with multimodality treatment. Patients can present as cough or neurological symptoms only and thus need high index of suspicion.

Anaemia among newly diagnosed cancer patients in India: A pilot study

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Background: Anaemia associated with cancer is a major public health issue. The gravity of this problem is likely to be higher in India due to already existing malnutrition in the general population. This study was undertaken to evaluate anaemia among newly diagnosed cancer patients at a cancer research institute in India. **Materials and Methods:** 62 consecutive patients of anaemia were identified out of 119 cancer patients (solid tumours) registered over a study period of 4 months. Iron parameters and clinical status were evaluated. **Results:** Anaemia was identified in 52.10% of the newly registered cancer patients. Iron deficiency (ID) was demonstrated in 59.61% of the anaemia patients. Severity of anaemia correlated with poor performance status (PS) ($p=0.002$). Most of the patients presented to us in stage IV disease which was statistically significant (Coefficient of correlation = 0.86, $p<0.00001$). Mild, moderate and severe anaemia was seen in 27(51.9%), 18(34.61%) and 7(13.46%) patients, respectively. Poor PS (ECOG 2-4) was seen in 24 (46.15%) patients while 28 (53.84%) patients had good PS 12 patients in the poor PS group had moderate to severe anaemia (50%) while in the good PS group, 13 patients had moderate anaemia (46.42%). Interestingly, all 7 patients with severe anaemia had poor PS and the result was statistically significant ($p = 0.002$). ID was identified in 31(59.61%) patients. None of our patient had absolute iron deficiency (ACD). Functional iron deficiency was seen in all patients. 21(40.38%) patients had TIBC low or within normal limits with raised serum ferritin, suggestive of ACD. **Conclusion:** Prevalence of anaemia in Indian cancer patients is high. ID is seen in a large proportion of patients. Large sample studies are required to better define the exact prevalence of ID, chemotherapy induced anaemia and anaemia in cancer subtypes.

Two Rarecases Of Intraoral Extramedullary Plasmacytoma

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Extramedullaryplasmacytoma occurs rarely (<1% of cases of multiple myeloma) and preferentially at level of head and neck,upper airways including nose-pharynx,tonsils,andparanasal sinuses and rarely in the oral cavity.Herein we report two cases of multiple myeloma who during their disease course presented as intraoral extramedullaryplasmacytoma.First case 45 years old male presented with bilateral buccal masses and FNAC of same was suggestive of plasmacytoma.Patient was started on palliative radiotherapy to buccal masses but during the course of radiotherapy he developed brain metastases and succumbed to his progressivedisease.Second case 54 years old male presented with intraoral mass over hard palate, biopsy of which was suggestive of plasmacytoma.He received palliative radiotherapy to intra oral mass to a dose of 30 Gy/10 # and thereafter patient is on follow up.

A Rare Case of Lymphangiomatosis

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We report on a rare case of lymphangiomatosis in a 3 year old child who presented as a diagnostic and therapeutic challenge.The child presented with chief complaints of progressive dyspnoea, abdominal distension and swelling of right hip joint.Imaging including chest roentgenogram,CT scan chest and abdomen and MRI Rt. thigh suggested multiple osteolytic lesions in rt. pelvis and femur,fluid in rt. side of peritoneum and massive right sided pleural effusion.HPR from hip lesion suggested LYMPHANGIOMATOSIS. As the child was progressively symptomatic breathlessness and abdominal distension he was treated with radiotherapy to a dose of 18 Gy/12# to rt. side of chest to which he responded symptomatically and on imaging also.

Segmentation of soft tissue structure in a CT slice corresponding to Liver. (Poster only)

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Background: CT has lower sensitivity in detecting liver lesion because of low contrast as compared to MRI. When digital contrast enhancement technique (DCET) is applied, overall contrast of the image is improved but the desirable contrast enhancement required in the soft tissues structure is not achieved. The aim of this study was to segment those soft tissue structures so that resulting image can be better improved using DCET. **Material and Methods**: Sixty four PET/CT scans of the HCC patients performed on Siemens Biograh mCT with 120 KVp with CareDose ON were included in this study. One CT slice corresponding to liver from each of 64 PET/CT scan were exported in JPEG format. A Matlab script was written that reads these images, converts the rgb data into gray scale, displays the histogram, and takes input from the user in the form of two threshold values, namely T1(lower threshold) and T2 (upper threshold), to produce segmented the image whose gray scale is between T1 and T2. The histogram was analyzed to determine T1 and T2, and were given as input and also recorded. The segmentation of image was based on the thresholding technique. **Result**: The mean value of T1 was 105 and it ranged from 75 to 135. The mean value of T2 was 153, ranging from 130 to 190. It was found that T1 as 75 and T2 as 190 segmented soft tissue structures from all the sixty four images successfully. **Conclusion**: The soft tissue structures in the CT slice corresponding to liver can be segmented by using the thresholding technique with parameters T1at 75 and T2 at 190.

A comparative study of hemodynamic responses to endotracheal extubation with priortreatment of lidocaine, verapamil and their combination.

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Objective: To evaluate the efficacy of intravenous (IV)Lidocaine, Verapamil and their combination for attenuating the hemodynamic responses to endotracheal extubationcomparativelyin the form of randomized, double blind interventional type of hospital based controlled study. **Method:** We evaluated 200 Patients (age 20-50 years) and divided into four groups of 50 cases each undergoing elective surgery of the duration 1-2hrs with American Society of Anesthesiologistgrade I and II. These groups are: Group A = 0.1 mg/kg Verapamilgroup,Group B = 1 mg/kg Lidocaine group, Group C = 0.1 mg/kg Verapamil plus 1 mg/kg Lidocainegroup and Group D = normal saline On completion of surgery, anesthetic agents were discontinued, muscle recovery was assessed with peripheral nerve stimulator and residual muscle relaxation was reversed. Three minutes later, the study drug was given intravenously (IV). The trachea was then extubated 2 min after administration of the study drugs. SAP(systolic arterial pressure), DAP(diastolic arterial pressure) and HR(heart rate)were measured at the end of surgery, at the time of study drug medications, at the time of tracheal extubation, until 20 mins after extubation were noted and compared among the four groups. **Result:** In our study hemodynamic responses were blunted to tracheal extubation by IV Verapamilalone and Verapamil+Lidocainecombination {SBP, DBP, MAP or HR ($p>0.05$)}. However, there is no significant difference in between these two. But , in the Lidocaineonly group , there were significant increase in DBP and SBP($P<0.05$) and HR($P<0.05$) at the time of tracheal extubation from the baseline values, and all hemodynamic parameters

were also found significantly raised in Lidocainegroup in comparison to Verapamil+Lidocainegroup.

Utility of Non-Invasive Emoglobin Measurement in Oncosurgery Patients.

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Introduction: Major Oncosurgeries involvemassive blood loss demanding frequent blood sampling to assess decreased haemoglobin caused by blood loss and need for replacement . Continuous non invasive method for hemoglobin monitoring (SpHb)using Radical-7®; Masimo Corp. , can prove a good resource during intraoperative management of oncosurgeries , guiding about blood transfusions. The device provides continuous Hb% ,we studied the utility of Radical-7®; Masimo Corp., in intraoperative management of oncosurgeries involving massive blood loss. **Method**: Fifty adult patients undergoing oncosurgery with anticipated blood loss more than 20%of blood volume were selected. Continuous noninvasive hemoglobin monitoring (SpHb) was doneintra-operatively with simultaneous laboratory hemoglobin (LabHb). Paired measurements of SpHbandLabHb were compared using Bland–Altman plot analysis. Blood transfusions were done on the basisofSpHb values. Accuracy to decide the intraoperative blood transfusions were analyzed using error grids analysis. **Result**: We studied 137 paired measurements of laboratory hemoglobin and noninvasive hemoglobin in 50 patients. Correlation of 72.7% ($p<0.001$) was found between LabHb and SpHb (Figure 1). In Bland Altman analysis the mean bias was -0.38g/dl with 95% of values within the limits of agreement of -2.92 to 2.16 g/dl. Error grid analysis on blood transfusion decision showed 95% of values in Zone A (least error). **Conclusion** : The Radical-7® has advantage of providing noninvasive hemoglobin value continuously to take early decision regarding blood transfusion thus avoiding unnecessary blood transfusionand related complications.

Key words – Noninvasive haemoglobin monitoring (SpHb)

Is there atie between risk factors cold environment and high cholesterol for cancer?

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Introduction: After cardiovascular diseases, cancer is the second-leading cause of morbidity and mortality of patients. Many extrinsic and intrinsic factors might increase the risk of cancer incidence and/or death. For example, some factors such as smoking, high fat diet, environmental toxin exposure, etc., have been connected positively with tumorigenesis. This is assumed to be by promoting oncogenic signals and/or altering epigenetic changes of cancer cells. This could be by either directly influencing the tumor cells or by favoring the tissue microenvironment. This study was planned to find out the potential risk factor(s) linked with cancer incidence and/or death.

Methods: Average annualtemperature (AAT), cancer mortality rate (CMR), cancer incidence rate (CIR), meat-, alcohol-consumption, gross domestic product, body weight, physical inactivity, smoking, obesity,CO_2 emission and serum total cholesterol of a country were collected.Statistical softwarewas used for data analysis. MTT and cell count assays were performed to see the effect of cold exposure on cancer cell proliferation. **Results:** Statistical analysis found that the AAT of a country may have a most potential contribution in regulating CMR, when compared to other factors such as alcohol and meat consumption. CMR is low in those countries situated near to the Torrid Zone, but it is high for those countries situated away from this zone. This indicated that cold temperature may have a contribution in increasing the risk of cancer. Furthermore, statistical analysis found a positive relationship between serum total cholesterol (ATC) and overall CMR. A similar correlation was found between ATC and different anatomical site-specific CMRs, including lung, bladder, ovarian, breast, and pancreatic cancers. Our analysis further found a negative association between AAT and ATC, similar to that of AAT and CMR. It was also observed that the result patterns of univariate analysis between AAT and CMR are very much similar with AAT and ATC. Moreover, geographic location of the top 50 countries having the highest CMR is very similar to top 50 countries having the highest ATC. Similarly, the least 50 countries having the lowest CMR are located in the same geographic region, similar to least 50 countries having the lowest ATC. Moreover, multiple linear model depicts that the behavior of CMR in presence of other these two regreesors (AAT and ATC) can be observed easily. **Conclusion:** This study, for the first time, documents that a relationship exists among AAT and CMR for overall, as well as, many specific cancers such as lung, bladder, ovarian, breast, etc. This epidemiological studynot only proposes that cold-induced brown fat activation could be an inducer of cholesterol, for increasing risk of tumorigenesis, but also unravels a novel area for cancer research. Cell culture based studies indicate that cold exposure might augment cancer growth.

Versatility of Rectus Abdominis Myocutaneous Flap in Primary Reconstruction of Defectsin Surgical Oncology

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Introduction: The vertical rectus abdominismyocutaneous(VRAM) flap is arguably the most versatile flap used in reconstructive surgery. It can be utilized in covering a wide range of defects from the head and neck, breast, chest wall to the groin and perineal region. Overtime it has come to be known as the 'work horse of reconstructive plastic surgery'. Reliable blood supply, ability to harvest a large bulk and a good cosmetic outcome make it a favoured option by most plastic surgeons. **Objectives:** To demonstrate the utility of VRAM flap in primary reconstruction of defects by measuring incidence of flap necrosis as a primary outcome andincidence of hematoma, seroma, incisional hernia, flap edema, wound dehiscence and infection as secondary outcomes. **Material and Methods:** A combined retrospective and prospective, single institution study was conducted from 2010 to 2015. Forty five patients undergoing primary reconstruction using the pedicled as well as free VRAM flaps were included. Defects ranging from breast (35), head and neck (8), groin (4), perineum (2)and chest wall (1)were included in the study. Twenty four subjects underwent either neoadjuvant chemotherapy or radiation or both. The primary outcome measured was incidence ofcomplete and partial flap necrosis while incidence of hematoma, seroma, incisional hernia, flap edema, wound dehiscence and infection were secondary outcomes measured. The patients were followed up for a minimum period of one year. **Results:** The incidence of complete flap necrosis was 4.4% while partial necrosis was 11.1%. Incidence of minor complications such as seroma was 8.2%, hematoma 4.4%, wound dehiscence 6.6%, flap edema 11.1%, infection in 12.7%. Incisional hernia was not seen in any patient after mean follow up of one year. **Conclusions:** This study demonstrates the versatility and reliability of the VRAM flap in primary reconstruction of surgical defects in surgical oncology. It can be harvested easily by surgeons with limited experience using cheap and readily available instruments, provides a large volume as well as contour that can be customized to the defect, making it an ideal flap.

Histopathological Examination of Placenta in Cases of Reproductive Failure

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The placenta is the organ that facilitates nutrition and gas exchange between the maternal and fetal compartments. The study was conducted in Dept. of Pathology in Mahatma Gandhi Mission's Medical College &Hospital, Navi Mumbai over a period of two and half years between May 2011-October 2013with the goal to investigate the association between placental pathology and IUFD.Routine histopathological examination was done with Haematoxylin and Eosin staining.Of the various pregnancy induced maternal risk factors encountered, the commonest risk factor was PIH (42%) followed by fever(32%) and DM(8%) with maximum cases of IUFD(42%) in primigravida (42%). We found almost same percentage of Oligohydramnios(6%) and Polyhydramnios(7%) followed by APH(5%). Our study revealed that the mean placental weight was slightly on the lower side in hypertensive patients than in non hypertensive patients. In comparison mean placental weight was found to be almost similar in diabetic and non diabetic patients. The commonest lesion encountered on microscopic examination was acute chorioamnionitis (38%) followed by IVH (11%) and infarction(10%), chorangiosis(7%) and retroplacentalhemorrhage(6%).

Profile of Cancer Patients at a Tertiary Cancer Center

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Background: Among various diseases, cancer has become a big threat to human beings globally. As per Indian population census data, the rate of mortality due to cancer in India was high and alarming with about 806000 existing cases by the end of the last century.The present study was conducted with an aim to determine the pattern of incidence, stage, morphology,age and gender distribution&histopathological types of cancers treated at Rajiv Gandhi Cancer Institute & Research Centre (RGCI&RC). **Methods:** Over a period of one year (2012), all the patientsregistered at Rajiv Gandhi Cancer Institute & Research Centre, Delhi were included in the analysis. The demographic, diagnostic, clinical and treatment details of the patients were extracted from the hospital medical records. **Results:** A total of 7785cancer cases were registered,of which 4081 (52.4%) took treatment and rest(47.6%) came for second opinion.Among the patients who took the treatment, 2203 (54%) were males and 1878 (46%) were females. A total of 2449(60%) patients were in the age group of 31-60 years. Also, 712 (17.4%), 1059 (25.9%) and 249 (6.1%)patients were treated by surgery, chemotherapy and radiotherapy alone, respectively while 2061 (50.6%) patients receivedmultimodality treatment. Among females, breast was the leading site of cancerwith 597(31.7%) cases followed by ovary171(9.1%) cases, cervix 156(8.3%), head &neck 149 (7.9 %) and gallbladder105 (5.5%) cases. Among female breast cancer patients,the commonest morphology was invasive ductal carcinoma in 537 (89.9%) cases. Also, 313 (52.4%) cases were early breast cancer, 176 (29.4%) cases were locally advanced and 108(18%) cases were metastatic.Among males, Head & Neck was the leading site of cancer with 573(26%) cases, followed by lung 268(12.1%), leukemias 211(9.5%), prostate 176(7.95%) and 113 colorectal (5.1%) cases.Among head & neck cancer patients oral cavity was the commonest site of primary lesion (51.5%) including lip, followed by pharynx and larynx with 37.2% and thyroid with 9.3% cases.Squamous cell carcinoma was reported in 517 (90.2%) cases. Also, moderately differentiated tumor grade was most commonly observed in 304 (53%) cases while 330 (57.5%) cases had stage IV disease at the time of diagnosis. **Conclusion:** Findings from the study indicates that majority of the patients are reported in the middle age group. Breast is the leading site amongst women and is reported in early stage while head & neck cancer is the leading site amongst males which is most commonly reported in advanced stages of the disease. The only way to fight this bane under such circumstances is to have realistic programmes and policies based on currently available scientific information and sound public health principles.

Evaluation of Possum Score in Predicting Morbidity and Mortality Following Major Oncosurgical Procedures.

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Background: Comparison of operative morbidity rates after major oncosurgical procedures between units may be misleading because it does not take into account the physiological variable of the condition of the patients. The aim of the present study was to evaluate the Physiological and Operative Severity Score for the enUmeration of Mortality and Morbidity (POSSUM) scoring system in patients undergoing major oncosurgical procedures at GCRI, Ahmedabad, Gujarat. **Methods:** Between January 2012 and June 2012, 300 patients underwent a major oncosurgical procedures. Final physiological and operative score calculated from POSSUM data sheet. The predicted morbidity and mortality calculated by POSSUM equation. After surgery paients observed morbidiy and mortality were noted for one month and compared with the predicted outcomes. **Results:** Pulmonary complications under the GIT group and wound dehiscence under GUT group was the most common cause of morbidity(10% each) in this study 6% mortality and 29..33% morbidity was observed. POSUM scoring system coud no accurately predict overall mortality (AUC=0.586) and morbidity (AUC=0.636) in our setup. AUC for both the equations were lower than acceptable AUC=0.7. Calibration of POSSUM morbidity equation was satisfactory (χ^2=8.431, p=0.392) while there was lack of fit of POSSUM mortality equation (χ^2=14.869, p=0.062).**Conclusions:** Overall, there is a lack of calibration of POSSUM among patients who undergo major oncosurgical procedures. Modification of the POSSUM mortality and morbidity scores by logistic regression analysis in larger pt setup is required to accurately predict the risk.

Surgical site infection after oncosurgery – Risk factors, Prevention and Management

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Background: Surgical site infection [SSI] is one of the most common complications resulting in significant morbidity and prolonged hospital stay. There is paucity of Indian data on the subject. The aim of the present study was to determine the prevalence of SSI at a tertiary cancer care hospital in North Karnataka. Secondary objectives were to identify the risk factors and to define the measuresto control SSI. **Material and Methods:** This is a retrospective review of a prospectively maintained database at Kerudi Cancer Hospital and Research Centre, Bagalkot, Karnataka. All patients undergoing surgical treatment for cancer were included in the study. Two hundred consecutive patients met the inclusion criteria. Perioperative antibiotic prophylaxis was according to the standard guidelines. SSI was graded according to Southampton grading system. **Results and discussion:** Head neck malignancies were the most common sub site followed by breast cancer. 20% patients developed SSI in the study period. Grade ¾ infection developed in 5 % patients whereas in the rest it was grade ½ SSI. Diabetic status as well as gastrointestinal surgeries were significantly associated with the risk of surgical site infection. SSI lead to significant prolongation of the hospital stay with delay in starting adjuvant therapy. **Conclusion:** Surgical site infection is a preventable complication of surgical oncology. Preoperative optimization of blood sugars and nutritional status plays a key role in preventing SSI.

Novel Mitochondria Targeted Photocytotoxic Cobalt(III) Complexes of Curcumin and Phenanthroline Bases for Application in the Photodynamic Therapy of Cancer

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Photodynamic Therapy (PDT) is an emerging modality for the treatment of cancer. There is currently a strong interest to develop metal-curcumin based photochemotherapeutic agents for such applications. We have synthesized and characterized a novel series of photocytotoxic cobalt(III) complexes of formulation $[Co(B)_2(L)](ClO_4)2$ (1–6), where B is a N,N-donor phenanthroline base, viz., 1,10-phenanthroline (phen; 1, 2), dipyrido[3,2-d:2',3'-f]quinoxaline (dpq; 3, 4), and dipyrido[3,2-a:2',3'-c]phenazine (dppz; 5, 6), L is acetylacetonate (acac; 1, 3, 5) or curcumin (bis(4-hydroxy-3-methoxyphenyl)-1,6-diene-3,5-dione, cur; 2, 4, 6). The crystal structures of 1 (as PF6- salt) and 3 show distorted octahedral geometries formed by the CoN4O2 core. Complexes 1, 3 and 5 having the acac ligand are prepared as control species. Complexes 2, 4, and 6 show remarkable visible-light induced cytotoxicity in HeLa cells giving respective IC50 values of 7.4 μM, 5.1 μM and 1.2 μM while being much less toxic in dark. Interestingly, complex 6 is significantly less photocytotoxic to MCF-10A normal cells when compared with the HeLa cells. The control complexes 1, 3, and 5 were inactive both in the light and dark. Fluorescence imaging experiments on HeLa cells reveal that complex **6** accumulates inside the mitochondria. The cell death is apoptotic in nature and is photo-induced by the ROS. Binding experiment shows that the complexes bind HSA with good affinity. Thus, complex **6** holds significant photochemotherapeutic potential.

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An Analysis of occurence of synchronous multiple primary malignant neoplasms : A Rare phenomena

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Introduction: Multiple primary malignant neoplasms is the term to malignancies arising from two different organs with different histology and having no relation which each other. Incidences of such cases have been reported to around. Two primary cancers occurring simultaneously in same patient are quite rare compared to Metachronousoccurrence of cancers. **Methods:** Prospective data collection of newly diagnosed double primary cases and retrospective data was gathered of patient being diagnosed with de novo second cancer between 2014-2015 . Warren and Gates criteria was used as a inclusion criteria. Synchronous cancer was defined as occurring either simultaneously or within 6 months of primary malignancy. Details such age sex site histopathology and treatment have recorded. **Results:** Of the eight synchronous malignancy that were recorded 6 were females and 2 males. The most primary presenting neoplasm was of breast with 3 patient having ductal carcinoma as presenting cancer. Out of synchronous breast also formed the primary as well as second cancer making it most frequent occurrence. Gall bladder adenocarcinoma was the next in frequency as 4 patients had such cancer as its primary or second malignancy. Cervix , Ovary , brain tumours and soft tissue sarcomas were the other malignancies to occur with . Most common association was found to be with breast primary occurring with gall bladder adenocarcinoma as the second malignancy. **Conclusion:** With increasing life expectancy and improvement in imaging and investigations there is a rise of reporting of such cases. Unusual presentation of any cancer should raise a suspicion of such occurrence . Proper Clinical assesment is needed to ruleout recurrence or metastasis from such cases, to help the appropriate management of the malignancy. Management of primaries may be complicated with different stages of individual malignancies. More data may be required to determine proper management of such patients .

Key words : Multiple primary, synchronus ,second malignancy, metachronous

Cancer and Opportunistic Infections among the People living with AIDS on ART in Eastern Nepal

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Background: Opportunistic infections (OIs) are more frequent and severe because of immune-suppression in HIV-infected persons, and are the major clinical manifestation of HIV patients. Cancer is a significant cause of mortality and morbidity in people infected with HIV; in fact 30% to 40% will develop a malignancy during their lifetime. The objective of this study was to find out the prevalence of Opportunistic Infections (OI) and Cancer among the PLWA on ART in eastern of Nepal. **Materials and Methods:** Descriptive cross-sectional research design was used to carry out the study. The PLWA receiving ART residing in eastern Nepal constitute the population of the study. Using convenient sampling technique 75 subjects were selected for study during the period of 15th June 2014 to 30th July 2014 of six weeks. **Results:** Majority of the PLWA (52.65%) were of age group of 35-45 years, Male (62.7%) and Hindu (81.3%). Among the PLWA about 13% were illiterate; 18.7% were farmer, 13.3% house wife, 10.7% were driver and 9.7% were labour. Most of the respondents (60%) were from Sunsari District and 61.3% belongs to rural areas. The common OIs found were Pulmonary Tuberculosis (33.3%), extra Pulmonary TB (14.7%), Oral Thrush (30.7%), fungal infection (22.7%), Herpes Zoster (14.7%) and Hepatitis-C (18.7%); whereas regarding Cancer it was found that 22.7% had Lymphandopathy, 18.7% had Skin Cancer and 2.7% had Kaposi-Sarcoma. **Conclusions:** It can conclude that the Opportunistic Infections among PLWA were Tuberculosis, Oral Thrush,Fungal infection, Hepatitis-C, and Herpes Zoster; whereas, cancer of Lymphnode, skin cancer and Kaposi-Sarcoma was found among the PLWA receiving ART in eastern Nepal.

Key Words: Cancer, Opportunistic Infections, People living with AIDS

Towards a healthy billion: Medical data digitization for doctorsand patients

Viviktha Ramesh

The Healthy Billion

Methods: A data digitisation product – THB Clinytics – was launched, in which all medical data including patient history, diagnostic tests and prescriptions were uploaded and managed. Diagnostic tests were booked by the patient through THB Clinytics, with the option to choose from a variety of labs. Samples were collected at home. Reports were then uploaded online. Patient history and prescriptions were uploaded through THB Clinytics. Patient could view all his health information in his personalized portal and the doctor could view the information of individual patients as well as their entire practice on THB Clinytics. Patients and doctors were asked for their experience of using THB Clinytics. The uses of this data were studied. **Results:** Patient personalized portal was used to view test results in the form of trends lines, and to consolidate all reports and prescriptions without the hassle of manual records. Most patients found the portal extremely convenient and hassle free. The doctors were able to monitor trends in the health of their patients and detect early changes. Data could be easily extracted for analysis, research and publication. There is also scope to use this data to predict patient trends, and more importantly, personalize healthcare and make record keeping easier than ever before. **Conclusion:** Data digitization can help doctors make their practice easier, improving patient management and follow ups, and contributing towards medical research conveniently. For patients, it becomes a tool to track their health seamlessly. Life-long storage of records becomes easy. Data analysis and monetization of this data at an aggregate level enables the user fee levied to be minimized and makes the tool accessible to all.

Cholesterol or cholesterol regulators: A friend or foe

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Introduction: Cholesterol is a magic molecule, which in excess toxic to the body; but pivotal for synthesis of cell membrane. Recent studies have shown cholesterol not only found on cell membrane but also on chromosomes in cell nucleus.Several studies also reported low plasma cholesterol in cancer; still it is unclear whether it is a risk factor for cancer development or due to the cancer.Hence, understanding of cholesterol or cholesterol regulators is one of the paramount interests to explore in malignancy. **Objectives:** This study was carried out to find out the insight of cholesterol or cholesterol regulators in the cancer viz. chronic lymphocytic leukemia (CLL). **Material and Methods:** Seventy fivemale subjects in the age group of >50 years were volunteered in this cross sectional study. Enzyme based plasma lipid profile estimation, isolation of peripheral blood lymphocytes and lysate preparation, SDS-PAGE and Western Blotting, dil-LDL uptake and ultracentrifugation were the part of the methodology used in this study. **Results:** Our study has shown hypocholesterolemia in CLL. While plasma cholesterol level falls down ($p < 0.0005$); hyper-expressions of cholesterol regulators viz. LDL receptor ($p=0.0001$), SREBP-2 (transcription factor of LDLR) ($p=0.0001$) and PBR (nuclear cholesterol channel protein) ($p=0.016$) are observed in lymphocytes isolated from CLL subjects in association with significant increase of intracellular cholesterol in nuclear ($p=0.036$) and cytoplasmic ($p=0.004$) compartments. **Conclusions:** This study has thrown some light on the utilization of cholesterol by the nucleus of highly proliferated leukemic cells. More work is needed to fill up the gap: the mechanism responsible to stimulate cell division by cholesterol component of the nucleus.

Mathematical Model development in assessing complete tumor response

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Introduction: Computer modelling in radiotherapy plays critical role since automation of many physical events and seeking close results to actual results with different algorithms (statistical (Monte Carlo), table based and model based). Not only in radiotherapy it helps in many other related divisions. **Objectives:** There is no single platform like Aria, lantis (which are database) for assessing complete tumour response. My aim is to bring all related fields on one single platform where the final tumour response can be assessed. **Material and Methods:** Six hypotheses(representation and decisions) are laid down in order to get tumour response. Tumour response model is developed and it has reception sectors where any modality can act on that. Each receptor can be active or inactive. If it is active and it brings response to tumour. Some of the conditions like any environmental condition like hypoxia, stage of the disease etc. can retard response. Provision for assessment due to any replaced modality to improve response. Flow chart has been made to deal with. Body should be represented not only with HU values and also with a/b values, which provides complete response curves. **Results:** Model has the capacity to include the parameters related to various modalities simple enough to predict nearby value. **Conclusions:** Radiotherapy should be main model(mathematically assumed) and chemotherapy, hormone therapy and other allied therapy should have impact on that.

Oncogenic Osteomalacia associated with PhosphaturicMesenchymalTumor of Thigh – A Rare Presentation

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Introduction: Oncogenic Osteomalacia (OOM) is an uncommon metabolic and bone disease caused by Fbroblast Growth Factor 23 (FGF 23), a phosphaturic factor produced by phosphaturicmesenchymaltumors (mixed connective tissue variant) characterized by phosphate leakage from the kidneys and subsequent hypophosphatemia. **Objectives:** To discuss the diagnostic evaluation, differential diagnosis and treatment of Oncogenic Osteomalacia associated with Phosphaturic Mesenchymal Tumor. **Material and Methods:** This was a single patient case report. A 50 year old woman presented to our hospital with the complaint of being unable to walk since 5 years. She had been initially diagnosed with low Phosphorus level and treated with oral PO4 powder for 3 years. On examination she had the worst hypophosphatemia(1.3 mg/dl) with a normal calcium and elevated PTH(163pg/ml) plasma values. FDG PET-CT showed a low grade metabolically active soft tissue nodular lesion in proximal right thigh, just lateral to the femoral vessels in anteromedial aspect of infratrochanteric region which needs biopsy evaluation as it raises suspicion of oncogenic osteomalacia. Trucut biopsy suggested the histologic findings consistent with a Phosphaturicmesenchymaltumor, in conjuction with the imaging suspicious of oncogenic osteomalacia. MRI scans revealed a well defined lobulated heterogeneous enhancing mass lesion in the anterior aspect of the right thigh in the intermuscular plane. **Results:** The patient underwent wide excision of the lesion in the right thigh. **Conclusions:** After surgery, the patient had complete recovery.

Impact of field length on dose, noise and contrast in cone beam CT

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Introduction: Cone beam CT is playing very important role in positioning patient in radiotherapy giving assurance to the treatment delivered on target properly. Resolution of ct is assessed by MTF and contrast is depending on noise present in image. **Objectives:** Since imaging dose is to be justified for the treatment, in this paper how field length is affecting the dose and noise, contrast is analyzed. **Material and Methods:**The dose at the center of CIRS phantom is measured by using diode having volume 1 mm^2 x 2.5 μm on Varian OBI. The field size factor was deduced by changing field length from 7cm to 20 cm while keeping the width remains same. The other parameters like kV, mA, pulse width and filters, reconstruction technique remain same. **Results:** The linear relationship is found with field size inside the field and off the field the curve fit quadratically. The scatter to primary dose was deduced by measuring dose outside the field and extrapolated to inside the field. Then the change in scatter to primary with respect to field size is deduced. This can be fit into formula like (std^2 is proportional to $((resolution)^3/(thickness*Dose))$. Same way the impact on contrast and noise also studied using catphan phantom. Filters changed and again the study is repeated. **Conclusion:** It is found that imbedding the field size into the formula also important in dealing the quality since it alters the scatter to primary in turn it changes noise and contrast.

Smart segmentation validation on eclipse

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Introduction : Fully auto or semi smart segmentation helps delineating the targets automatically and efficiently which reduces the labor of doing manually. **Objectives:**To evaluate stability and efficiency of smart segmentation in eclipse planning system since segmentation is governed by lots of modeling. **Material and Methods:** Eclipse planning system has smart segmentation which provides automatic segmentation for the organs at risk. If the gradient persists then then segmentation can be done either with derivative or laplacian. If the interface does not have any kind of cleavage then models must be used to deal with. Five patients contours

are analyzed in order to check the stability and efficiency of contouring. These scores compared with eclipse contouring score. **Results:** Dice similarity coefficient, distance to agreement were used and the concepts of target coverage index and conformity index also introduced to see how best segmentation is merited. **Conclusion:** It is found it is possible to merit and the models can also be merited.

Pharmacogenetics-Cytochrome P 450 2D6 Polymorphisms Central role in Tamoxifen, Opioid metabolism and Antid epressant related drug interactions.

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Background: Genetic polymorphisms in Cytochrome P450 2D6 expressed in the liver ,Gastrointestinal tract and Brain lead to interindividual variation in the activity of this non inducible enzyme .Various phenotypes of this enzyme system include ultrarapid metabolizers (UMs), extensive metabolizers (EMs), intermediate metabolizers (IMs) and poor metabolizers (PMs). **Methods:** A literature search containing the following terms Tamoxifen or Opioids or Anti depressants and Cytochrome P 450 2d6 was performed on Pub Med and information from articles pertaining to the subject under discussion was identified ,scrutinized and included in this review. **Results:** CYP2D6 catalytic activity is highly important in tamoxifen-treated individuals, because this enzyme has a key role in the biotransformation of N-desmethyltamoxifen into endoxifen.Ultrarapid metabolizersof tamoxifen are more prone to adverse effects whereas poor metabolisers are liable to treatment failure.Genetic inactivation of CYP2D6 renders Codeine ineffective owing to lack of morphine formation, decreases the efficacy of tramadol owing to reduced formation of the active metabolite O-desmethyl-tramadol ,reduces the clearance of methadone and precipitates opioid toxicity in sub therapeutic dosages .Concomitant usage of Tamoxifen with SSRIs like Paroxetine and SNRIs like Venlafaxine whichinhibit CYP2D6, thus significantly loweringEndoxifenconcentrationsshould be discouraged. **Discussion:** Three recent trials have reported no clinical significance of the interaction between Tamoxifen and CYP 2D6 polymorphisms although the derivation of DNA from the tumor tissue and potential misclassification of CYP2D6 genotypes due to loss of heterozygosity (LOH) might have influenced the results.NCCN recommendations state that it is reasonable to avoid the use of potent CYP2D6inhibiting SSRIs in patients taking tamoxifen.Citalopram, fluvoxamine, and sertraline do not sharethis inhibitory property and do not cause CYP2D6specific interactions. **Conclusion:** Variation in activity of other drug-metabolizing enzymes, due to genetic polymorphisms or concomitant medications, involved in the metabolism of tamoxifen may affect the interindividual response to tamoxifen. The combination of a US FDA-approved test, such as the AmpliChip CYP450 Test, and an FDA definition of CYP2D6 as a 'valid biomarker' makes CYP2D6 genotyping a prime candidate to be the first successful pharmacogenetic test. However,NCCN Breast Cancer Panel does not recommend CYP2D6 testing as a tool to determine the optimal adjuvant endocrine strategy.Therapeutic drug monitoring (TDM) is likely to be the optimal strategy for individualization of tamoxifen treatment.

Performance Status Assessment In Patients Treated With Anti- Cancer Therapy

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Background: Principle of measuring the impact of treatment on a patient's well-being is the subjective evaluation. Treatment of cancer improves the performance statusThis measurement of performance statuswell accepted in healthcare research.The effects of performance status on cancer treatment have been studied a lot. However, few studies have reported on the association between successful anticancer treatment and improvement in performance status.we conducted a case control study to assess the impact of anticancer treatment on performance status. **Methods:** In our study group 100 patients with histopathologically proven malignancy were included. These were the patients which were treated with surgery followed by adjuvant chemotherapy/radiotherapy with curative intent. Control group was formed by 100 healthy volunteers of comparable age , sex & socioeconomic status and was constituted by the attendants of patients.The performance status was assessed before start of anticancer therapy and at 6 & 12 weeks after completion of the therapy in study group. Functional status was assessed by using Karnofsky performance scale (KPS). **Results:** KPS was evaluated as status of functional capabilities. There was improvement in KPS with anticancer treatment.Statistically highly significant improvement in performance status was noticed in study group and this improvement gradually increase over time ($p=0.01$). KPS as functionl status improved earlier as compared to weight gain over period of time. Improvement in functional capabilities were more per unit time. According to our experience cognition enhancement leads to improved appetite and weight gain. hemoglobin and serum Albumin level increased linearly along with KPS, but again KPS improved faster and earlier. **Conclusion:** Successful anticancer treatment does improve KPS and improvement in KPS is accompanied by improvement in nutritional indicators.

Key words: Performance status, KPS, Anticancer treatment:

Experience with patient advocacy for rare diseases: Need and Challenges in India

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Patient advocacy groups are organizations, generally non-profit, that focus on specific diseases or aspects of healthcare and cater to a small group of patients or disease. Patient advocate is a liaison between patients and healthcare providers (HCPs) with specific goals to aid care. In India, cancers still attract a lot of social stigma and fear and often need help, information and support outside of medical advice. Patient advocacy and support groups fill in this gap and have a major role to play in this arena. Creating a connect with patients while assuring privacy is undeinably critical to their role.Rare disease advocacy specially becomes challenging for non profit support groups in India due to lack of awareness among HCPs as well as patients, often inadequate interest and financial support from philanthropists as well as difficulty in finding and connecting withthe actual patient population. Reaching out to large illiterate rural and suburban public remains a challenge unique todevelpoing countriesand innovative approach with non conventional media and means isneeded. Besides, with heavily overburdened government healthcare delivery system, encouraging HCPs and healthcare policy makers to focus on rare diseases is indeed difficult. Sensitization of HCPs as well as patients and caregivers remains important, as well as information dissemination among general public which may help in early detection. The internet may also be utilized as a powerful partner in information dissemination and creating awareness amongst general public.

Outcomes of adult medulloblastoma treated with a multimodality approach: A tertiary cancer center experience

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Background: Adult medulloblastoma (≥18 years of age) (AMB) is a rare central nervous system tumor. We aimed to analyze the treatment outcomes of AMB treated with surgery followed by craniospinal irradiation

(CSI) and adjuvant chemotherapy(AdCT). **Material and Methods**: We retrospectively evaluated the treatment charts of 31 patients of AMB treated from 2003-2011. 45 patients were found to have AMB (total CNS-1487 cases), constituting 3.02% of all CNS cases. The patient demography, treatment details and survival data were collected in a predesigned proforma. KaplanMeier method was used to analyze disease free survival (DFS) and the impact of prognostic factors was determined by univariate analysis (log rank test). **Results:** Male: Female ratio was 21:10. Median age (years) 26 (range: 18-49). 10 patients aged more than 30 years. Cerebrospinal fluid dissemination was noted in 16% cases. The distribution as per chang's stage was M3 in 4 patients and M2 in one patient. Surgery was contemplated in all patients. The median time gap between surgery and initiation of RT was 30 days (range: 21–35 days). Medium pressure ventriculo peritoneal shunt was placed in all cases prior to surgery. 24 patients underwent a GTE and 7 patients underwent subtotal resection (STR). CSI (36 Gray at 1.8 Gray/fraction to entire neuraxis and 20 Gray at 2 Gray/fraction boost to posterior fossa) was used in all cases. 26 patients received AdCT (carboplatin plus etoposide). Remaining 5 patients received radiation alone. Median number of AdCT cycles was 6 (range - 3–6). Of note 20 patients received the planned 6 cycles of chemotherapy whereas 6 patients received <6 cycles. 10 (33%) patients developed grade III or higher hematological toxicity and 6 patients developed febrile neutropenia. 3 patients developed Grade IV hematological toxicity.Median follows up was 26.85 months (9.47-119.73 months). The estimated 3 and 5 years DFS was found to be 84.9% and 50.7% respectively. On univariate analysis, tumor located laterally had a trend towards better DFS (HR 3.04; 95%CI 0.722 to 12.812; $P = 0.07$) compared to midline tumors. Other factors likeadjuvant chemotherapy, age, gender, surgical extent had no statistically significant impact on survival.The most common site of failure was the posterior fossa (7 patients). Only one patient developed isolated spinal metastasis, and one had a local failure with CSF dissemination. One patient underwent re-excision and salvage chemotherapy was used in all cases. However, all but one patient progressed after salvage therapy. **Conclusions:** Maximal safe surgical resection remains the cornerstone of therapy for AMB. In our experience of 31 patients, adjuvant CSI, followed by chemotherapy is well tolerated with minimal morbidity and descent survival outcomes. Tumors with lateral location tend to have a better outcome than centrally located tumors.

Prognostic factors and survival outcomes of intracranial ependymoma treated with multimodality approach: A tertiary cancer centre experience

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Introduction: Intracranial ependymoma (ICE) is a rare central nervous system tumour accounting for <2% of all brain tumors. There is paucity of literature on management of ICE in Indian patients. **Objectives:**We aimed to analyze the treatment outcomes of ICE treated at our institute with multimodality treatment of surgery, radiotherapy and chemotherapy. **Material and Methods:** We retrospectively evaluated the treatment charts of 40 patients of ICE treated from 2005-2012. The patient demography, treatment details and survival data were collected in a predesigned proforma. All patients underwent a maximal safe resection. Patients also received adjuvant radiotherapy and chemotherapy. Kaplan Meier method was used to analyze disease free survival (DFS).Univariate analysis (log rank test) was used to assess the impact of age (</>20 years), extent of surgery, radiotherapy dose (56 Gray versus 60 Gray), grade of tumour (grade II versus III), MIB labelling index (</>20) and adjuvant chemotherapy on DFS. Multivariate analysis was done using Cox-proportional hazard model. $P < 0.05$ was taken as significant and SPSS version 21.0 was used for all statistical analysis. **Results:** Male: Female ratio was 29:11. Gross total resection: subtotal resection or less was 42.5%: 57.5%. 16 patients (40%) had anaplastic histology. All except two patients received adjuvant radiotherapy. Median radiotherapy dose delivered was 56 Gray (45-60 Gray). Cranio-spinal irradiation was delivered in 5 patients, rest received focal conformal radiotherapy. Median duration of radiotherapy treatment was 50 days (range 42-58 days). 4 patients received concurrent chemotherapy (temozolomide) and 10 patients received adjuvant chemotherapy (6 carboplatin plus etoposide; 4 temozolomide). Median follows up was 18 months (2-60 months). The estimated 1, 2 and 3 year DFS was found to be 55.1%, 41.3% and 31% respectively. At the last follow-up 24 patients were found disease free. On univariate analysis, patients receiving higher radiation dose (56 Gray versus 60 Gray; HR 0.33; 95% CI 0.117 to 0.928; p=0.02) and lower MIB labelling index (<20 versus ≥20; HR 0.279; 95% CI 0.0859 to 0.910; p=0.0188) had a better DFS [Figure 2-3]. Higher MIB labelling index continued to be a poor prognostic factor on multivariate analysis (p=0.0121). The commonest site of failure was tumour bed [12/16 patients]. 3 patients had elsewhere brain failures and 2 patients had spinal deposits (one had both tumour bed and spinal recurrence). **Conclusions:** Maximal safe resection followed by post-operative radiotherapy to a higher dose of 60 Gray (particularly for anaplastic ependymoma) should be used in ICE. Higher MIB labelling index confers poor prognosis. Role of chemotherapy remains controversial and radiation therapy should not be delayed even in young patients.

Extremely Rare and Unusual Cases of Intracranial Hemangiopericytoma

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Introduction: We report two extremely rare and unusual cases of Grade II and Grade III Intracranial Hemangiopericytomas which either in primary or recurrent setting have rarely been reported in Indian and world literature. HPC is an uncommon neoplasm arising from Zimmerman pericytes around capillaries and post capillary venules. Most HPCs are located in the musculoskeletal system and the skin. Central nervous system Hemangiopericytomas are extremely rare and aggressive accounting for less than 1 % of all intracranial tumors which recur locally or distantly in the neural axis or as distant extra-neural metastases. The local control, disease-free survival and overall survival rates are much greater when patients receive adjuvant radiotherapy. **Objectives**: The current prospective study was undertaken to evaluate two patients who presented with extremely rare and unusual cases of intracranial hemangiopericytomas and to define the clinicopathological findings, role of adjuvant radiotherapy in the management of this disease, the treatment tolerance and outcome with subsequent follow up. **Materials And Methods**: This prospective study was done through a thorough history and physical examination along with routine haematological and biochemical parameters for the initial evaluation of the two patients who presented to our institute during the natural course of their disease. Local evaluation in the form of MRI brain was done along with metastatic workup in the form of computed tomography of chest, abdomen and pelvis. Literature search was done and relevant information was incorporated from published case series and standard textbooks. **Result**: First case: A 28 year old male presented with complaints of headache and vomiting. MRI brain showed an ICSOL in left parieto-occipital region. Underwent craniotomy and excision. Histopathology (HPR) showed Hemangiopericytoma Gd II, Vimentin and CD 34 positive on immunohistochremistry (IHC). Second case: 31 years old male presented with history of headache. MRI brain showed an ICSOL in left frontal lobe. Bi-frontal craniotomy and excision was performed. HPR revealed Anaplastic Hemangiopericytoma Gd III, Vimentin positive and EMA negative on IHC. Both patients were treated with adjuvant radiotherapy to brain. Presently on regular follow up with no evidence of recurrence or metastases. **Conclusion**: Hemangiopericytomas have an indolent course but are notable for high rates of recurrence and metastasis many years after treatment. Studies have suggested that high mitotic rates and proliferative indices may portend malignant behaviour. Though surgery remains the initial management, conformal radiotherapy remains the mainstay of adjuvant treatment as it increases the overall survival and quality of life in patients.

Keywords: Hemangiopericytoma, intracranial, anaplastic, radiotherapy.

Retrospective analysis of outcome and toxicity associated with extended adjuvant temozolomide in patients newly diagnosed with Glioblastoma

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Introduction: High grade gliomas comprise 38% of primary brain tumors. Glioblastoma accounts for approximately 75% of all high grade gliomas. If untreated, patients with Glioblastoma usually survive upto 5 months only. Currently, standard treatment of Glioblastoma is Surgery, which is followed by radiotherapy given concurrently with temozolomide (TMZ) and then, 6 further cycles of adjuvant TMZ given monthly. With this, median survival has improved upto 14.6 months. Recently published data suggests that extended adjuvant TMZ in patients with stable or responsive disease has proved beneficial. However, data demonstrating the benefit is scarce. **Objectives:** To evaluate the outcome and toxicity in patients, newly diagnosed with Glioblastoma, and treated with extended (more than 6 cycles) adjuvant temozolomide after surgery and concomitant chemoradiotherapy. **Materials and Methods:** Records of 116 patients treated for Glioblastoma at our institution between November 2009 and September 2014 were analysed. 23 patients (~20%) were found to be meeting our eligibility criteria. Progression free survival (PFS) was calculated from day of surgery to the day of progression as noted on MRI and/or Re-Surgery. Overall Survival (OS) was calculated from the date of diagnosis to the date of last follow up/ death. Median survival data was calculated for the cohort, and compared with survival data published in landmark trial standardizing 6 months of adjuvant temozolomide. Patterns of recurrence were evaluated as the secondary end point of the study. **Results:** The patient-data was analyzed till October 2015. The patients received an average of 11 cycles of adjuvant temozolomide (Range 7-21 months). These patients progressed at a median of 15 months, and had a median overall survival around 20 months (vs 14.6 months). 12 month survival rate was 87% in the cohort. Only 2 (<1%) patients developed toxicity requiring discontinuation of treatment. On evaluation of patterns of recurrence, it was found that nearly 90% patients recurred within radiation field. **Conclusion:** Majority of patients (>50%) diagnosed with Glioblastoma progress within 6 months of initiation of treatment. Extended adjuvant temozolomide is associated with favourable outcome in terms of PFS and OS, and is reasonably well tolerated.

Outcomes of craniopharyngioma treated with multimodality approach : A 20 years experience from a tertiary cancer center

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Introduction: Craniopharyngioma is a benign intracranial tumor and treatment options include radical or limited surgical resection followed by Radiotherapy (RT). **Objectives:** To present the demographic profile, interventions and outcomes of patients with craniopharyngioma treated with limited surgery followed by conventional or conformal RT along with endocrine therapy from a tertiary care hospital in northern India. **Material and Methods:** Between March 1990 and Oct 2013, 67 patients with craniopharyngiomawere registered in the department of Radiotherapy. Medical records were retrieved for referral patterns, demography, surgical, RT and endocrinological therapy practices. Progression free survival (PFS) and overall survival (OS) were computed by Kaplan-Meier method. **Results:** 67 patients underwent limited surgery followed by conventional/conformal RT and endocrinal assessment and therapy. 37(55%) patients belonged to peadiatric age group (< 18 years) and median age at presentation was 17 years. 48(72%) patients were male. Presenting symptoms were headache, vomiting, diminution of vision, field defects, amenorrhea and polydipsia/polyuria with a median of 12 months. 93% were referred from the department of Neurosurgery after undergoing one in 44(65%), two in 19(28%) or more surgeries in 4(7%), consisting pterional/transcranial craniotomy in 57(85%) and trans-sphenoidal surgery in 10 (15%). 21(31%) had ventriculo-peritoneal shunt while 12(18%) had an Ommaya reservoir placement. Tumor was confined to the sellar and suprasellar region in 59(88%).Indications for adjuvant RT included residual tumor after first surgery in 43(64%), after second or more surgeries in 13(19%) and recurrence or progression after one or more surgeries in 11(17%). Median gap between surgery to start of RT was 3 months. Conventional RT was given using 2 or 3 fields at telecobalt machine in 18(27%) or conformal RT at linear accelerator in 49(73%) to a median dose of 54Gy. With a median follow up of 5 years, disease was stable in 36(54%), progressive in 3(5%) while 28(42%) were lost to follow up. PFS and OS was 93 %, 93%, 93% and 98%, 98% and 98% at 5,10 and 15 years respectively. Post-surgery 47(70%) developed pituitary hypofunction. Additional 13(20%) patients had endocrine deficiency following RT and required hormone replacement therapy. No formal neuro-cognition assessment was done however no obvious neuro-cognitive disability was seen in any patient. **Conclusions:**Conventional/conformal RT following a limited surgery along with endocrine therapy in patients of craniopharyngioma is safe and effective for tumor control. Challenges for management include reliable long term follow up and formal neuro-cognitive assessment.

Spinal metastases from GlioblastomaMultiforme (GBM).

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Objective: To report a case and review the literature on Glioblastomamultiforme (GBM) with drop metastases in the spine.

Background: GlioblastomaMultiforme (GBM) was first described by Rudolph Virchow in 1863 and represents the most common and most lethal malignancy of the brain, usually arising between the ages of 40 and 60 years. Extra-cranial and visceral metastases of GBM is extremely rare with frequency of only 0.44%. Macroscopically evident and symptomatic spinal metastases from GBM are quite uncommon and have been reported in up to 2-5% of patients. Although involvement of the spinal cord has been noted with increasing frequency in recent years, literature provides only a few well documented cases. We present one such rare case of symptomatic leptomenigneal metastases of GBM in a patient who has been operated surgically with primary subtotal resection and underwent adjuvant concomitant radiotherapy and chemotherapy with Temozolamide. The patient developed widespread lesions within 4 months of his primary brain surgery. **Material and Method:** A 51 years old male reported in the month of June 2014 with symptoms of headache, vomiting and generalized tonic and clonic convulsions . He was investigated and MRI of the brain done on 15th June 2014 showed 40x24x36 mm size multi-lobular mass lesion with heterogenous signal intensity on T1/T2 and flair images in the region of left temporal lobe. The lesion showed intense enhancement on post contrast studies. No hydrocephalous noted. The patient underwent Craniotomy and subtotal resection of the lesion on 16th June 2014. Histo-pathology of the operated lesion from the left temporal lobe of brain revealed 3.3x1.2x0.5 cm lesion with moderate nuclear pleomorphism , micro-vascular proliferation , multiple mitotic figures and necrosis, suggestive of GlioblastomaMultiforme (GBM). Immunohistochemistry staining (IHC) showed Vim+, WT-1 and p-53 positivity. The Ki proliferative index was

30%. GFAP was non contributory. Thus, a final diagnosis of GBM(WHO Grade IV) given. His post operative scan done on 24th 2014 June showed residual lesion at operated site. The patient received adjuvant postoperative Radiotherapy (60 Gy/30 fractions/6 weeks) along with concomitant daily oral Temozolamide. He completed radiotherapy on 1st September 2014. Thereafter, he was started on a monthly 5 days course of oral Temozolamdie . Just after the first course of oralTemozolmide, he developed severe low back pain, weakness in the lower extremities and difficulty in walking. Contrast enhanced MRI of spine showed areas of meningeal thickening particularly at the level of C6-D5. There was epidural enhancing mass lesion at the level of L1 compressing conus from left and posterior side. Thickened enhanced caudaequina roots were also seen down to L4. MRI features were suggestive of extensive spinal leptomenigeal and intradural metastases. MRI of the brain showed a large lesion in the operated site with irregular enhancement and cavitation. All ventricles were dilated with peri-ventricular interstitial fluid. The patient underwent spinal surgery in the form of laminectomy and removal of epidural soft tissue mass lesion at the L1-L2 region . The histo-pathological examination of the lesion was reported as metastatic Glioblastomamultiforme similar to the primary in the brain. Following surgery, the patient was started on a course of local palliative radiotherapy over L1-L4 region . Later on the patient developed bilateral pulmonary embolism and septicemia. He died due to uncontrolled and progressive malignant disease, pulmonary embolism and septicemia. **Conclusions**: Extra-cranial spread of GBM is very uncommon. Clinicians should be familiar with the possibility of extra-cranial spread of GBM because as treatment improvement provides better control of primary tumour and improving survival , metastatic disease will be increasingly encountered. Finally Clinicians, Oncologists and Neurosurgeons should always suspect spinal metastases in a patient with known diagnosis of GBM whenever there is back pain or some new neurological impairment is noted.

Primary Cns Lymphoma in Immunocompetent Patients – Case Series

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Introduction: Primary Central Nervous System lymphoma (PCNSL) is a rare, aggressive subtype of NonHodgkins Lymphoma, limited to the cranio spinal axis. It is seen in patients with immunodeficiency syndromes, although present in the immunocompetent population as well. It represents a challenge to the treating physician as the biologic knowledge is incomplete. **Method and Material**: We present a series of 20 cases of immunocompetentPrimaryCNS lymphoma with varied clinical presentations. In all patients a detailed history & clinical examination, neuro imaging, tissue diagnosis, CSF studies, ophthalmologic evaluation, Bone marrow studies and whole body PET CT Scan was documented at admission.4 - 6 Chemotherapy with a median dose of 3.5g/m2 of Mtx was given along with various combinations. 3 patients received HD Mtx with High dose AraC. All were followed by Cranial RT around 40Gy. Response to therapy at completion of therapy and follow up documented. **Results and Discussion**: Of the 20 patients, majority were males (80%), most common symptom was headache, the most common histology was DLBCL; the most common site of involvement was frontal lobe. 62.5% attained CR, 25% had disease progression. 12.5% had PR. 66% patients receiving HDMtx +HD AraC attained CR post therapy, compared to 60% with only HDMtx. Grade 3—4 haematological toxicity was more common in the Mtx + AraC group than in the Mtx group. **Conclusion:** PCNSLis a rare disease with protean manifestations. Therapy with HDMtx + HDAraC offers good response, compared to HD Mtx alone, with acceptable toxicity profile.

Precision of CT-MRI fusion vs CT-alone for contouring of primary intracranial malignancies.

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Aim: Development of imaging techniques, computed tomography (CT),magnetic resonance imaging (MRI) & positron emission tomography (PET) made great impact on radiotherapy treatment planning by improving the localization of target volumes. Improved localization allows better local control by minimizing geographical misses & decreased dose to the organs at risk. The aim of this study was to validate the CT-MRI image fusion method & compare delineation obtained by CT versus CT-MRI image fusion for patients with primary brain tumors in our centre based on the contour ratio* for GTV & brain stem.

*Contour ratio = Contour Volume_CT/Contour Volume_Fusion

Materials & methods: Thirty patients with different primary brain tumors who underwent 3D conformal radiotherapy were included in this study. CT & MRI imaging in treatment position was done for all the patients after surgery. The first step correlating CT & MR images is image registration. Image registration is the process in which two image data sets are put into the common coordinate system. The most often is a combination of CT & MR images. CT set was used as a reference, &MRimage set was reoriented & registered to the CT coordinate system using pixel data in the eclipse treatment planning system V 8.9.10. The GTV(Gross Tumor Volume)& Brain stem volume on CT & CT-MRI fusion were delineated &measured [GTV-CT &GTV-F (Fusion) respectively]& contour ratio was derived. **Results &Discussion:** Theaverage contour ratio obtained for GTV was>1 while for brain stem volumeit was <1. The graph plotted between the average contour volume of the tumor on CT & CT_MRI fusion& the contour ratio for GTV depicts this findingFusion allows defining smaller more accurate volumes which may decrease dose to normal tissues & improve tumor coverage& can help escalating the dose to the tumor. The OARs are better spared in the fused images due to better delineation of the organs. **Conclusion:** The result showed that MRI is an essential modality in radiotherapy for accurate delineation ofintracranial malignancies & the OARs.CT-MRI fusionfusion allows better visualization for organ delineation & planning of target volumes that may permit better treatment individualization, organ sparing or functional avoidance. It is also clear that CT-MRI fusion allows strategies of dose escalation. Future dynamic imaging modalities like, PET, SPECT & functional MRI should be included in our practice.

Key words: CT-MRI fusion,Contourratio,primary intracranial malignancies

Title: A study of quality of sleep in cancer patients in a tertiary care hospital in India– "The quality matters too!"

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Background: Insomnia, poor sleep quality and short sleep durations are common problems in cancer patients. These may interfere with their ability to cope effectively with the symptoms and treatment, andthus affect their quality of life leading to poor outcomes. Various studies have confirmed that Pittsburgh Sleep Quality Index (PSQI) is a reliable valid instrument to assess quality of sleep in various groups of cancer patients. Hence this study was undertaken to assess the prevalence of sleep disorders and to study the quality of sleep among the cancer patients admitted for chemotherapy. **Materials and methods:** This cross-sectional study was conducted at Medical Oncology department. The participants were included by random sampling method after obtaining written informed consent. Evaluation of these patients was done only once. The Pittsburgh Sleep Quality Index (PSQI) questionnaire was administered and compiled by a nurse who had no training in psychology. The questionnaire consisted of seven sub-scores (subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances,

use of sleeping medication, and daytime dysfunction) with a possible score of 0 to 3 each, making the possible total range of score from 0 to 21. A PSQI total score of ≤ 5 was suggestive of good quality of sleep and a score of > 5 was indicative of poor quality of sleep. All questions referred to the quality of sleep over the last one month. Data collected was tabulated and analyzed in Microsoft excel sheet. **Results:** 92 consecutive consenting cancer patients admitted for chemotherapy in the medical oncology ward wereinterviewed. 67 (72.8%) were females and 25 (27.2%) were males.31 patients (33.7%) had early stage of cancer (stage I and II) and 35 (38%) patients had stage IV metastatic disease. The median age was 53 years in females and 57 years in males. The mean scores of PSQI were 6.89 (SD 3.64) in females and5.72 (SD3.04) in males.36 patients (39.1%) complained of sleep of less than 6 hours duration of which 26 were females. 36 patients (39.1%) complained of sleep disturbance and 30 patients (32.6%) had day dysfunction due to sleepiness. There were 53 patients (57.6%) who were found to have poor total PSQI score of which 39 (73.5%) were females and 14 (26.5%) were males.This study showed no correlation of the PSQI scores with the stage, education and the prior treatment. **Conclusions**: This study showed that Indian cancer patients have short sleep duration and poor quality of sleep. Sleep disorders are under diagnosed in cancer patients and there is a higher prevalence among female cancer patients as seen in this study. Early recognition and management will significantly decrease the psychological burden and may improve the outcomes. Thus PSQI questionnaire can be a cost-effective way of screening cancer patients for poor quality of sleep.

Key words: Sleep, Pittsburgh sleep quality index, cancer

Symptomatology of cancer related fatigue and impact on quality of life of palliative care patients: a prospective observational study

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Background: Fatigue and other symptoms affects quality of life (QOL) in advanced cancer patients. This study looks into the factors associated with fatigue, its impact on QOL at baseline and predictors of improvement of same at first follow-up visit. **Methodology:** A prospective, observational study was conducted in the outpatient clinic of Department of Palliative Medicine from January to June 2014. Registered adult advanced cancer patients with PC clinic meeting the inclusion criteria (ECOG </=3, ESAS fatigue score >/=1) were assessed after taking informed consent for symptom burden (ESAS) and QOL (EORTC-QOL PAL15) along with demographic details. They were given standard treatment for those symptoms. They met the PC team or were telephonically contacted for the same domains after an interval of 15-30days. Descriptive statistics, comparison of baseline and follow up data, correlation and multiple linear regressions between fatigue and symptoms at baseline, logistic regression model to determine factors associated with improvement in fatigue were performed.CTRI no.: REF/2014/02/006537. **Results:** Among 500 subjects assessed at baseline, 402 followed-up (median age, 52 years; 51.6% male). Significant change in fatigue score was observed ($p<0.001$) at follow-up. Hemoglobin, albumin levels, type of cancer, sites of metastasis, ECOG score, body weight, ESAS items except drowsiness, overall QOL, emotional functioning and constipation were found to be significantly associated with fatigue at baseline ($p < 0.05$). The logistic regression model showed that changes in hemoglobin and albumin levels, pain, dyspnea, physical functioning, insomnia on QOL scale significantly contributes to the improvement in fatigue. **Conclusions:** Fatigue is strongly associated with certain physical, emotional and biochemical parameters; some of which are predictive of improvement of fatigue. As it is a single centered referral based study, its generalizability needs to be ascertained in a larger study.

Keywords: Fatigue, Advanced cancer, palliative care, Symptom control

Prevalence and impact of dyspnea in patients with advanced cancer

Supportive Care and Palliation

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Background: Dyspnea is a subjective, multidimensional experience of breathing discomfort, commonly seen in patients with advanced cancer that influences all aspects of patient's life. To find the impactofdyspnea on the quality of life in this population, it is important to understand the prevalence and factors influencing dyspnea. Aim: The aim of this study was to determine the prevalence, intensity and factors influencing dyspnea in advanced cancer and determine its impact on overall quality of life. **Methods:** The study was a prospective cross sectional study. Prevalence of dyspnea and its impact on quality of life was determined on 500 patients registered with Palliative Medicine OPD. The patients were asked to fill a set of questionnaires which included the Cancer Dyspnea Scale (translated and validated Hindi and Marathi versions), Visual Analogue Scale for dyspnea and EORTC QLQ C 15 PAL. Other details of symptoms, disease, treatment and the demographics were collected from the case record form of the patient. Descriptive statistics, univariate and multiple regression analysis were used to calculate results. **Results:** 44.37 % of the patients experienced dyspnea. The factors of dyspnea increased with increase in anxiety, depression, fatigue, loss of appetite, loss of wellbeing, pain, lung involvement by primary or metastatic disease, performance status and deteriorating overall quality of life and emotional well being on EORTC QLQ C15 PAL. **Conclusions:** Prevalence of dyspnea in advanced cancer population is as high as 44.37% and it causes a negative impact on overall quality of life of patients.

Exploring the level of cancer related fatigue among patients receiving chemotherapy: a subjective analysis of disease and treatment related outcomes of cancer therapy in Indian patients and its implications on their psychosocial wellbeing.

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Introduction: Fatigue is a highly predominant condition among cancer patients, which most them report as major obstacle in maintaining normal daily activities and quality of life. Although clinician from across the globe stress upon evaluating all patients presenting with significant fatigue, however it is seldom identified and treated in clinical practice in India and therefore hardly documented. This is why it remains unidentified in majority of the Indian patients. The main objective of this study is to find out the prevalence of cancer related fatigue (CRF) and its implication on psychosocial wellbeing among Indian cancer patients. **Methodology:** An exploratorydesign was adopted for the study. Using purposive sampling method, patients (N=132, M: 56 & F: 76) undergoing chemotherapy at Rajiv Gandhi Cancer Hospital and Research Center, Delhi, India; aged 16-77 years were included. The level of fatigue was assessed using 16-item Multidimensional assessment of Fatigue (MAF) scale and a semi structured in-depth interview schedule. These interviews were recorded, transcribed and analyzed. **Results:** Irrespective of age and education, 88% of all patients experience clinically significant fatigue, of which extreme level of fatigue was reported by 47% patients requiring immediate clinical intervention and 41% patients reported moderate level of fatigue, which is also clinically significant. The level of fatigue was reported more in females than males. Top three psycho social issues reported were apprehension of chemotherapy side effects (20%), anxiety during chemo therapy (19%) and combination of multiple psycho social issues by 14 %, followed by loss of apatite by 13%, financial issues by 12% and fear of pain during chemo therapy (10%). Among all the patients, (66%) were aware of their diagnosis, of which 11% were either fully aware or partially aware about the prognosis (20%). **Conclusion :** Fatigue

remains one of the most important clinical parameters among majority of the patients receiving chemotherapy, with females reporting it more as compared to their counterparts.Among Indian cancer patients, fatigue is neither assessed by clinicians nor reported by majority of the patients. Nearly one third of the patients report fear of chemotherapy and anxiety as their pressing concerns during chemotherapy. Loss of apatite, financial issues and fear of pain associated with chemotherapy are also reported by a significant number of patients. Indian patients should be evaluated for treatable conditions that might contribute to this symptom. Exercise, educational material and psychotherapeutic interventionsshould also be developed to prepare and support them during their treatment phase, which will ultimately lead to reduced symptoms and better quality of life.

Insights of a breast cancer patient and anxiety levels via going through palliative care with relationship to quality of life! How do counselling work via going through relapsing deadly onco therapies? Phenomenon to synchronized anxiety packets w.r.t psychosocial assessment/ clinical parameters!

Yamini Malhotra

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Introduction: Fatigue and fear of relapsing cancer had a major impact on every 89/100 women that not only effects their psychological well being but too their inner insights of insights including anxiety, distress, schizophrenic circumstances, obsessive meditation cum rickety life quality , that nurtures negative more because of the feeling of being paralysed, heaviness, psychological continuation of dystole cum systole leads to pending thoughts that impacts daily routine of day and night into traumatic stressful disbalance well being! **Objectives:** Via examples correlating menopause and breast jelly as if its menstruation blood changing position from vaginal discharge to breast pus , self healing abilities, theotherapeutic technical inventories is the objective only to gain confidence in breast cancer patients! **Material and Methods:** Clinical inventories, Catharsis techniques, norms, scoring keys, hue pendulum phenomena devices showing statistical approach towards quality of life, different poetries, jokes, examples to relate psychosocial issues unto peace giving attributes, emotional support and reassurance and confidence levels to comply with treatment like guidance and counselling! **Results:** Psychological reactions w.r.t statistical analysis using Chi square and Fisher's test with mode and median of socio behavioural aspects including adjustment, coping up symptoms, DD,PTSD, personality traits and et al gave reduction levels via intervention with psychological trial! **Conclusions:** Meeting the patients several times during treatment provided emotional support and confidence to combat with fear and fatigue via going through different onco targeted therapies!

Improvement in quality of life and prolongation of survival time of terminal cancer patients treated with herbal medicines

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Background: The increasing usage of Complementary and Alternative Medicine (CAM) in patient with cancer is a global phenomenon. In many instances the oncologists have very little idea about the various CAM used by patients. In a country like India conventional cancer treatment is beyond the reach of many economically challenged patients. Moreover, due to lack of awareness in public, shortage of oncologists and cancer treatment hospitals most patients present to a clinic with very advancedincurable disease. As a result in many cancer patients curative therapy is not possible. Hence, these patientsare compelled to try various complementary and alternative therapies like Ayurveda, homeopathy, herbal, traditional medicine etc. **Materials and methods:** A poly herbal combination of Azadirachtaindica, Curcuma longa, Embelicaofficinalis, Ocimum sanctum, Semecarpusanacardium, and Tinosporacordifolia was tried for treatment in 100 terminal cancer patients who were refused convention treatment due to advanced disease. **Results**: Improvement in quality of life was observed in 40 % of patients, reduction of cancer related pain in 15% patients, unexplained prolongation of survival time in 10% patients, complete regression of cancer/tumor in 3% patients. The anticancer potential of the various herbal medicines used in the present investigation are proven in vitro and in vivo experimental studies. The anticancer activity of medicinal plants is due to the presence of antioxidants present in them. Medicinal plants also promote host resistance against infection by re-stabilizing body equilibrium and conditioning the body tissues. **Conclusions:** We believe that in absence of any conventions therapy the poly herbal combination may have been responsible for the observed effect. As unprecedented number of cancer patients worldwide are resorting to CAM. Hence, serious attention should be given to alternative cancer medicine.

Integrating Positive Psychology in the Oncology Field : A Therapeutic Approach in bridging the gaps

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Every single human being on the planet has cancer cells (Dr..David Serven Screiber, 2007). The process of cell- division is usually controlled ; but this normal pattern gets hindered when exposed to carcinogens leading to cancer evolution and progression. The stress and burden posed by cancer experience triggers negative affirmations in the brain leading to psychological disturbances that immensely reduce one's quality of life (Michael.A.Andreykowski.et.al.2008: Psychological Health in Cancer Survivors). Twenty studies on the effect of positive psychology for improving Quality of life (QOL) in cancer patients have been reviewed in this paper. It has been found that positive psychology builds individual strengths and civic virtues by making them thrive through situations. It has implications in the field of of oncology in imparting hope for future, positivity, life satisfaction and adherence to life issues by considering them at an optimal grade : thereby improving the Quality of Life (QOL). The researches reviewed demonstrate how positive psychology builds coherence with oncology ; filling gaps in the oncology field : creating positive psychological states and health outcomes among the patients , suggesting its role in the treatment and prevention of cancer.

Keywords: *Positive psychology, Quality of life (QOL), life satisfaction*

Clinico pathological factors predicting regional lymph nodes metastases in Marjolin's Ulcer.

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Introduction: Marjolin's ulcer is a rare malignancy. There are no formal guidelines for the management of this malignancy. It is described as a local problem arising in old neglected trauma scars. There is lack of regional lymph node involvement as per the literature due to alteration of local lymphatics in the area of wound scars. These are associated with super added infection often leading to palpable regional nodes. We analyze our patient's data that underwent regional lymphadenectomy along with the resection of Marjolin's ulcer to determine factors associated with the pathological involvement of the regional nodes. **Methods**: We retrospectively analyze our data of biopsy proven 62 patients of Marjolin's ulcer who underwent surgery including regional lymphadenectomy at our department in King George Medical University from January 2013 to 2015. Clinic-pathological data was analyzed to see the factors associated with the pathological node positivity. Statistical analysis was done utilizing SPSS version 21. **Results:** Age ranges from 19-72 years with mean age of 47 years. Male to female

ratio was 0.87:1. Total 40 (64.5%) patients had burn scars and remaining 22 (35.5%) had chronic trauma history. Forty-six patients had ulcer located in lower limb and remaining 16 had upper limb ulcer. Total 20(31.2%) patients had clinically positive nodes. Wide local excision was done in 48 patients, amputation was done in 12 patients and 2 patients underwent hip disarticulation. All patients underwent regional lymph node dissection. Final histopathology revealed squamous cell carcinoma in resected ulcer in all patients with clear margins. Total 15 (23.4%) patients had lymph node metastasis pathologically. T size (>4 cm vsupto 4cm) and clinically significant nodes (>2cm vsupto 2 cm) was significantly associated with pathological node positivity (p= 0.05 and 0.0001 respectively). Other factors including thickness of tumor (upto 1cm vs>1 cm), depth of infiltration (superficial to muscle vs muscle or bone infiltration), grade of tumor (well vs moderate vs poor differentiation) and perineural invasion were not significantly associated with pathological node positivity. **Conclusion:** Regional lymph node involvement is not uncommon in marjolin's ulcer. Risk of nodal metastasis is high when tumor size is > 4 cm and clinically palpable node is >2cm. Prophylactic regional lymphadenectomy should be contemplated whenever risk of occult metastasis is high.

Popliteal lymphadectomy forcutaneous malignant melanomawith synchronous in-transit, palpable popliteal and groin metastases -a case report

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Context: Metastatic disease of the regional lymph nodes and presence of in-transit metastasis in patients with malignant melanomas have been associated with poor prognosis. In cases of melanoma located in the distal lower extremity, the lymphatic dissemination most commonly observed is in the inguinal chain for which selective lymphadenectomy (sentinel lymph node biopsy) or therapeutic inguinal lymphadenectomy have been recommended. On the other hand, involvement of the popliteal chain is very rare. In such clinical scenario, popliteal lymphadenectomy is indicated which is rarely performed operative procedure. Local excision is a reasonable approach for a solitary or a localised cluster of in-transit metastases because of low morbidity in this procedure, as compared to isolated limb perfusion with chemotherapy plus tumour necrosis factor- alpha. **Case Report:** We report a case of 35 years old female presented with non ulcerated melanoma of right heel with in-transit metastasis with popliteal and inguinal nodal chain involvement. She underwent wide local excision of primary lesion, along with resection of in-transit metastases with popliteal and ilio-inguinal lymphadenectomy, with a good postoperative course. **Conclusion:** The present case described a rare surgical problem of dissemination of melanoma of distal lower extremity with peculiarity of presence of synchronous in-transit and palpable popliteal and groin node metastasis. However, this particular presentation is resolved by a therapeutic approach with thorough knowledge of anatomy and surgical technique that is safe and effective despite only being used exceptionally. Survival benefit of this mode of treatment has not been proven due to rarity of this manifestation and resultant lack of randomized trials.

Key words: Malignant Melanoma. Lymphatic metastasis. Popliteal lymphadenectomy. Ilio-inguinal, lyphadenectomy. Lower extremity.

A Single Institution Experience Of DermatofibrosarcomaProtuberans In South India With Clinicopathological Review- ACase Series Of 21 Patients.

Arun Pandey

Background: Dermatofibrosarcomaprotuberans (DFSP) is an uncommon cutaneous sarcoma of low malignant potential, which has a propensity to show locally aggressive and infiltrative behaviour. It has a high tendency for local recurrence. **Patients and Methods:** It is a retrospective study of 21 patients with dermatofibrosarcomaprotuberans who were treated at Kidwai Memorial Institute Of Oncology, a regional cancer center in south Indiaover a period of8years (2007-2014). The primary treatment modality was surgery with or without adjuvant radiation therapy. This study analyses epidemiological and clinicopathological factors associated with DFSP with special reference to disease-freeinterval, as well as recurrence rate. **Results:** Of the 21 patients included, 13 patients had recurrent DFSP (initially treated elsewhere), 8 were primary lesions. Three of these patients also had pulmonary metastases at presentation.The median age at presentation was 40 yrs (range 15-72 years). In our study, male patients marginally outnumbered the female patients. All patientswith non-metastatic disease were treated with wide local excision, while 4 patients were also given adjuvant radiation therapy. Of the 21 patients, 5 patients developed recurrence. **Conclusion**: Wide excision with histologically negative margins is the mainstay of treatment for DFSP. Historically, high recurrence rates have been described in the literature, particularly whenconservative resection is employed.Role of radiotherapyhas been described in close postoperative margins, or in cases with positive margins when re-excision may not be possible due to anatomical constraints. Adjuvant radiation therapy decreases localrecurrences. All patients withdermatofibrosarcomaprotuberans should be followed up foran extended period, beyond the usual recommended 5-yearfollow-up, because late recurrences may occur.

Photodynamic Therapy and Hematoporphyrin Sulfonamides: Novel Approach of Treatment for Melanoma

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Introduction: Skin cancer is one of the most widespread tumors. However, despite the progress achieved in all clinical diagnostic techniques, the most severe of different tumors-cutaneous melanoma whose frequency continues to climb. Melanoma has increased to the level of a serious public health problem during the past 20 years. Melanoma tumor is accounted for 2·6% of the global cancer incidence and 1·1% of cancer-related deaths. Even if these data rank melanoma eighth or ninth in incidence, its doubling rate every 10–20 years is more worrying. The combination of intentionally increased sun exposure with diminished ozone protection has led to an epidemic increase in skin cancers. Macroscopically, malignant melanoma (MM) is diagnosed by the so-called ABCDE rule (asymmetry, border irregularity, colour variation, diameter generally greater than 6 mm, and elevation). Nowadays D may stands for dark colour.Based on the stage of the cancer and other factors, treatment options may include surgery, Chemotherapy, Immunotherapy,Targetedtherapy, Radiationtherapy and Photodynamic therapy. Photodynamic therapy (PDT)is a modality of cancer treatment based on light-induced killing of cells after administration of a photosensitizer. It gives good cure rates for superficial skin tumors. The results of photodynamic therapy in the treatment of hyper-proliferative diseases, especially in the skin, are most encouraging and have the potential of treatment ofchoice. **Objectives:** The purpose of studyto the tumortargeting Hematoporphyrin sulfonamide derivatives (HPDs)has been designed to getpotent antitumor drugs with low toxicity, enhance selectivity, increased absorption, and to determine whether Hp or its derivatives once inside tumors, can act as a selective photodynamic agent for the destruction of malignant melanoma cells. **Material and Methods:** Hematoporphyrin (Hp), sulfadiazine (SDZ), sulfamethoxazole (SMX), sulfadimidine (SDD), hematoporphyrin, cell line (B16F10), *p*-nitrosodimethylaniline (RNO), methyl thiazole tetrazolium (MTT). **Results:** HPDs showed significant phototoxicity against mouse melanoma cells (B16F10). In comparison, Hp alone did not lead to any phototoxic effect which is in agreement with previous report on photodynamic efficacy of Hp in human lung cancer cells and in mouse Levis carcinoma tumors. Our results on RNO bleaching

showed that free Hp did not produce significant singlet oxygen upon irradiation with red light (630 nm ± 20 nm) and all HpDs displayed higher singlet oxygen generation. Phototocatalytic bleaching of RNO by Hp and HpDs (30 μL; 1 mM in PEG system) on different time intervals (0, 2, 4, 6, 8 and 10 min) and different light dose (0, 0.75, 1.5, 2.25, 3.0, 3.75 J/cm2) were determined. at 630 ± 20 nm. It was found to vary from 100 to 100.48 ± 1.68 for Hp; 100 to 91.40 ± 5.35 for HpSDZ; 100 to 89.61 ± 5.07 for HpSMX; 100 to 88.35 ± 2.71 for HpSDD, at above said time intervals and light doses. The cell viability of MMCs (B16F10) was determined by MTT assay. The cells were exposed by irradiation at 630 ± 20 nm. The light doses at the position of the cells were 0 J/cm2, 1.18 J/cm2, 2.38 J/cm2 and 3.54 J/cm2 for 0, 5, 10 and 15 min respectively. Percentage phototoxicity of melanoma cells was found to be 102.24 ± 14.77, 40.32 ± 14.09, 29.31 ± 3.12 and 43.10 ± 9.56 for Hp, HpSDZ, HpSMX and HpSDD respectively at 15 min exposure of 3.54 J/cm2 light dose by PDT. The percentage phototoxicity of melanoma cells was found be least in HpSMX. This means that maximum B16F10 melanoma cells death was achieved by treatment with HpSMX at 15 min exposure of 3.54 J/cm2 light dose by PDT. **Conclusions:** The sulfonamides constitute an important class of drugs, which display a variety of activities including antibacterial, anti-carbonic anhydrase, diuretic, hypoglycemic effectiveness as well as anticancer activity. The sulfonamide moiety appears to be a crucial functionality to interact with cellular targets and is used as potent anticancer agents. Porphyrins are powerful photodynamic agents that render cells vulnerable to light. HpSDZ, HpSMX and HpSDD were subjected to *in vitro* studies using different tests i.e RNO bleaching, MTT assay and cellular uptake by B16F10 melanoma cells. The results showed higher activity of HpDs as compared to Hp, in the presence of PDT. The maximum efficacy was exhibited by HpSMX.

MELANOMA – Experience at Tertiary Care Center of Northern India

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Introduction: The incidence of melanoma is continuing to increase worldwide. UV exposure is a known risk factor for this cancer. Thus, geographic location is known to influence UV exposure and incidence of melanoma. In 2015, it is estimated that there were 73,870 new cases of melanoma of the skin and an estimated 9,940 people died of this disease. Melanoma is more common in men than women and among individuals of fair complexion and those who have been exposed to natural or artificial sunlight (such as tanning beds) over long periods of time. There are more new cases among whites than any other racial/ethnic group. The number of new cases of melanoma of the skin was 21.6 per 100,000 men and women per year based on 2008-2012 cases.Advanced-stage cutaneous melanoma has a median survival time of less than 1 year. Multidisciplinary approach of Surgical removal, radiotherapy, chemotherapy, targeted therapies and a variety of immunotherapies have been utilized in the treatment of melanoma. Our aim was to complete a retrospective chart review of MM from a tertiary institution within rohtak over a 5 year period (2011-2015). The clinical features and treatment modalities were identified and correlated with outcomes. **Methods:** Data was collected from the PGIMS, ROHTAK for five years. **Results:** A total of 21 cases were found. Mean age was 56.95 years. Maximum age was 80 years and minimum was 39 years. There were 10 females and 9 males. Two were excluded due to inaccessible data. Out of 19 cases, the majority were cutaneous melanomas (10/19). Two (2/19) originated in the nasal cavity. Nasal tumour patients presented with epistaxis or obstruction. One (1/19) patient presented with hard palate swelling, one (1/19) patient had mass in maxillary antrum, another one (1/19)patient presented with conjuctival mass, one (1/19) presented with aryepiglottic fold mass, one patient (1/19) had melanoma of mixed type in right eye ball and remaining two (2/19) showed exophytic mass in anal canal. All patients were offered surgical excision. **Conclusion:** MM is a rare and aggressive malignancy associated with poor long term outcomes. Despite technically adequate surgical management, 80% of deaths are due to distant metastasis. Further research of this rare tumour is required to determine the ideal treatment protocol.

Key words: Melanoma, malignancy, metastases.

Malignant Tumors of Head and Neck in Pediatric Patients : A Ten Year Retrospective Study

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Objectives:

- Our study aims at discussing the commonest clinicalpresentations,diagnosis,types of treatment and outcomesin cancers of the head and neck region in paediatric age group
- To compare the results with other similar studies.

Methodology: It is are trospective study of the last 10 years period between January 2002 and august 2012 conducted in Gujarat Cancer And Research Institute a tertiary regional cancer centre in Gujarat, in separate pediatric oncology department. All patients were investigated thorough lyaccording to the Standard protocols. Children under the age of 17 year were included. Lymphomas and primary ophthalmic tumours were excluded. **Results and Conclusions:** This 10 year (2002 2012) retrospective review identified 59 Children under the age of 17 yrs who presented with malignant tumors of the head and neck. Nasopharyngeal cancer was the most common diagnosis Followed by rhabdomyosarcoma, parotid and thyroid cancers. Nasopharyngeal cancer, parotid and thyroid cancers were most common in age group more than 10 year where as Rhabdomyosarcoma was common in 05 years age. Commonest nasopharyngeal cancer wasun differentiated carcinoma. Common estparotidtum or was mucoepidermoid carcinoma. Common estthyroidtum or was papillary carcinoma. Most commonlinical presentation was necks welling. Most common site for rhabdomyosarcoma was paranasalsinuses. Nasopharyngeal and rhabdomyosarcoma was treated primarily with chemoradio therapy and surgery used for salvage. Parotid and thyroid cancers were treated primarily with pfront surgery. Surgical management was done in 18/59 (30.5%) and the rest were managed either with chemotherapy or radiotherapy orc hem orad io therapy. Primary line of treatment for nasopharyngeal and Rhabdomyosarcoma was nonsurgical. In Rhabdomyosarcoma, salvage surgery was performed in 21% Most common surgeries done were parotidectomy (4.4%) followed by thyroidectomy (27.7%), craniofacial resection (5.5%). Parotid malignancies underwent superficial parotidectomies(50%) and radical parotidectomy (50%).

Key Words: Head and neck, malignant tumors,paediatric patients,

Incidence, risk factors and outcome of t-AML: single centre experience from a paediatric oncology unit

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Introduction: Therapy related acute myeloid leukemia (t-AML) is a rare though devastating late effect of cancer treatment. Alkylating agents, DNA topoisomerase II inhibitors and radiotherapy have been mainly implicated as causative agents. Six cases of t-AML were observed amongst 1020 cases of pediatric cancer treated between 1998 and 2014. The profile of these patients is described below. **Material and Methods:** This was a retrospective analysis of the hospital e-data base. **Results:** Among 6 children, 5 were males and median age was 12 years. The incidence of t-AML among patients of sarcoma (one each with Ewing's sarcoma, 1/80, osteosarcoma, 1/70, and rhabdomyosarcoma, 1/41), B-non-Hodgkin lymphoma and acute lymphoblastic leukemia was 3/191, 2/77 and 1/408 respectively. The patients of Ewing's sarcoma and rhabdomyosarcoma received cumulative doses of cyclophosphamide (equivalent dose 27.7g/m2), etoposide of 4 g/m2 and

adriamycin of 300mg/m2 while the child with osteosarcoma received total cumulative doses of adriamycin (375 mg/m^2) with cisplatin (500 mg/m^2). The cumulative doses of etoposide and cyclophosphamide were 1.8 g/m2 and 6.8g/m2 for the two patients with NHL treated for group C disease on LMB 96 protocol. One patient with acute lymphoblastic leukemia received cyclophosphamide dose of 3g/m2 and daunorubicin of 240mg/m2. Presenting symptoms included pyrexia, bone pains, gingival hyperplasia and median latency period was 12.5 months (range 4-52 months) from completion of therapy. None had a preleukemic phase. The FAB morphology was M2 (1) and M4/M5 (5) and MLL rearrangement was detected in 4/6 patients. Treatment in the form of chemotherapy followed by allogenic BMT was offered and accepted by 4/6 patients. Three achieved remission of which only one is a long term survivor. **Conclusions**: We observed a high incidenceof t-AML in children with pediatric sarcoma and group C NHL. Shorter latency period, absence of preleukemic phase, presence of MLL gene implicate epipodophyllotoxin to be the probable causative agent. In view of poor outcome with conventional therapy, novel strategies need to be considered.

Study of Induction Outcome in Pediatric Patients with Philadelphia Positive Acute Lymphoblastic Leukemia

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Introduction: The Philadelphia (Ph) chromosome is the most common cytogenetic Abnormality associated with adult ALL. Until recently, Ph-positive ALL carried a dismal prognosis in both children and adults. Patients with Ph-positive ALL who received conventional chemotherapy reportedly had long-term survival rates of approximately 10%.Philadelphia translocation confers poor risk. Treatment response was shown to be a robust predictor of induction failure. **Objectives: 1 .** To determine the induction outcome of pediatric Philadelphia positive acute lymphoblastic Leukemia.2. To determine the prognostic factor, responsible for poor inductionoutcome in pediatric Philadelphia positive acute lymphoblastic leukemia. **Material and Methods:** All new peadiatric Patients (age <19) suspected of ALL, where subjected to all routine blood tests such as Complete heamogram, uric acid, lactatedehydrogenase, serum albumin and other routine liver function tests and renalfunction tests. Patient where counseled for, and screened for any co morbidHIV, HbSag and HCV infection. Besides subjecting to bone marrow aspirationand biopsy, Immunophenotyping and karyotyping was done routinely on ALL patients. Patients were screened for Philadelphia chromosometranslocation by Fluorescence in situ hybridization (FISH) on bone marrowsample.Those who tested positive for Philadelphia chromosome on FISH were selected,as case, for looking induction outcome. **Results:** Results of our study were as follows, 21 out of 25 (84%) patients were in remission, following induction Chemotherapy. Regardless of the chemotherapy protocol used i.e. BFM90 or MCP 841. Besides the start of imatinib, also, did not significantly affect the induction outcome. Average age of the patients in our study was 9.48 years. (Range 3-18). Males were 18 (72%) and females were 7 (28%). The ratio of male: female was 2.57:1. Amongst the age group, 1-10 and >10 yrs, CALLA positive subsets, were uniformly distributed 11/12 (91.66) vs 7/11 (63.6) respectively. (p=0.76) Patients were classified in different age groups, which are known to impact induction outcome. Age 1-10 years and >10 years , to negate the confounding due to age. But this did not affect the outcome. (p=0.73) According to Day 1 Total leucocyte count, patients were classified into different groups, based on total leucocyte count on Day 1 of induction. These groups were those with 10,000 to <50,000, >50,000 to 1,00,000 and >1,00,000 counts . To see the impact of day 1 TLC on induction outcome. Although there was trend towards inferior outcome from 100% CR in 50,000 to 1,00,000. But it failed to achieve significance (p=0.18). **Conclusions:** In our study, induction outcome was independent of all risk characteristics such as age, CALLA, cytogenetics, day 8 blasts, and day 1 total leucocyte count. Age, day TLC and Day 8 Blasts have been related poor outcome in ALL, but it does not affect the induction outcomeAs compared to other study induction outcome in our study was 84% complete remission rate. Other studies had complete remission rate of 86.44.

A Single Institute Experience in Hepatoblastoma - Paediatric Liver Resections

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Back ground: Hepatoblastoma is the most common primary liver tumor in children, accounting for just over 1% of pediatric cancers. The etiology is unknown, but it has been associated with Beckwith-Weidemann syndrome, familial adenomatosispolypi, and low birth weight. The primary treatment is surgical resection, however, chemotherapy plays an important role by increasing the number of tumors that are resectable. The prognosis for patients with resectable tumors is fairly good, however, the outcome for those with nonresectable or recurrent disease is poor. **Material and Methods**: All patients of liver tumours treated at our institute from february 2010 to date were included in the study.They were staged according to the **SIOP**staging system.Operable lesion were taken up for primary surgery the rest were given Neoadjuvant chemotherapy and later operated. All patients with residual viable cells were offered adjuvant chemotherapy. **Results** The mean age of patients was 2yrs (range: 7months–13 years).The most commonly seen in male childrens (60 %) .Sixty percent (n=12) of the pts have lesions in rt.segments of liver.Majority were in stage 3. Neoadjuvant chemotherapy made 70% cases to be resectable.

Conclusion :

- Hepatoblastomas are relatively common tumors in children
- Majority of pts.present with locally advanced disease.
- Neoadjuvant chemotherapy made these pts resectable
- Operative procedure related complications and morbidity is very less in experienced hands
- Hepatoblastomas are eminently curable with surgery and chemotherapy

Spectrum of Solid Malignant Tumors of Infancy and Childhood in a tertiary care hospital

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Background: The aim of this study is to evaluate the pattern and frequency ofpediatric solid malignant neoplasmsat our hospital to understand the epidemiology of tumors in children in our region being a significant cause of death among children. All the cases were treated by multidisciplinary approach of surgery, chemotherapy and radiotherapy. **Materials and Methods**: This is a retrospective analysis of 137 cases of pediatrictumorsat tertiary care hospital excluding neurosurgery, cardiothoracic and hemato-lymphoid malignancies. The records of all the tumors diagnosed by means of histopathological or cytological examinations in addition to ultrasonography, computed tomography and magnetic resonance imaging findings were included in children ≤14 years of age during a period of 5-year (2011-2015) in department of Pathology, Pt. B.D. Sharma, PGIMS Rohtak. **Results**:137 children were diagnosed with malignant tumors. The commonest tumor was wilmstumor (31 out of 137 cases) with commonest age of presentation being 3-5 yearswith increasing trend towards early age of presentation followed by neuroblastoma (25 of 137cases) with commonest age of presentation being 1-4 years. Male predominance was seen. The mean age of presentation was 3 year. Bone tumors (23 out of 137 cases) were next common in frequency followed by germ cell tumors (15cases out of 137) followed by Rhabdomyosarcoma(12 cases out of 137) with mean age of presentation

being 2-4 year and five cases each of primitive neuroectodermaltumor (EWS/PNET) and malignant sacrococcygealteratoma. Three cases each of hepatoblastoma, retinoblastoma, papillary carcinoma thyroid and nasopharyngeal carcinoma. Nine cases were included miscellaneous category. **Conclusions**: Wilms' tumor is the most common solid childhood malignant tumor at our centre. Documentation of cases, advanced diagnostic methods like IHC, cytogenetic studies and treatment modalities with close follow up is needed to achieve better statistical evaluation of the problem to decrease morbidity and mortality. Histological type is important for understanding etiology and progression of disease. The likelihood of a given type of tumor being present in a particular age or sex group or particular site may heighten the index of suspicion and ultimately influences etiology, biology, and natural history, relative incidence and distribution frequency, clinical presentation and manifestations, and response to therapy and outcome.

Key words: Children, histopathological, tumors

Stage IV Pelvic Chondrosarcoma Treated with Extracorporeal Radiation and Reimplantation, Metastatectomy: A Case Report of 6 Years Follow up

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Introduction: A 25 year old lady presented with history of swelling and pain in left flank and hip region for 4 months.Pain was also present on rest, associated with painful restriction of left hip movements. **Method:** Radiographic evaluation with plain radiographs, CT andMRI of the pelvis were done which showed large expansile lytic lesion in the left ilium and acetabulum. Histology on needle biopsy was Conventional Chondrosarcoma. Staging was done with CT Thorax, showed 4 lung nodules in left lung. She underwent Internal Hemipelvectomy Type I + II of left Hemipelvis, followed by extracorporeal radiation with 50 Cgy. This ECRT graft was soaked in vancomycin solution and reimplanted into the defect with plate and screw osteosynthesis. In the same sitting, Lung Metastatectomy was performed.She was allowed non weight bearing ambulation from 4 post-operative day and maintained until union of osteotomy sites which was by 9 months of follow up. **Result:** At present follow up of 6 years, the patient is alive, disease free without any events.At latest follow up, the patient walks with lurch to affected site with functional MSTS score of 26/30. **Conclusion:** The highlight of the case is the approach taken to clear the tumor completely, the method of reconstruction and aggressive approach to resect lung metastases during primary surgery corroborated by the event free and disease free survival at 6 years follow up. Of note, the patient of childbearing age had uneventful pregnancy and gave birth to healthy child in 4th year of follow up.

Extracorporeal radiation & reimplantation for primary malignant bonetumours

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Introduction & Purpose: Extracorporeal radiation&reimplantation is innovative and established method to treat bone sarcomas, especially long bone and pelvis. This study was performed to analyse the results of extracorporeal radiation &reimplantation after excision. **Material &Methods:** Retrospective data of 16 patients treated between years 2009-2015 were analysed. Histological diagnosis was 9Osteosarcomas, 6 PNETand 1 Chondrosarcoma. Femur was involved in 6, Tibia in 4, Humerus in 3 and Pelvis in 3. Pre-operative chemotherapy was given in 13. 16 patients with mean age 15 years underwent wide excision of involved diaphysealor pelvic bone segment followed by 50 cGy irradiation in sterile conditions. This irradiated tumour graft was soaked in vancomycin solution and reimplanted with various osteosynthesis methods. Average surgical time was 6 hours, average blood loss was 540 ml. Median follow up was 29 months with longest at 72 months. **Results:** At latest follow up, 12 were alive and disease free, 1 had skull metastasis, 2 died during post- operative chemotherapy and 1 died due to local and distant metastasis. Average time to unionat osteotomy sites was 9months.Major complications were observed in 6patients whosubsequently underwent surgeries. This included 2 implant removal for late infection (ECRT graft had incorporated), delayed union in 2 patients requiring autograft and osteosynthesis, dual plating for screw backout in 1 and 1 superficial infection requiring debridement. Functional outcome in 12 patients at latest follow up according to MSTS was 24/30. **Conclusion:** Reconstruction of diaphysealand pelvic tumours is a challenge with reported rates of success and complications. Irradiated bone can be a biological and economical solution in this situation. Precise planning, execution and strict postoperative rehabilitation is key for success of this technique.

Single centre experience of various operableprimary axillary masses and their management.

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Introduction: Axillary masses are an uncommon alterations when detected as an isolated finding. They may be associated with a gamut of benign and malignant diseases. Axilla contains various mesenchymal elements from which various disorders can develop, the lymph nodal metatstasis from breast cancer being commonest. Soft tissue masses ,though rare should always be considered as a prime differential while approaching a case of axillary mass. **Objectives:** The objective of our study was to describe the myriad pathologies of axillary masses , their clinical behaviour, the multidisciplinary approach in their management and their outcomes. **Material and Methods:** Amongst the patients with a clinical diagnosis of axillary mass seen at our service from 2011 to 2015 , we retrospectively selected 10 patients who presented with masses anywhere in the axilla, which were deemed operable after evaluation. Patients with alterations of breast or ipsilateral limb , chest wall , inoperable axillary masses, metastasis, Lymphomas and Tubercular lymphadenopathy were excluded from our study. **Results:** In our study of 10 patients , 5 were males and 5 females. The mean age of presentation was 39.1 years. 4 patients had spindle cell sarcoma,1 had alveolar Rhabdomyosarcoma,1 had Malignant schwannoma, 1 PNET,1 Hemangiopericytoma/Solitary fibrous tumour,1 was Benign peripheral nerve sheath tumour and 1 had Intramuscular hemangioma with secondary haematoma.All patients underwent surgery with 1 patient receiving neoadjuvant chemotherapy and 2 patients received Adjuvant radiotherapy as a treatment protocol. **Conclusions:** Isolated axillary masses are a rare entity. Clinicians should have a high index of suspicion in detecting such masses early in the disease course when it is still amenable to curative treatment and has got fairly good survival with the multidisciplinary approach.

Evaluation of role of Interstitial Brachytherapy in Soft Tissue Sarcoma: A single institute experience

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Background: Soft tissue Sarcomas are rare group of solid tumors comprising of 1% of all solid tumors. The management of soft tissue sarcomas have evolved due to advancements in imaging, histopathology, cytogenetics, and the use of multimodality treatment. The treatment strategies emphasizes on the control of disease locally, sparing of limb function and improvement in the quality of life. High dose brachytherapy has formed a part of the

management and has the advantage of providing concentrated dose to tumors and sparing of surrounding normal tissues. In this study we examined the clinical outcome of High dose Brachytherapy for STS at our Hospital through retrospective analysis of the prospective database maintained. **Objectives:** To review the clinical outcome and quality of life in patients with Soft Tissue Sarcoma treated at our center through High dose rate interstitial brachytherapy. **Methods:** Eleven patients with different sites and grades of Soft Tissue Sarcoma underwent surgery and Intraoperative catheter implantationsin single planein biopsy proven Soft tissue sarcoma cases. These patients then underwent High Dose Brachytherapy with Iridium – 192. The patients received average dose of 3.5Gy per Fraction (Two fractions per day 6 hours apart) with total dose of 35 Gy/10 Fr/5 Days and after completion of treatment were followed up at 1 month and later every 3 monthly for 2 years; Followed by 6 monthly interval. **Results:** The Patients were followed up for range of 1 – 42 months (Median 12 months) and overall control rate was 72.72%. The Local recurrence was noted in only one patient (9.09%) and two patients developed distant metastases (18.18%). **Conclusions:** The results in our study suggested the importance of HDR Brachytherapy in management of Soft Tissue Sarcoma. The local control rate was 72.72 %. The dose of 35Gy over 10 fractions over 5 Days was found to be effective in local control and limb salvage in case of Soft Tissue Sarcoma as practiced at our Centre.

Key Words: Soft Tissue Sarcoma, Interstitial Brachytherapy, High Dose Rate

Primary tumours and tumourous lesions of the clavicle.

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Abstract : Primary tumours and tumourous lesions of the clavicle are very rare , and little literature is available regarding their characteristics, outcome and management techniques including biopsy. The method of biopsy is controversial in the clavicle due to the risk of injury to the neighbouring neuromuscular bundle. We studied the clinical, radiological and histopathological characteristics of the patients with lesions involving the clavicle who presented to us between 2013-2015. Seven patients presented to us with lesions involving the clavicle during the above mentioned study period. Two patients had metastatic disease (Carcinoma breast and lung) with the clavicle being a part of the systemic spread of the disease. They were treated with palliative therapy as per the guidelines. Ewing's sarcoma, Bone cyst (simple and aneurysmal), Gaint cell tumour and Mixed fibroma constituted the remaining cases. All the patients underwent resection of the clavicle (medial end > lateral end). Functional and oncological results were good. The distribution of tumours in the clavicle is quite different from those in the long bones. No form of reconstruction was required.

Key words: Tumour, Clavicle, Resection.

Day-3 ACOS 2016

Activation of Caspase Activated Dnase by Benzophenone Pyridine -Na-1 Analogues Promotes Apoptosis Hallmark in Lymphoma

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Introduction: Programmed cell death plays a crucial role in the manitaince of tissue homeostasis by regulating cell death, but failing mechanism leads to formation of malignant tumour, opening new gateway that induction of apoptosis is important mechanism for cancer therapy. Molecular events underlying stimulation of apoptotic characteristics is through activation of caspase activated endonucleases (CAD) by dissociating CAD+Inhibitory CAD complex and nuclear translocation of the CAD leading to cleavage of the cellular DNA , making a key strategy for cancer treatment. **Objectives:** To develop a novel drug with target specific activity by promoting apoptotic pathway. **Material and Methods:** Antiproliferative studies by MTT, LDH and Trypan blue assay, cell cycle arrest through FACS, *In-vivo* antitumor activity using murine Daltons Lymphoma, Mechanisim of Apoptotic activation by cell fractionation and nuclear localization studies of CAD/ICAD by immunoblot, CAD activity by endonuclease assay, DNA fragmentation assay and cellular changes by Giemsa stain. **Results:** NA-1 exhibited potent synchronized cytotoxic activity with Ic-50 value of 8.5 μm against Murine Daltons Lymphoma ell lines in different methods of antiproliferative study. The cytotoxic results were validated through FACS where population of cells undergoing apoptosis is in significant number .The *In-vivo* antiproliferative effect of NA-1 resulted in dose dependent regression of the tumor parameters like cell proliferation and ascetic fluid accumulation. The mechanism behind antitumor activity is due to activation of CAD by cleaving the ICAD/CAD complex through the expression of caspase-3. Activated CAD translocated to nucleus and induces DNA fragmentation resulting the change in cellular parameters such as cellshrinkage, membrane blebbing and irregular shape with apoptotic bodies. **Conclusions:** NA-1 is a novel molecule with potent cytotoxic activity and propapototic nature which activates Caspase-3 mediated DNA damage which could be further investigated for drug development for the treatment of cancer in future.

Breast Cancer Metastasis to Stomach- A Case Report and Review of Literature

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Background: Breast cancer metastasis to the stomach is rare. It is very important to distinguish a breast cancer metastasis to the stomach from a primary gastric cancer on the basis of clinical, endoscopic, radiological and histopathological features, in order to administer the appropriate treatment. **Case presentation:** A 52 year post menopausal female presented with lump in right breast of 5 months duration with history of back ache and laminectomy done one year back. Mammogram showed a 4x5cm mass in upper-outer quadrant , which on FNAC came as infiltrating lobular carcinoma breast. Metastatic workup by chest X-ray, ultrasound abdomen and bone scan were all negative. Patient was operated by right breast conserving surgery with axillary dissection. Final HPE report- invasive lobular carcinoma, grade 2, ER positive, PR negative, her 2/neu positive, stage- T2N2aM0. Patient received 6 cycles of adjuvant TAC chemotherapy, 18 cycles of herceptin and IMRT 50.4 Gy in 28 fractions. After 2 years patient developed supraclavicular and bony metastasis as seen in PET scan. Patient was given palliative chemotherapy with 3 cycles of gemcitabine, carboplatin and zolendronic acid. On this regime patient developed severe thrombocytopenia and hence was started on abraxane for 11 cycle. Following this patient developed complaints of pain abdomen and constipation. Repeat PET scan showed – interval development of focal wall thickening of greater curvature of stomach with exophytic projection, likely representing an ulcer. Upper GI endoscopy showed an ulcer along greater curvature in body of stomach and multiple biopsies taken. Biopsy report was consistent with signet ring carcinoma, which after IHC analysis showed positivity for Her2/neu, GCDFP-15 and mammoglobulin. Because of poor general condition, patient was referred to palliative care unit for further management. **Conclusion:** Breast cancer metastasis to the stomach can be differentiated from primary gastric cancer by comparing the biopsies from the gastric metastasis with the original histological slides from the primary breast tumor. Appropriate systemic treatment for metastatic breast carcinoma is the preferred treatment, whereas surgical intervention should be reserved for palliation or may be indicated in cases of solitary resectable gastrointestinal tract metastases.

A Case of Malignant Peripheral Nerve Sheath Tumor of Breast(Mpnst) In Male Patient. A Rare Case Report

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Malignant peripheral nerve sheath tumor (MPNST) is very unusual type of soft tissue sarcoma (STS) and occurs mostly in patients of neurofibromatosis. The occurrence of MPNST in breast tissue is particularly rare. Only 8 cases have been reported till date in absence of history of neurofibromatosis. We are reporting such case in a 30 years old male who presented with hard and painless breast lump for 3 months. Patient was treated with wide local excision and surgical specimen was submitted for histopathological examination. Microscopic examination revealed a malignant spindle cell tumor of low grade. Immunohistochemistry (IHC) was performed which showed positivity of vimentin and negative for LCA (leukocyte common antigen), CD99, desmin, Bcl-2, S-100. Final diagnosis MPNST was put on the basis of morphological appearance and IHC. Patient was treated with postoperative radiotherapy in dose of 50 Gy in 25 fractions in view of unknown margin status. At present patient is on regular follow up.

Neuroendocrine Carcinoma of Breast: How we treated

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Introduction: Primary neuroendocrine carcinoma of the breast (NECB) was originally described in breast cancers with carcinoid like growth patterns. Because it can mimic some of the most common histologic subtypes of breast cancer, primary NECB is difficult to diagnose and therefore remains under-recognized. Herein we report the case of a patient initially diagnosed with invasive ductal carcinoma (IDC) that was postoperatively found to have a primary NECB. We describe a case of a 43-year-old woman who presented with a breast lump with FNAC and mammography suggestive of a malignant lesion. After undergoing modified radical mastectomy the final surgical pathology showed evidence of alveolar-type primary neuroendocrine carcinoma of the breast. The patient was treated with cisplatin/etoposide followed by paclitaxel/carboplatinum. Thirteen months after surgery the patient is alive, disease free. **Conclusions:** The breast in situ component of primary neuroendocrine carcinoma of the breast may prevail on a core biopsy samples increasing the probability of underdiagnosing this tumor

preoperatively. Being aware of the existence of this disease allows for timely diagnosis and management. Optimal treatment requires simultaneous consideration of both the neuroendocrine and breast in situ tumor features. We present How we treated a case of NECB.

Post Mastectomy Radiotherapy in Patients of Implanted Cardiac Pacemaker

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Introduction: Adjuvant post mastectomy radiation therapy for breast cancer in women is the standard component of multimodality treatment. With the increase in prevalence of cardiac morbidity, patients with pacemakers requiring radiotherapy has increased. Pacemakers are usually implanted subcutaneously, overlying the pectoral muscles and thus may be affected by radiation used in treatment of cancers of breast, lung, chest wall and lymphomas. Therapeutic irradiation may cause pacemaker malfunction due to the effect of ionizing radiation or electromagnetic interference. Most cited guidelines for the management of radiation oncology patients are American Association of Physicists in Medicine (AAPM) guidelines. They recommend that these patients should not be treated with a betatron, pacemakers should not be in the direct treatment field, to limit the accumulated dose to the pacemaker to 2 Gy. **Case Summaries :** We present two cases with carcinoma breast with implanted pacemaker who received adjuvant radiotherapy at NIMS. **Case I :** 41yr old female, Permanent pacemaker placement in Dec 2012. Diagnosed as Ca Right breast and Underwent Right modified radical mastectomy (MRM) in Apr 2013 and received adjuvant chemotherapy. No local recurrence or distant metastasis. Cardiology consultation taken , detailed 2D Echo done, reprogramming done before starting RT. **Treatment Plan :** Adjuvant RT by 3DCRT to right chest wall and right SCF, 2Gy/fr,25 fractions to a total dose of 50 Gy. Dose to pace maker was restricted to 0.6Gy mean and max of 1.8Gy. Patient was monitored daily with ECG , cardiology review. Doing well on follow up. **Case II:** 68 yr old female, non diabetic, non hypertensive with pacemaker implantation 7 yrs ago for sick sinus syndrome was diagnosed with Ca left breast in Jan 2014 and underwent left MRM. After adjuvant chemotherapy planned for adjuvant radiotherapy . Pre treatment ECG showed incomplete Right bundle branch block and 2DEcho showed normal study. Cardiology consultation taken , detailed 2D Echo done, reprogramming done before starting RT. After explaining the consequences to the patients and attendant and with their consent the treatment was given. **Treatment Plan:** Adjuvant RT by 3DCRT to left chest wall and left SCF, 2Gy/fr,25 fractions to a total dose of 50 Gy. Dose to pace maker was restricted to 0.7Gy mean and max of 2.2Gy. Patient was monitored with ECG, pacemaker function assessment regularly. Patient doing well on follow up. **Conclusions** The patient's coronary and pacemaker status should be assessed by cardiologist before, during and soon after the completion of radiotherapy. Planning radiotherapy to minimize the dose, close monitoring throughout the treatment and with strong support from the Cardiologists these patients can receive adequate treatment.

Primary Stromal Sarcoma of Breast: A Rare Entity

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Introduction: Primary soft tissue sarcomas of the breast constitute less than 5% of all soft tissue sarcomas and less than 1% of malignant breast cancers. The rarity of this tumor limits most studies to small retrospective case reviews and case reports. Primary breast sarcomas are locally aggressive tumors as evidenced by the high rate of local recurrence when excisional surgery is performed.

Case Report: We report a case of 45 year old female, who presented with a large ulcerated breast mass and was diagnosed as carcinoma breast on fine needle aspiration. Modified radical masectomy was performed and microscopic examination revealed numerous haphazardly arranged spindle cells with variation in cellular size along with few benign appearing glands entrapped in between. Sections were subjected to immunohistochemistry, vimentin and CD10 were positive in tumor cells, Hence patient was diagonsed with primary breast stromal sarcoma, which is a rare entity. **Discussion:** Primary sarcomas of the breast are extremely rare with less than 1% of all malignant tumors of the breast and there are only a few hundred cases reported in the literature. Primary breast sarcomas occur over a wide range but most occur in women in their fifth or sixth decade of life Sarcomas can occur anywhere in the human body. The treatment for breast sarcomas is planned by a multidisciplinary team and follows the treatment model of sarcomas in other locations. However, there is still no definitive consensus regarding the treatment of primary breast sarcomas (PBS). Surgery represents the only potentially curative modality. A contemporary multidisciplinary approach to therapy including surgery, radiation, and chemotherapy is advocated.

Keywords: Breast, Histopathology, Sarcoma.

History of Endometrial Cancer as a contraindication for Tamoxifen, a Case Study. Time to amend the British National Formulary?

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Introduction: Both breast and endometrial cancer are increasing in our ageing population and share similar epidemiological characteristics. Oestrogen is strongly implicated in the genesis of the majority of cases. Tamoxifen has been extensively used as an adjuvant treatment for Oestrogen Receptor(ER) positive breast cancer and is increasingly being prescribed to healthy women as a prophylactic. However, paradoxically, at the level of the endometrium, Tamoxifen is associated with propensity for neoplastic change. **Methods:** We report the clinical course of a woman who developed two independent endometrial adenocarcinomas intersected by an episode of ER positive breast cancer and discuss the implication of the endocrine management in the genesis of her relapse. In addition, we examined several data sources listing contraindications to the use of Tamoxifen. **Results:** A 65 year old was treated for stage I well differentiated deeply invasive endometrial cancer. Three years later she developed a T2, N1 ER positive breast cancer. Adjuvant Tamoxifen was prescribed and three years later a vaginal recurrence of her ER positive endometrial cancer was excised for histology. The Tamoxifen was switched to the aromatase inhibitor Anastrazole (market name: Arimidex) and seven years later she remains free of disease at either site. **Conclusion:** Although Arimidex has been shown to be as efficacious as Tamoxifen as adjuvant treatment for breast cancer but is more frequently prescribed. The British National Formulary, pharmaceutical company data sheets and national guidelines in the United Kingdom warn of the adverse endometrial side effects of Tamoxifen. However, none of these publications define a pre-existing history of an endometrial cancer as a contraindication to taking Tamoxifen. We believe the above case supports why these documents should be amended. Woolas, J.D Medical Student Plymouth University School of Medicine and Dentistry Rahimi.S Consultant Histopathologist, Queen Alexandra Hospital Portsmouth Woolas, R.P Consultant Gynaecologist, Queen Alexandra Hospital Portsmouth

Extra-mammary solid tumours metastasizing to the female breast – A Report of 3 cases

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Introduction: Metastasis to the breast from extra-mammary solid tumours is a rare event. This is due to large areas of fibrous tissue with poor blood supply. Review of literature shows only 0.2-1.3% incidence of metastasis to breast. **Material and Methods:** Between 2011 and 2015, we reported three cases of metastasis to the female breast from extra-mammary solid organ tumours at the Department of Surgical Oncology, King George's Medical University, Lucknow. First Case : 30 year old lady presented with Melanoma of hard palate with Breast metastasis Second Case : 40 year old lady with Carcinoma lip with Breast metastasis Third Case : 45 year old lady with Carcinoma Gallbladder with Breast metastasis **Conclusions:** Although breast is a rare site for metastasis by solid tumors, the possibility should always be kept in the differential diagnosis of a breast mass.

Gingival Metastasis from Carcinoma Breast : A rare case report

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King George's Medical University Metastases

From malignant tumors to the jaw and the oral cavity are seldom seen and constitutes 1% of all oral malignant tumors. Furthermore, in the absence of any other metastasic site, isolated solitary tumor seedling of oral soft tissue is extremely rare and constitutes 0.1% of all oral malignancies. Jaw bones are more commonly affected than the oral mucosa in a ratio of 2.5:1. Oral region is not a preferred site for metastasis. Oral metastasis arises as a result of secondary spread from other metastatic lesions specially the lungs. In nearly 30% of cases, the metastatic lesion in the oral region is the first indication of an undiscovered malignancy at a distant site. Lung and breast carcinoma account for the majority that metastasize to oral cavity, constituting 50-60% of all such tumors. Breast cancer in females, is the malignant lesion that most frequently metastasises to the jaw bones especially to the mandible, and it is followed by malignant tumors of the lungs and the kidneys. However, breast carcinoma metastatic to the oral soft tissues is extremely rare. Because of their rarity, metastasis to oral cavity is challenging to diagnose and treat. Metastatic disease to oral cavity is evidence of widespread disease and indicates grave prognosis. We present here a case report of 44 year post menopausal lady with solitary gingival metastasis treated at our institute. Patient initially presented to us with locally advanced carcinoma right breast (cT1N1M0) and was treated with neoadjuvant chemotherapy followed by surgery and adjuvant chemotherapy and hormone therapy. Patient however defaulted on adjuvant radiotherapy. Patient remained asymptomatic for eight years and presented with right upper quadrant pain, massive nodular hepatomegaly with multiple liver metastasis and 4x3 cm asymptomatic exophytic soft tissue growth over right gingivobuccal sulcus. There was no mucosal breach , mandibular erosion or cervical lymphadenopathy. An incisional biopsy confirmed metastasis from ductal carcinoma breast. IHC was suggestive of ER/PR + and Her2/neu –ve tumor. Patient was started on palliative chemotherapy with follow up suggestive clinical response.

Keywords: gingival mmetastasis, carcinoma breast, jaw bone

Silent Mediastinal Mass in Carcinoma Breast: A Horse of another Colour

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Background- Tuberculosis and malignancy represent major health problems claiming millions of life and inflicting dreadful morbidity worldwide. Although, the simultaneous occurrence of tuberculosis and lung cancer has commonly been described in literature but the coexistence of tuberculosis and carcinoma breast is an uncommon event. The concomitant incidence of both the diseases produce clinical and radiological diagnostic challenges and may lead to delay in the commencement of radical treatment. **Case report-** A 39 years old female was incidentally diagnosed with a mediastinal mass and left breast lump during pre-anaesthetic check-up for cholecystectomy. Chest X- ray reported right hilar prominence ? Nodal mass. CECT thorax reported mass in upper, inner quadrant of left breast and a large paratracheal mass from thoracic inlet to subcarinal region. Biopsy from breast lump reported infiltrating ductal carcinoma. Whole Body PET CT scan reported metabolically active lesions in left breast (SUV- 28.7)- mitotic , left axillary lymph nodes and conglomerate lymph nodal mass in paratracheal and subcarinal locations (SUV- 24.5)- likely infective. Endobronchial ultrasound and guided biopsy from the mediastinal mass reported granulomatous lymphadenitis, AFB positive on ZN staining, consistent with tuberculosis. She was managed with breast conservation surgery followed by adjuvant chemotherapy & radiotherapy and simultaneously, antitubercular therapy was started. **Discussion-** Patients with cancer are vulnerable to develop tuberculosis because of immunocompromised status and due to use of cytotoxic drugs, further during the course of treatment. The coexistence of tuberculosis and carcinoma was first described by Boyle's in 1810 as cavitation cancereuse. Kaplan et al (1974) reviewed 58, 245 malignancy patients and identified 201 cases of coexisting tuberculosis. Highest prevalence of tuberculosis was noted in Hodgkin's disease and lung cancer followed by lymphosarcoma and reticulcum cell sarcoma. Out of 14,742 cases of breast cancer, only 28 had coexisting tuberculosis. In breast cancer cases, lymph node involvement with metastatic disease is one of the most significant prognostic factors and an accurate staging is very important before planning the management of patient. Active granulomatous infections like tuberculosis, fungal infections and sarcoidosis should also be considered in breast cancer patients as it may altogether change the intent as well as modality of treatment.

Malignant Mesenchymal Tumours of Breast : A Report on Two Cases

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Introduction: Malignant Mesenchymal Tumours of Breast : A Report on Two Cases. **Objectives:** Malignant tumors originating from mesenchymal tissue occur very rarely in the breast. It includes metaplastic carcinomas ,malignant phyllodes tumour and primary stromal sarcomas. Pure primary sarcomas are the rarest malignancies in mammary tissue. Here we are reporting two cases of malignant mesenchymal tumour. **Material and Methods:** Formalin preserved lumpectomy specimen were grossed as per CAP guidelines. Section taken were then processed, paraffin embedded blocks were prepared, and H&E stained slides were made. Later Immunohistochemistry was performed. **Results:** On histopathological examination tumours comprised of preserved duct with marked mesenchymal spindle cell proliferation showing lipoblastic differentiation in one case and undifferentiated tumour cells in another were identified. Further IHC was performed. **Conclusions:** malignant mesenchymal tumour are rare tumours of breast

Primary Atypical Carcinoid Tumor of Midgut Mesentery. A Case Report

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Primary atypical carcinoid tumor of the mid gut mesentery is a rare entity. Carcinoid tumors are slow growing tumor with neuroendocrine characteristics on histology. Carcinoid tumors most commonly arise in the gastrointestinal tract and lung, with an incidence of more than 90% of neuroendocrine tumor of whole body. Although, carcinoid tumor is the most common primary malignant tumor of the small intestine and most frequently arises in the terminal ileum. The incidence of secondary mesenteric involvement of small bowel carcinoid tumors is reported about in 40% to 80% of cases. Other than carcinoid, primary solid tumors of the mesentery are fibromatoses, neurofibromas, teratomas, germ cell tumors.

Previous reported cases of preimary mesentery carcinoid tumor are typical as histological features, herein we present a case of primary atypical mesentery carninoid tumor.

Keywords: Midgut mesentry; carcinoid; atypical

Primitive Neuroectodermal Tumor of the Kidney

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Background: Primitive neuroectodermal tumors (PNETs) are originally categorized as small, round-cell tumors of neural crest origin usually arising in the cardinal neural system (CNS). It was first reported by Arthur Purdy Stout in 1918. Later, it is reported in the peripheral organs including the genitourinary tract, testis, ovary, uterus or pancreas. These tumors are closely related to Ewing's sarcomas due to the same chromosomal abnormality: t (11; 22) (q24; q12). It can also occur as primary renal mass like other extraskeletal sites. PNET kidney is characterized by an aggressive clinical course and poor prognosis. **Objective:** Our aim is to determine the clinico-pathological features, treatment and prognostic features of primitive neuroectodermal tumor of the kidney. **Material and method:** We searched the patient's records that were diagnosed with primitive neuroectodermal tumor of the kidney between January, 2009 and December, 2014 at a Regional Cancer Centre in South India. We noted the demographic parameters, clinical features, diagnosis, treatment and follow-up of all the patients and we are presenting a case series study. **Results:** We found four cases of PNET of the kidney over the period of six years. Three patients were male and one was female with age of range 21 to 67 years. Two patients presented with heamaturia and other two with pain in loin. All patients undergoing CECT abdomen and all were diagnosed having heterogenous mass in kidney and underwent nephrectomy. One patient, 67 year male presented with advance stage. The tumors were mainly composed of small blue cells on haematoxylin and eosin staining. The pathologic findings were consistent with PNET in all cases, confirmed by immunohistochemistry with diffuse membrane positivity of CD99 in the cytoplasm of the neoplastic cells. Cytokeratin AE1/AE3, desmin, S100, chromogranin, synaptophysin, MyoD1 were negative. FISH revealed the translocation 22q12 for the EWSR1 gene 22q12 in t(11;22)(q24;q12) in all cases. Two of them were on regular follow up without any evidence of local or systemic recurrence in the absence of adjuvant treatment. One patient died within three months of diagnosis and one male patient was found to have multiple lung metastasis after 2 years of primary diagnosis and he received palliative chemotherapy.

Keywords: primitive neuroectodermal tumor; kidney tumor; round cell tumor; CD99

Epitheloid Hemangioendothelioma of Liver masquerading as GIST: An unusual Case

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Introduction: Epitheloid hemangioendothelioma (EH) is a rare neoplasm of vascular origin that may develop at different sites, such as in soft tissue, the lungs, or the liver. It usually affects adult females. Compounds such as oral contraceptive pills, poly vinyl chloride, and Thorotrast have been identified as risk factors for subsequent disease development. It has unpredictable malignant potential ranging from benign hemangioma and clearly malignant hemangioendothelioma. **Methods:** In the current study, the authors describe a patient with primary Epitheloid Hemangioendothilioma of the liver masquerading as exophytic Gastrointestinal stromal tumour (GIST) arising from pylorus of stomach. **Results:** Most patients present with nonspecific symptoms, such as right upper quadrant abdominal pain or weight loss. We present a case of this rare disease in which the tumour presented as exophytic GIST arising from Pylorus & abutting left lobe of liver which on exploration was found to be left hepatic mass. The definitive diagnosis of Epitheloid Hemangioendothelioma was based on histological evidence. Patient was managed with Left hepatectomy. This case is highly illustrative of the one of the ways in which hepatic EH can present (nodular or diffuse) and of its diagnostic and therapeutic management. In general, the key to diagnosis was the demonstration of cells containing factor-VIII-related antigen. **Conclusions:** Epitheloid Hemangioendothelioma of the liver is a very rare clinical entity & it masquerading as GIST arising from stomach is even more exceptional. The primary treatments of choice are radical hepatic resection or orthotopic liver transplantation. However, this disease seems to be resistant to chemotherapy and to be lethal in some cases. The 5-year survival of 55.5% is significantly better than for other hepatic malignancies.

Key words: Epitheloid, Hemangioendothelioma, GIST

Giant Carcinoma Ex Pelomorphic adenoma of parotid – A case report

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Introduction: Carcinoma ex pleomorphic adenoma (CXPA): carcinoma arising from primary or recurrent benign pleomorphic adenoma .It's incidence is 3.6-4% of all salivary gland neoplasms. **Objectives:** This is a case report of gaint myoepithelial CXPA- a rare subtype of parotid gland carcinoma, one of the very few reported in literature. **Material and Methods:** A 35 years old male presented with 26 x 21 cms multi-lobulated, hard, fixed, ulcerated left sided neck mass with history of pre-existing swelling below the angle of left jaw since 10 years with rapid increase in size for past 6 months and anemia. Chronic smoker with hypertension, diabetes mellitus and systolic dysfunction (ejection fraction of 35%). **Results:** The patient underwent wide local excision + parotidectomy + left modified radical neck dissection as the lesion was found to arise from the lower part of parotid. Post operative image . Immunohistochemistry revealed Myoepithelial CXPA (positive for S100, CD10 and CK) . Pathological staging was pT4aN0M0 .Post operative radiotherapy of 45 Gray given for 5 weeks as the deep margin was focally positive. **Conclusions:** CXPA of parotid though a rare malignancy of head and neck should be considered in the differential diagnosis. Careful history taking, detailed clinical examination with correlation of cytology, IHC and imaging features guide in appropriate diagnosis and management of such cases.

Complete Response in Patient of Renal Cell Carcinoma Treated with Cytoreductive Nephrectomy followed by Sunitinib

Shyam Agarwal

Sir Ganga Ram Hospital

Background: Currently targeted therapy is the standard of care in metastatic renal cell carcinoma patient. Role of cytoreductive nephrectomy in renal cell carcinoma needs to be explored in current era. **Case Presentation:** A metastatic clear cell renal cell carcinoma patient underwent cytoreductive nephrectomy. Patient was given Sunitinib post-operatively. Adverse events were manageable with dose modification. Patient demonstrated complete response after 22 months of therapy. Patient is still in excellent condition after stopping Sunitinib for more than 4 years. **Conclusion:** A case report of complete response attained with Sunitinib after cytoreductive nephrectomy.

Keywords: Complete response, Sunitinib, Renal cell cancer

Case Report of Prolonged Stable Disease with Modified Schedule Sunitinib In Metastatic Renal Cell Carcinoma

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Background: To manage toxicity, sunitinib was prescribed 2 weeks on and 1 week off in a patient of metastatic renal cell carcinoma, at dose of 37.5 mg. For more than 72 months, patient had stable disease. **Case Presentation:** A patient was diagnosed left sided renal cell carcinoma with metastatic spread to pleura and lungs. He underwent left sided radical nephrectomy and started Sunitinib post-operatively. To manage toxicities, the dose and scheduled were modified to 37.5 mg and 2 weeks of Sutent followed by one week of drug holiday. He showed significant improvement on sunitinib therapy demonstrating stable disease. He continued sunitinib for more than 72 months for reduced and modified schedule and on progression responded to increased dose with manageable toxicities. **Conclusions:** This is a case study for prolonged stable response attained with sunitinib with modified dose schedule.

Keywords: Stable disease, Sunitinib, Renal cell cancer

Unilateral Renal Metastases After Definitive Chemo-Radiation In Squamous Cell Carcinoma of Esophagus. A Case Report and Review Literature.

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Kidney is considered to be fifth most common site of metastases of esophageal carcinoma. Most of the metastatic renal tumours are bilateral but a unilateral renal metastasis is extremely rare. There are only ten cases of unilateral renal metastases after curative treatment reported in literature. Herein, a case of solitary, unilateral renal metastasis in a case of carcinoma oesophagus after definitive chemo-radiation treatment is reported.

Keywords: Carcinoma esophagus; definitive chemo-radiation; squamous cell carcinoma; unilateral renal metastases

Gall Bladder Cancer Metastasis to Cervix: A Rare Entity

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Background: Gall bladder cancer is usually diagnosed once it has progressed to advance stage either infiltrating to multiple adjacent structures or distant metastasis. Metastasis to cervix from a primary arising from gall bladder cancer is extremely rare and based on extensive literature review, only 4 cases reported till date. Here, we report a case of gall bladder cancer in a middle aged female patient along with Krukenberg tumor and Sister Mary Joseph's nodule. **Case Presentation:** A 35 years old lady presented with history of irregular menstruation for 6 months. On gynecological examination an ulceroproliferative growth involving cervix was found. Ultrasound of whole abdomen revealed a 9 x 7.6 cm right adnexal mass with thickening of gall bladder wall. CA-125 was within normal limit and biopsy of cervix reported poorly differentiated carcinoma. Then she was referred to us. On physical examination we found an infra umbilical subcutaneous hard palpable nodule which was missed earlier. CECT scan of abdomen and pelvis showed asymmetrical wall thickening at body and fundus of gall bladder, and ill defined interface with hepatic parenchyma. Two large well defined heterogeneously enhancing lobulated lesions arising from both adnexa were seen. Apart from these findings there was a small nodular enhancing lesion in umbilical region and also enhancing lesion in cervix. CA 19-9 was 590 U/ml. US guided FNAC from gall bladder mass, umbilical nodule and adnexal masses were suggestive of poorly differentiated adenocarcinoma. On IHC, tumor cells were positive for vimentin, negative for CK7 and CK20; however, strong cytoplasmic expression for CEA and strong nuclear expression for CDX2 in tumor cells was seen. On basis of imaging, tumor markers, histopathology, and IHC final diagnosis of gall bladder poorly differentiated adenocarcinoma metastasizing to cervix and adnexa as well as Sister Mary Joseph's nodule was made. Patient was started on gemcitabine and cisplatin based palliative chemotherapy. She had good response to chemotherapy and alive after 8 months of diagnosis. **Conclusion:** Gall bladder cancer is highly lethal disease with dismal prognosis and poor outcome. We highlight the role of immunohistochemistry and proper imaging to search the primary site of malignancy and plan the further management.

Non-Fdg Avid Facial Cutaneous Metastases from Carcinoma Esophagus

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Introduction: Cutaneous metastases from gastro-intestinal malignancies are rare (0.4-5%). Esophageal cancer, unlike colorectal cancer, rarely metastasizes to the skin. While there are anecdotal reports of face or scalp metastasis from carcinoma esophagus, ours is one of few series that includes both squamous cell carcinoma(SCC) and adenocarcinoma(AC). **Objectives:** To present a case series of esophageal carcinoma with synchronous or metachronous cutaneous metastases to face or scalp and analyse their clinic-pathological parameters and outcomes. **Material and Methods:** We retrospectively analysed our data from August 2014- 2015. PET-CT was done as staging work-up in all patients. Cutaneous lesions were confirmed as metastasis by biopsy, histopathological examination by two pathologists and immunohistochemistry. **Results:** Four patients of carcinoma esophagus were found to have solitary face or scalp nodules as the only site of metastases. Three were synchronous with a symptomatic primary. All patients were male smokers, 50-70 years, with performance status of 0-1. Though all PET scans were negative for systemic metastases, skin lesions were detected to be metastatic due to thorough clinical examination and subsequent biopsy before initiating therapy. All patients had intra-dermal nodules initially, without fungation - an unusual presentation. The metachronous lesion was picked up on routine follow-up in a patient who developed an asymptomatic nodule after being disease-free for 18 months following neoadjuvant chemotherapy and surgery. All patients received palliative treatment after skin biopsy confirmation. One patient died three months after diagnosis, while the remaining are still alive. **Discussion:** PET-CT scan may not be sensitive for early cutaneous lesions. A high index of suspicion coupled with a low threshold for biopsy of cutaneous lesions is warranted in locally advanced cases of esophageal carcinoma for appropriate prognostication and further intent of therapy. Cutaneous metastases from esophageal carcinoma may initially masquerade as benign face and scalp nodules and may be wrongly treated dermatologically, until they progress. **Conclusion:** The purpose of this presentation is to report esophageal metastases may present as asymptomatic skin nodules, undetected even on PET scan. All nodules, even if benign-looking should be investigated before treatment initiation. The rarity is that all metastases were confined to face and scalp.

Patient	1	2	3	4
Stage at initial presentation	IV	IV	IV	IIIA
Location of the primary	Mid-1/3	Mid-, lower-1/3	Mid-1/3	Lower-1/3
Histology	SCC	SCC	SCC	AC
Nodal status	cN+	cN+	cN+	ypN1
LVI/PNI	Not applicable(NA)	NA	NA	Yes
Location of metastases	Ala of nose	Scalp	Scalp	Forehead
Overall survival, months	3	5	6	20

Extrapelvic extension of Carcinoma Rectum - An unusual mode of spread

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Diseases arising from the pelvic organs may spread by direct extension of disease through the pelvic foramina or along the pelvic vessels and muscles and present elsewhere from the site of origin. The knowledge of these pathways of extrapelvic extension and their modes of presentation will help in early diagnosis and avoid delay in initiation of treatment. We present a case of Carcinoma rectum with progressive disease post neoadjuvant chemoradiotherapy with extension of the disease along the greater sciatic foramen and presenting as a palpable mass in the gluteal region.

Small cell carcinoma of the pancreas with temporary radiological complete response to chemotherapy consisting of CPT-11 + CDDP; a case report

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Background: In 2010, WHO classified pancreatic neuroendocrine tumor (pNET) as follows; G1, G2 and NEC according to the Ki-67 index. Chemotherapy consisting of CPT-11+CDDP has been used widely for the treatment of extrapulmonary NEC as for small cell lung cancer (SCLS) because their genetic, pathological and clinical features are very similar. But we don't know how long this chemotherapy regimen has been used for extrapulmonary NEC, though it is usually used for SCLS within 6 courses. We reported a case of small cell carcinoma of the pancreas (SCCP) with temporary radiological complete response to chemotherapy consisting of CPT-11 + CDDP over 6 courses. **Material and Methods:** A 55-year-old woman visited a hospital because of back pain. Abdominal ultrasonography revealed a mass, 25 mm in diameter, in the tail of the pancreas. She was referred to our hospital for further examination in March, 2012. A computed tomography (CT) scan revealed a low-density heterogeneous mass of 35 mm X 20 mm in size in the tail of the pancreas and multiple metastases to liver, lung and bone. We performed Endoscopic ultrasound - guided fine needle aspiration biopsy (EUS-FNAB). Histological examination revealed spindle-shaped cells with scanty cytoplasm, hyperchromatic nuclei and positively immunohistochemical staining with synaptophysin, chromogranin A and Ki-67. Pancreatic small cell carcinoma was finally diagnosed (stageIVb). **Results:** She underwent chemotherapy (repeated every 4 week) with irinotecan (60 mg/m2/day, day 1, 8, 15) and cisplatin (60 mg/m2/day, day 1). However temporally radiological complete response (CR) was achieved after 12 courses, she was finally died due to recurrence. Progression free survival and overall survival were 15 months and 26 months, respectively. **Conclusions:** Our case showed that continuing this chemotherapy over 6 courses made it more suppressed. We suggest the chemotherapy consisting of CDDP + CPT-11 over 6 courses for SCCP might be used and more effective if adverse events are acceptable.

Unusual Site of Origin of Extraintestinal Gastrointestinal Stromal Tumor – A Case Report

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Introduction: Extraintestinal gastrointestinal stromal tumors (E-GIST) are rare types of GIST most commonly involving the mesentry, omentum and retroperitoneum. Parietal wall E-GIST are very rare. Very few cases have been reported in the literature. **Case report:** 18 year female presented with pain abdomen and abdominal lump for 9 years. The mass was gradually increasing in size. On examination there was a smooth, firm mass in left upper quadrant moving with respiration. Ultrasonography of the abdomen showed 62 X 58 X 56mm well defined hypoechoic solid mass with cystic areas noted in left upper quadrant separate from solid organs. Contrast enhanced computed tomography of the abdomen showed a heterogeneously enhancing well defined spherical soft tissue density mass in the left upper abdominal cavity likely to be arising from the omentum. Trucut biopsy revealed spindle cell neoplasm and immunohistochemistry staining showed tumor cells positive for CD117. Laparoscopic resection of E-GIST was planned. Surprisingly there was approximately 6 X 5 X 4 cm mass arising from the parietal wall of abdomen without any visceral attachment . The mass was dissected from the parietal wall and delivered through a midline incision in supraumbilical region (Figure 5).Other organs were normal. Cut section showed a solid mass with central cavity. Patient on regular follow up every three months. **Conclusion:** E-GIST is a rare condition often confused with other soft tissue tumors. Early diagnosis requires a high index of suspicion in combination with different investigations.

Key Words: E-GIST, parietal wall

Management of Hepatic Encephalopathy in Advanced Cancer in the non ICU Setting

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Introduction: Metabolic encephalopathy is an important cause of delirium in advanced cancer. In the absence of any inpatient admission facility in the ICU for advanced cancer patients who are not receiving cancer directed treatment,the decision to manage hepatic encephalopathy can be fraught with many challenges. **Subjects and Methods:** The diagnosis of hepatic encephalopathy was made upon first liason after referral from the primary unit in the casualty in the setting of advanced malignancy of the hepatobiliary tract. A decision to manage the condition outside the Intensive care unit in the inpatient setting was taken given the need of the hour and the deteriorating general condition of the two patients .The Evaluation, Plan of management and subsequent outcome of these two patients along with the therapeutic challenges faced, logistical issues encountered and ethical dilemmas are discussed below. **Results:** The first patient was a case of carcinoma gall bladder with nodal and liver metastasis who had documented disease progression despite two lines of chemotherapy who subsequently underwent PTBD with SEMS and developed fever along with worsening of the jaundice and altered sensorium without any sign of hepatic decompensation. He was managed as hepatocholangiitis with hepatic encephalopathy with stent block.The second patient was a 50 year old female patient a known case of

metastatic cholangiocarcinoma with documented disease progression despite multiple lines of chemotherapy who presented with bleeding per rectum and was managed as cholangitis with stent block with hepatic encephalopathy with hepatic decompensation .A decision to optimise the patient prior to PTBD procedure was taken and she was started on pharmacological management of hepatic encephalopathy, Bowel decontamination, Broad spectrum antibiotics and fresh frozen plasma infusion along with correction of hypokalemia. **Discussion:** The first patient developed hepatorenal syndrome ,was advised inj Octreotide plus Midodrine plus albumin in the inpatient setting as infusing terlipressin without cardiovascular monitoring was not advisable. Despite a Gastroenterology referral and rigorous efforts at Bowel decontamination and adequate supportive measures he succumbed to the metabolic encephalopathy. The second patient was being prepared for a PTBD Procedure and the INR had been brought down to 1.7, but she could not survive despite institution of optimum management of Encephalopathy and Cholangitis. **Conclusion:** Better optimisation and minimisation of time lost in transferring the patient to the supportive care setting can prove vital in prolonging the patients life.The concept of a Palliative ICU is a relevant and practical measure for inpatient management of critically ill patients.

Key words: Hepatic Encephalopathy Advanced Cancer PICU

Carcinoma Prostate with Bilateral Testicular Metastases.

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Introduction: Secondary neoplasms of the testis have been reported with an incidence of 0.02% to 2.5% on autopsy. Moreover, prostate cancer metastases to the testis are rare despite the proximity. Testicular metastases generally are painless and are detected incidentally in up to 4% cases after orchiectomy for treatment of advanced prostate cancer. Less than 80 cases of prostate carcinoma with testicular metastasis have been reported so far in literature. **Case report:** Here we are present a case of 60 year old male who presented with urinary retention and back pain .USG KUB showed grade 1 prostatomegaly. CECT abdomen showed heterogeneously enhancing prostatic mass with lobulated outlines with focal loss of fat planes with base of bladder, sclerosis of D12 vertebra with lytic component and lytic lesion involving posterior half of left eighth rib. Serum PSA was 100 ng/ml. Tc-99m bone scan showed abnormal tracer uptake in D6 and D12 vertebrae and left 8th rib. TRUS-guided prostatic core biopsy showed adenocarcinoma with Gleason's score 3+4=7. He underwent bilateral orchidectomy. Histopathological evaluation of the orchidectomy specimen showed metastatic deposits of adenocarcinoma with lymphovascular emboli in both testes. Adult filarial worms were seen in the lymphatic channels. The adjascent testicular tissue was atrophied and few seminiferous tubules showed thickened basement membrane. Immunohistochemistry was strongly positive for PSA and AMACR. Serum PSA at one month post orchidectomy reduced to 7.3 ng/ml. He was treated with palliative radiotherapy to the pelvis and vertebral metastatic lesions. He had good subjective reponse to palliative radiation. **Conclusion:** The prognostic significance of testicular metastases from prostate cancer is still unknown because of the rare occurrence. To the best of our knowledge, this is the only case of bilateral tesiticular metastases from prostate cancer with co-existing filariasis.

Second-line Pembrolizumab for diffuse type gastric cancer: Report from a 29 year old patient treated in Qatar

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Background: The efficacy of second-line chemotherapy in metastatic gastric cancer is variable with an overall survival between 3 to 9 months (Mahipal A et al 2015). Promising results with Immunotherapy have been reported in this dismal disease. In the KEYNOTE-012 trial, a phase Ib study in treatment naïve metastatic gastric cancer exploring the checkpoint inhibitor pembrolizumab , progression free survival at 6 months was 24% (K Muro; GIASCO 2015). The CheckMate 032 study , a phase I/II study in pretreated upper GI cancer reported a median OS of 5 months with nivolumab. (D Le; GIASCO 2016). Here we report preliminary results of a patient with diffuse type gastric cancer treated with pembrolizumab in second line. **Clinical Presentation:** A 29-year-old female patient from Sudan without a family history of cancer underwent a sleeve gastrectomy for morbid obesity. Postoperatively an ulcer in the surgical specimen was diagnosed as diffuse type adenocarcinoma. The invasive tumour showed mild infiltration by lymphocytes of which less than 1% were positive for PD-1. Tumour cells were all negative for PD-1. Staging revealed an enlarged right-sided ovary as well as subcutaneous tumor infiltration. Given her age and pathognomic precursor lesions upon histologic review, the patient was referred for genetic counselling and mutational analysis of E-Cadherin (CDH1) was recommended. Within 3 months the patient developed abdominal pain; radiologically tumor progression was noted in the peritoneum, right ovary and subcutaneous area of the abdomen. On chemotherapy with Docetaxel, Cisplatin, 5-Fluorouracil (modified DCF) symptoms rapidly subsided. Treatment was complicated by two episodes of neutropenic fever. A partial response was achieved after three months. 8 months after treatment start there was tumor progression in the right ovary confirmed by histology. Clinically the patient remained asymptomatic.. In absence of a standard treatment option in 2nd line, unavailable clinical trials and in line with institutional procedures treatment with pembrolizumab 2mg/kg iv q3weeks was started and subsequently well tolerated. TSH assessment prior to starting the 2nd treatment revealed significant hypothyroidism for which the patient was adequately substituted with no other complaints reported. After 12 weeks (4 treatments) imaging showed stable disease and treatment continued. **Conclusion:** Second line Pembrolizumab shows activity in metastatic diffuse type gastric cancer progressing under 1st line chemotherapy with acceptable toxicity profile. Treatment is ongoing and updated follow-up will be shown at the congress.

An Unusual Case of Carcinoma Esophagus and Individualized Management

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Background: Carcinoma of middle esophagus is common cancer in India. Generally, they present in advanced stage and even after surgical resection many of them develop systemic metastases – most commonly in lungs and liver and succumb to disease. Isolated bone metastases are rare. Here, we are presenting a case of localized squamous cell carcinoma of esophagus with isolated single bone metastases and its management with long term survival. **Case report:** Fifty eight years male, presented with dysphagia of 3 months duration with some weight loss. He also has history of rt mid-thigh mild pain of same duration. On investigations, localized mid esophageal squamous cell carcinoma was diagnosed with small cyst (5 mm) in rt femur. He underwent transthoracic esopahgectomy in April 2013. Histopathology showed pT2N0 lesion and he was kept on follow up. His thigh pain continued and progressed over time. CT scan done 3 months later showed bone destructions with significant soft tissue component. Biopsy was suggestive of Squamous cell carcinoma. On PET CT scan, there was no evidence of disease elsewhere. First he received palliative Radiotherapy to thigh followed by 6 cycles of chemotherapy and then kept on follow up. On follow up, 10 months after the surgery, he developed fracture of femur at metastatic site. PET CT showed FDG avid lesion in femur only. He underwent resection of involved segment of femur with fibular graft and plating. Histopathology showed no viable tumour. Patient is doing well on follow up. **Conclusion:** Metastases

in small localized esophageal cancer without lymph node involvement are rare, but when develop is generally a death warrant to patient. Sometime individualized management approach and proper selection of cases can give good quality of life and survival to patient as happened in this case. Thus each case should be managed on its merits and demerits.

Keywords: Esophagus cancer, bone metastases, survival, individual management

Squamous Cell Carcinoma Oesophagus with Scalp Mets, A Rare Presentation: A Case Report

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Introduction: Oesophageal carcinoma is a major health problem worldwide and it has one of the highest mortality rates of all cancers. The two most common types of carcinomas arising in the oesophagus are squamous cell carcinoma and adenocarcinoma. The common sites of metastasis are lymph nodes, liver lungs and bones. Like other solid tumours cutaneous metastasis is extremely rare in oesophageal cancers especially in squamous cell carcinoma. In this case report we present a case of squamous cell carcinoma oesophagus metastasizing to scalp **Case report:** 58 year old gentleman known diabetic and hypertensive who is a chronic smoker and alcoholic presented to a hospital with progressive dysphagia of 2 months duration and loss of appetite of 1 month duration. He was evaluated with upper GI Endoscopy and it showed a proliferative growth in mid thoracic oesophagus and scope could not be negotiated beyond the lesion. Biopsy of the lesion was reported as squamous cell carcinoma. He was referred to Regional Cancer Centre Trivandrum for further management, He was evaluated with CT scan of chest and abdomen and it showed thoracic oesophageal growth with multiple liver metastasis. With the diagnosis of metastatic squamous cell carcinoma he was started on palliative chemotherapy with Cisplatin and 5FU.After 3 cycles of chemotherapy there appeared a 2*2 cm firm swelling in his scalp. CT scan done showed a deposit in scalp on right side.FNAC from the lesion was suggestive metastasis from squamous cell carcinoma. Due to the incidence of bleeding from the scalp lesion and occurrence of severe pain he was given palliative radiation to scalp using electrons. After 4 cycles of chemotherapy reassessment scan showed a response but dysphagia was persisting. He was then treated with palliative short course radiation to the primary lesion. **Conclusion:** This case reports shows a very rare presentation of squamous cell cell carcinoma oesophagus with metastatic deposit in scalp.

Key words: squamous cell cell carcinoma oesophagus, scalp metastasis, cutaneous metastasis

Rectal Leiomyosarcoma Mimicking as a Pararectal Gist : A Case Report

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Background: Rectal leiomyo sarcomas are rare tumors originating from smooth muscle cells. Differential diagnosis includes Gastrointestinal Stromal tumors (GIST), leiomyomas or schwannomas, and the differentiation of these tumors is usually made through immunohistochemistry. Due to its rarity, the standard treatment has not been defined. **Materials and Methods:** A 55 year old gentleman came with presenting complaints of bleeding per rectum and tenesmus. A CT scan Abdomen and Pelvis was ordered which showed a rectal mass occluding the lumen. Colonoscopic biopsy was suggestive of leiomyosarcoma of rectum and the Immuno Histo Cytochemistry was negative for c – KIT and thus excluding GIST and positive for smooth muscle actin ,desmin and CD -99 favoring leiomyosarcoma. The patient was managed with Abdominoperineal Resection and permanent end colostomy. The patient was discharged without any complications on postoperative day 7th. **Results**: The patient had an uneventful postoperative course and was discharged on 7th postoperative day without any abdominal and urinary complications. Histopathological analysis of the full specimen revealed a grade 3 leiomyosarcoma, $10 \times 9 \times 7 cm^3$ in size, with free mucosal resection margins. The mitotic count was 5 per 10 high-power fields, and an area of necrosis was identified. The tumor cells had characteristically elongated, pleomorphic, and blunt-ended nuclei and eosinophilic to pale cytoplasm . On immunohistochemical staining, the tumor cells were positive for smooth muscle actin, desmin, and CD99 but negative for S-100 protein and CD34, consistent with a diagnosis of rectal leiomyosarcoma. On follow up after 3 yrs the patient is having no problems with the stoma functions and is leading a normal life without any evidence of the disease recurrence right now in imaging and clinical examination. **Conclusions**: The rectum leiomyosarcoma is a very very rare entity which can be on imaging or clinical examination can easily mimick a pararectal GIST and thus can alter management strategies.If IHC is made use of then it can be but can be dealt with easily with surgery like Abdomino Perineal Resection or a local wide excision pararectally with an excellent survival.

Key Words : Rectal leiomyosarcoma , Abdominoperineal Resection , Immuno HistoChemical staining.

Non functioning Neuroendocrine tumour of pancreas in a 14 year old child- A rare case report

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Introduction: Pancreatic NETs are rare subgroup of pancreatic tumors and represent about 1-2% of all pancreatic neoplasms. The incidence and prevalence of overall NETs has increased substantially Neuroendocrine tumors (NET) account for approximately 25% of pediatric pancreatic masses. NET arise from endocrine tissues of the pancreas and are classified as either non-functioning or functioningPancreatic tumors in children rarely present with biliary obstruction, owing to the expansive rather than infiltrative growth patterns of the common pediatric pancreatic neoplasms. **Objectives:** To study the varied presentations of Pancreatic Neuroendocrine tumour and importance in consideration as a differential in pancreatic head masses. **Material and Methods: - -** A 14 year old male child presented t with 2 episodes of convulsions and loss of consiousness for 2 hours. On history, the child had intermittent jaundice since 6 months .CT scan showed a 4*4.3*4.3 cms resectable mass in head and uncinate process of pancreas . Total bilirubin was 5.2mg/dl with direct of 4.1mg/dl.EUS FNA revealed a Well differentiated neuroendocrine tumour Grade I/II infiltrating the duodenal wall .MRI Brain showed a Fronto temporal infarct in the left lobe and on investigations, no specific cause could be ascribed for the brain infarct .Conservative management was done for the infarct and the patient improved without any sequelae.Endocrinal workup revealed non functioning tumour. **Results:** Patient underwent a Whipples procedure for the mass, the histopathology was confirmatory for Neuroendocrine tumour of head of pancreas (IHC Chromogranin,Synaptophysin positive) with free resection margin.Post operatively , the recovery was uneventful and the patient is on regular follow up. **Conclusions:** Pancreatic tumors in children and adolescents are rare. Pancreatic NETs only represent 25% of these neoplasms. Unlike adults, these tumors rarely present with biliary obstruction and have a good prognosis if complete surgical resection can be achieved,hence should be kept as strong differential . Overall survival is significantly better among children with localized disease compared to those with distant spread.

Metastatic gall bladder cancer masquerading as myositis

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Background: Gall bladder cancer has one of the worst prognoses among hepatobiliary cancers. Metastatic spread usually involves lymph nodes and liver. Reported unusual sites include brain and bones. There have been no reports of metastasis to skeletal muscles. **Case report:** A lady aged 55 yrs presented with diffuse painful swelling of the right thigh for 2 months. She was managed as a case of myositis prior to presenting at our institute. On further workup there was diffuse enhancement on T2W MRI of the anterior compartment muscles of right thigh. A core needle biopsy showed metastatic carcinoma. A thorough search for the primary revealed a gall bladder mass which turned out to be adenocarcinoma. With a poor performance status patient was deemed unfit for chemotherapy and received supportive care. **Discussion:** This case highlights a very unusual presentation of a deadly malignancy. To our best knowledge this represents the first case of its kind in literature.

Keywords: carcinoma gall bladder, muscle metastasis.

Duodenal Obstruction Caused by Urinary Bladder Metastasis: A Case Presentation With Review of Literature

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Introduction: Bladder cancer is the most common malignancy of the urinary tract. The majority of patients present with lower urinary tract symptoms or painless hematuria. Initial presentation with metastatic disease is rare. To date, only few cases of duodenal obstruction caused by bladder cancer has been reported in the indexed literature. Here we describe a rare presentation of duodenal obstruction caused by retroperitoneal metastasis with fibrosis from carcinoma urinary bladder metastasis which lead to duodenal obstruction at the level of third part of duodenum. **Case report:** We report a case of 50 year old male who presented to us with history of bilious projectile vomiting, abdominal distension and weight loss since last 2 months. He doesn't have any classical symptom of carcinoma urinary bladder like lower urinary tract symptoms or painless hematuria. On examination he was dehydrated, palpable stomach with a succussion splash in the upper abdomen. On Digital rectal examination patient had the hard nodular prostrate. On Radiological imaging it demonstrated over distended featureless stomach with large air fluid level without any obvious obstructing mass lesion around duodenum, mild diffuse mesenteric and retroperitoneal fat stranding with multiple subcentric mesenteric & retroperitoneal lymph nodes and mild bilateral hydroureteronephrosis with mural thickening of urinary bladder. Upper GI endoscopy demonstrated normal dilated first and second part of duodenum but there was no abnormality in gastric and duodenal mucosa however they failed to comment on third part of duodenum or beyond it. Cystoscopy revealed the proliferative growth from the left posterior wall of bladder, from which biopsy was taken which showed transitional cell carcinoma. Tru cut biopsy from the prostrate showed the transitional cell carcinoma. After a preoperative preparation, exploratory laparotomy with a midline incision was done. Intra operatively, Stomach and first & second part of duodenum was dilated, retroperitoneum fibrosis was present with multiple subcentric mesenteric and retoperitoneal lymph nodes. Small nodular growth was palpable in the left posterior wall of urinary bladder. There was no ascites and metastasis to other solid organs. In view of advanced stage palliative surgery, antegrade gastrojejunostomy was done to relieve the duodenal obstruction with multiple biopsy from the retroperitoneal tissue and sampling of mesenteric and retropertoneal lymphnode was under taken. Histology from retroperitoneal tissue demonstrated the transitional cell cancer. Post operatively patient developed deep vein thrombosis and later succumbed to pulmonary embolism. **Conclusions:** Lymph nodes, bones, lung, liver, and peritoneum are the most common sites of metastasis from bladder cancer. Secondary involvement of retroperitoneal nodes around the duodenum is common in metastatic disease, but causing duodenal obstruction is not. Few case reports of duodenal obstruction secondary to metastases from ovary, testis, prostate, colon, caecum, and synovial sarcoma do exists. Patient presenting at advanced stage of carcinoma urinary bladder generally presents with LUTS or hematuria. Atypical initial presentation due to liver and lung metastasis are rare. Carcinoma urinary bladder with retroperitoneal metastasis presenting as duodenal obstruction is extremely rare entity.

Keywords: duodenal obstruction, urinary bladder metastasis, retroperitoneal fibrosis

Nsaid (Diclofenac) Induced Apoptotic Colitis-A Case Report and Review of Literature

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Objective:- Colon can be involved by a variety of etiological agents like infection (bacterial or viral), parasitic (entamoeba), idiopathic (Inflammatory bowel disease -Crohn's disease or ulcerative colitis), ischemic colitis and various drugs. The patient usually presents with pain abdomen, bleeding per rectum and diarrhea. Colonoscopic examination shows erosions,ulceration and strictuers involving the colon and colonic biopsies are usually taken for histopathological diagnosis. Sometimes histopathological findings may show unusual morphological findings which may help in making a diagnosis. Here we describe one such case of drug (NSAID) induced colitis. **Methods:-**A 75 year old female presented with diarrhea and bleeding per rectum for last one year. On colonoscopy there were multiple ulcers present in left colon. Histopathological examination showed multiple colonic fragments with maintained crypt architecture. The lamina propria showed dense mixed inflammation rich in eosinophils with focal areas of hyalinisation. Some of the crypts showed partial loss of lining epithelium and some showed flattening of epithelium. In addition many crypts showed apoptosis with cytoplasmic and nuclear remnants.The cypts showed reactive atypia with mitotic figures.Crypt abscesses were also seen. No basal plasmacytosis, crypt distortion, crypt branching,granuloma or infectious organisms seen. **Results:-** Based on these histopathological findings a detailed clinical history was taken including drug intake.She was suffering from osteoarthritis for last 5 years and was taking NSAIDs (Diclofenac) since last three years. No history of organ transplantation was present. Finally, a diagnosis of diclofenac induced apoptotic colitis was made based on clinical and histopathological findings. **Discussion:-** Colon can be affected by variety of drugs which may cause colitis.The drugs commonly cause colitis includes mycophenolate, antimetabolites, TNF-inhibitors, colchicine, taxane, NSAIDs etc. These drugs can produce different pattern of injuries like focal active colitis, chronic colitis,apoptotic excess, dilated damaged crypts, erosions,stenosis, epithelial atypia, increased mitotsis and malakoplakia etc[4]. The presence of increased apoptotic bodies (normal <1 per 20 crypts) should always raise the possibility of apoptotic colitis which is commonly associated with graft versus host disease or mycophenolate mofetil, an immunosuppressive drug used in organ transplantation. Rarely, NSAIDS can cause increased crypt apoptosis resulting in apoptotic colitis. A study by Lee et al[1] showed increased apoptosis in NSAID induced colitis. Also in this biopsy, there was focus of laminal propria hyalinization and withered appearance of the crypts, suggestive of ischemic etiology. This could be related to vasoconstriction by NSAIDs because of inhibition of prostaglandin synthesis. Hence , a drug history (NSAID ingestion) should always be considered in the differential diagnosis of colitis in patients who present with lower intestinal symptoms(diarrhea, abdominal pain, anemia etc) with or without radiologically demonstrable lesions. **Conclusion:-** Biopsy sampling is mandatory in cases of colitis and we should always take history of drug intake in patients presented with colitis having unusual morphological features on biopsy.Because rapid therapeutic response can be achieved on discontinuation of NSAID.

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Primary Carcinoma of the Cystic Duct: An Extremely Rare Malignancy. Case & Review.

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Introduction : The incidence of extrahepatic bile duct malignancies is about 2-3.6% of all gastrointestinal malignancies. Primary carcinoma of cystic duct is an extremely rare condition comprising a fraction of all extrahepatic bile duct malignancies. Early diagnosis can be difficult and if accidentally detected may add to surgeon's dilemma. **Case summary :** A 65 year old average built female presented to surgery outpatient department for recurrent right upper abdominal pain for last 3 months. General physical examination, abdominal examination and laboratory parameters were essentially normal. Ultrasonography showed gall bladder distended with multiple small stones (ranging 2-5mm), normal common bile duct, no mass or lymph nodes. Magnetic resonance imaging revealed mucocoele of GB and no other significant findings. Patient was taken up for elective laparoscopic cholecystectomy. During surgery a hard structure (stone/node) was found at cystic duct-common bile duct junction which was not amenable for clear dissection. The procedure was converted to open and the patient underwent extended cholecystectomy with resection of CBD with Roux-en-Y hepaticojejunostomy with regional lymphadenectomy. The patient made uneventful recovery and is doing well after 1.5 years of surgery. On section cystic duct showed a polypoidal, solid growth projecting into the lumen of CBD. Histological examination of the growth revealed moderately differentiated adenocarcinoma arising from duct epithelium and protruding in the lumen. **Discussion :** Primary carcinoma of the extrahepatic biliary tree has an incidence of 0.14% of all malignancies with commonest site as the CBD (40.1%) whereas primary carcinoma of cystic duct is extremely rare. The primary carcinoma of cystic duct is predominant in males and gallstones are less often associated, being found in only 25% of the cases. It is proved that inflammation of the biliary duct epithelium due to irritation from reflux and stasis of pancreatic juice and bile leads to malignancy over a period of time. However the risk factors for carcinoma of cystic duct are unclear. Its clinical presentation is nonspecific and mostly is similar to biliary calculus disease. The tumour is either discovered at laparotomy or on histopathological examination of the specimen. Farrar's first described diagnostic criteria for primary carcinoma of cystic duct. i) growth restricted to the cystic duct, (ii) absence of neoplastic process in the GB, hepatic, or CBD, and (iii) histological evidence of carcinoma. The new classification(s) defines carcinoma of cystic duct as a tumor with its center located in the cystic duct. Prompt surgery with en bloc resection of gallbladder, cystic duct, common bile duct and regional lymphadenectomy is the mainstay of treatment.

Keywords : Carcinoma of cystic duct; Adenocarcinoma; Common Bile Duct (CBD); Magnetic Resonance Imaging

Combined Hepatocellular cholangiocarcinoma-Clinical and Imaging Findings

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Introduction: Combined hepatocellular-cholangiocarcinoma (cHCC-CC) is a rare variant of primary hepatic cancer, with the reported incidence varying between 0.4 and 4.7%. Limited literature in the form of case series and reports are available. The demographic and clinical profile of cHCC-CC is intermediate between CC and HCC with a more aggressive behavior and poorer dismal prognosis than either HCC or CC . Thus it is important to familiarize with this unique and rare entity. We present 2 such cases who reported to our hospital for management. **Material/Methods and Results**: Case 1- A 36 years old male, symptomatic for 2 months presented to us with large bowel diarrhoea , anorexia and weight loss for 2 months. There were no complaints of pain abdomen, jaundice, gastrointestinal bleed , ascitis and fever. Patient was a non-alcoholic, non smoker with no history of diabetes or hypertension. On examination, he was anicteric, had hepatomegaly and no ascites. Spleen was not palpable. Laboratory investigations showed a hemogram of 12.7 g/dl, Total leucocyte count (TLC) of 8000/cmm, platelets=187000/cmm , prothrombin time(PT) of 14/13 secs, Serum bilirubin(S.Bil) 0.7 mg/dl, AST/ALT=21/55 IU/ml, serum alkaline phosphatese(SAP) 584 U/L, Total protein(TP)/ Serum albumin (S.Alb)=7.2/4.4 g/dl. His serum alphafetoprotein(AFP) was normal(6.35 ng/ml), CA 19-9 was 26.2 ng/ml . Markers for hepatitis B/C were negative and endoscopy normal. Ultrasound abdomen (US) revealed multiple hepatic masses with no features of chronic liver disease (CLD). Multiphasic MRI liver revealed the masses were hyperintense on T2w sequence, showing peripheral enhancement in the arterial phase (AP) which gradually increased in the venous phase (VP) and the enhancement was retained in the central part of the mass with peripheral washout in the delayed phase (DP). Case 2- A 23 years old female complained of right upper quadrant abdominal pain for 4 months, mild to moderate in intensity, nonspecific in nature and non-radiating. There was no history of anorexia, weight loss, gastrointestinal bleed, ascites or encephalopathy. She had jaundice 4 years back. On examination apart from diffuse hepatomegaly there was no other positive finding. Laboratory investigations revealed Hb12.8 g/dl, TLC=7900/cmm, Platelets=151000/cmm, S. bil 0.77 mg/dl, AST/ALT was 51/14 IU/ml, SAP=215 U/L and TP/S. Alb 7.2/3.4 g/dl. He was positive for hepatitis B (HBsAg positive, HBV DNA=28000 IU/ml and serum AFP was elevated (1810 ng/ml). Upper gastrointestinal endoscopy showed no oespohageal varices. Abdominal US revealed a large right lobe hepatic mass with no features of CLD. MRI liver showed a multiple variable sized masses in both lobes of the liver exhibiting peripheral enhancement in AP and progressive heterogeneous enhancement in the VP and DP. Biopsy from the hepatic mass in both these patients was suggestive of cHCC-CC classical type. The first patient was started on Sorafenib and responded well whereas the second took therapy for hepatitis B only and refused oral chemotherapy. **Conclusion:** cHCC-CC is a rare entity and should be suspected when atypical imaging findings are encountered and the diagnosis is always confirmed on histopathology. Accurate diagnosis and aggressive treatment planning can are vital in appropriate patient management.

Can be the Right Kidney be Salvaged in the Surgical Management of Leiomyosarcoma of the the Inferior Vena Cava. A Case Report

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Introduction: Leiomyosarcomas are mesenchymal tumours most commonly seen in the retroperitoneum and the uterus [1]. In the vasculature it has predilection for the venous system. These are most commonly seen in middle aged females in the mid segment of the IVC [2]. Only about 200 cases have been reported in literature since 1871 [3]. Symptoms are

nonspecific and may precede the diagnosis by many years [4]. Diagnosis is challenging as patients present with non specific complaints such as dyspnoea, malaise,weight loss, abdominal or back pain [4]. Computer tomography (CT), Magnetic resonance imaging (MRI) individually or in combination with cavography, ultrasound (US), and echocardiography, allow an early and accurate preoperative diagnosis[4]. Curative surgical resection is the choice of treatment for primary leiomyosarcoma of the IVC. We describe an unusual case of primary leiomyosarcoma of the IVC which was unique because we could salvage right kidney despite IVC resection. **Case Report:** A 70 year old male patient presented with vague abdominal discomfort of one year duration. Physical examination was normal. Our patient had been taking symptomatic treatment underwent an ultrasound of the abdomen which detected a mass in the retroperitoneum with mixed echogenicity, following which a CT scan of the abdomen with intravenous contrast was performed which revealed a 10.5 X 6 X 6 cm lobulated heterogeneously enhancing luminal mass with necrotic changes in the retrohepatic and supra-renal inferior vena cava (segment I &II). Surgical excision of the tumour was planned. On exploration a 10 X 6 cm mass was palpated in the suprarenal IVC extending to the left renal vein ostium with development of collaterals. En bloc resection of the tumor with 1cm cuff of IVC with closure of the lower end of IVC was performed with excision of a cuff of the liver which was adherent to the IVC. Reversed saphenous vein graft was anstomosed between the right renal vein to lower end of IVC in an end to side fashion. Histopathology revealed tumour mass composed of spindle cells arranged in sheets and fascicles. Tumour cells showed nuclear atypia with increased N:C ratio, hyperchromatic nuclei and significant mitotic activity (10-15 mitotic figure/ 10 hpf in cellular area). The tumour cells were immunopositive for smooth muscle actin , desmin, KI-67 (positive, 12-15%) , CD 34 (focal weak positive) and negative for S100 , consistent with Leiomyosarcoma. **Conclusion:** Leiomyosarcoma of IVC is an extremely rare entity. Patients often present with non-specific symptoms. Various imaging modalities have allowed early diagnosis, staging, treatment planning and subsequently better outcomes. Both the kidneys can be preserved with careful planning as was in our case where we avoided a right sides nephrectomy and created an anastomosis between the right renal vein and the infrarenal inferior vena cava with a reversed great saphenous vein graft. This procedure has not been reported in literature till date.

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Rare Site Metastases from Prostatic Carcinoma – A Showcase

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Objectives: Prostate-specific membrane antigen (PSMA) is a cell surface protein with high expression in prostate carcinoma. Our extensive experience with Glu-NH-CO-NH-Lys-(Ahx)-[(68)Ga(HBED-CC)]((68)Ga-PSMA) has shown various uses for this tracer in clinical setting for staging, response evaluation, restaging and pre radioligand therapy evaluation in prostate cancer. PSMA PET can detect tumor and metastatic lesions with high sensitivity, specificity and accurate lesion detection with high contrast images. **Methods:** We routinely performed Ga68 PSMA PET with contrast enhanced CT imaging for staging, restaging, pretherapy evaluation and treatment response evaluation at our centre. 3 mCi Ga68 PSMA was injected and whole body PET imaging was performed 60 minutes post injection. **Results:** In this presentation, we showcase a collection of four cases with rare site metastases to brain, radius, penis and breast from carcinoma prostate detected on PSMA PET imaging. **Conclusion:** A review of published literature shows an overall incidence of <5% for each of these metastatic sites in carcinoma prostate patients. Metastatic sites of carcinoma prostate can be detected with high sensitivity and specificity with PSMA PET imaging.

Renal Cell Carcinoma Presenting as Solitary Bone Metastasis

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Introduction: Renal cell cancer (RCC) is among the 10 most common cancers in both men and women. It comprises 2-3% of all malignancies . Approximately one third of patients with newly diagnosed RCC have metastatic disease at the initial presentation. Metastases to bone occur in 35% to 40% cases, second in prevalence of metastases to the lungs. These metastases are highly destructive and hypervascular which are difficult to manage. Compared to other types of carcinoma frequently affecting bone the prognosis of RCC is better than for lung cancer. The main reason for the poor prognosis is the poor response of RCC metastases to radiation and chemotherapeutic regimens. Here we present a case of clear cell RCC metastatic to bone which was clinically misdiagnosed as giant cell tumor. **Case Report:** A 55 year old male presented to orthopaedic OPD of our institute with progressively increasing swelling on dorsum of hand since 6 months. Swelling was approximately 4x3 cm, diffuse and non tender. Overlying skin was free. There was no associated disability of hand movements. Before presentation, he was in usual state of health. He had no history of trauma. X-ray was performed and revealed a lytic lesion in the distal end of left second metacarpal. It was suggestive of giant cell tumor. Biopsy was received in our department for confirmation. On microscopy, tumor cells with abundant clear cytoplasm and hyperchromatic nuclei were seen, favoring clear cell neoplasm. On immunohistochemistry, these tumor cells were cytokeratin, vimentin and CD10 positive. Based on above findings, diagnosis of metastastic clear cell RCC was made. Ultrasonography of abdomen and pelvis was advised, which revealed 2 cm hyperechoic lesion on upper pole of right kidney and the diagnosis of RCC was confirmed. **Discussion:** The majority of RCCs are sporadic. The clinical manifestations vary, but classic manifestations include hematuria, flank pain, and a palpable abdominal mass; however, more than 60% of RCCs are discovered incidentally because of the increased use of abdominal imaging. The mechanisms responsible for tumor growth in bone are complex and involve tumor driven stimulation of the osteoclasts, osteoblasts and other components of the bone microenvironment. Contrary to the pattern in some other tumor types such as prostate cancer, bone metastases from RCC are predominantly osteolytic and associated with bone destruction. Skeletal involvement is commonly an aggressive, lytic process which causes substantial morbidity through skeletal related events (SREs), defined as a pathological fracture, surgical intervention, requirement for palliative radiotherapy to bone, spinal cord compression or hypercalcemia. Surgery is the primary treatment of skeletal metastases from renal cell carcinoma, because radiation and chemotherapy frequently are not effecting the survival. **Conclusion:** RCC is usually not included in the differential diagnosis in patients with osteolytic lesions of small bones. This rare case suggest that metastasis from RCC may be considered in the lesions with morphology conforming to clear cell neoplasm when no other primary tumor is found. In such cases early diagnosis is helpful in preventing most devastating complications seen in advanced stage of this malignancy.

Extra mammary Paget's disease of vulva - a case report

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Extra mammary Paget's disease (EMPD) is a rare condition involving the vulva, anogenital region and axilla. Vulvar disease usually presents as a slow growing well defined itchy plaque with crustations or ulcerations over the affected area in postmenopausal women. Well established guidelines for diagnosis and management are not available for this rare condition. Our patient is a 64 year old postmenopausal woman with a history of similar complaints of 2 years duration, not responding to multiple topical treatments. She was diagnosed with EMPD on incisional biopsy and treated with surgery at our centre.

A Case Report on Adenoid Cystic Carcinoma of Uterine Cervix: A Rare Occurrence

Adenoid cystic carcinoma constitutes around 0.5%-2% of all carcinomas of uterine cervix. It usually presents in elderly age group. Very few cases have been reported in young age group. Adenoid cystic carcinoma is a rare variant of adenocarcinoma cervix. It is a locally aggressive tumour which is capable of distant metastasis in its early stage. This is a case report of Adenoid cystic carcinoma of uterine cervix, Stage III that was successfully operated upon and followed by radiotherapy.

Key words: Adenoid cystic carcinoma, Adenoid basal carcinoma, adenocarcinoma, metastasis, uterine cervix

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Introduction: Adenoid Cystic carcinoma is also called cylindroma is most commonly seen in salivary glandand respiratory tracts. Adenoid cystic carcinoma of uterine cervix is found rarely and it resembles Adenoid cystic carcionoma of salivary glands histopathologically. It constitutes 0.5-2% of all carcinomas of cervix .In this case report Adenoid cystic carcinoma of an elderly woman is presented who was treated successfully with no recurrence or metastasis of the tumour. **Case Report:** A 62 year old elderly woman, Gravida-5, para-4 was admitted to Patna Medical College & Hospital, Patna with complaint of genital bleeding for 10 days. On per speculum examination: The portio had a grayish white cauliflower like growth that infiltrated anterior wall of vaginal fornix. Bimanual and rectal examination revealed that the tumour had infiltrated to both sides of parametrium and left pelvic bone as well.Cervical punch biopsy was performed and the specimen was sent for histopathological examination. The histological findings showed round nests of basaloid cells that were arranged in cribriform pattern having eosinophilic homogenous secretions. Immunohistochemistry was performed that showed that tumour cells were positive for CK17,CK19, Pancytokeratin but were negative for CK. Chest X-ray, Abdominal imaging, GI endoscopy and cystoscopy revealed no findings of metastasis to other organs or lymph nodes. Tumour markers like CEA, EMA were within normal limits. Patient was diagnosed to be suffering from Carcinoma Cervis Stage III .The tumour was surgically removed and followed with radiotherapy .On follow up-patient was well without any evidence of recurrence of tumour or any distant metastasis after 5 year of treatment. **Discussion**: Irrespective of its anatomic location, Adenoid cystic carcinoma has a characteristic histological appearance[1]. Its common sites of occurrence are salivary glands, respiratory tract, nasopharynx, nasal sinuses and lacrymal glands. It is a highly aggressive tumour capable of local and distant metastasis. Uterine cervix is a rare location for Adenoid cystic carcinoma[2].Grossly it usually has a solid appearance and an infiltrative pattern of growth. Histologically typical adenoid cystic carcinoma has cribriform pattern with nests and columns of cells arranged concentrically around glandlike spaces(pseudocysts) filled with homogenous eosinophilic Periodic acid-Schiff(PAS) positive material. There is presence of both true and false glandular lumina which is required to make a diagnosis of adenoid cystic carcinoma[3]. The different patterns of growth in adenoid cystic carcinoma are tubular(most common), solid and sclerosing. It is mostly associated with neural invasion.The main ultrastructural features of Adenoid cystic carcinoma are pseudocysts, intercellular spaces, abundant basal laminn and true glandular lumens. The cell types present combine features of intercalated ducts, myoepithelial cells, secretory cells and pluripotential reserve cells. Immunohistochemically tumour cells are positive for keratin, lysozyme, CD117. T. **Conclusion:** Adenoid cystic carcinoma is a very rare carcinoma reported at uterine cervix notorious for its local recurrence and metastasis to distant organs. A radial surgery with chemo-radiotherapy is the.

Isolated Clavicular Metastasis in a Patient with Endometrial Adenocarcinoma

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Endometrial adenocarcinoma metastasizing to bones is rare, and isolated metastasis to clavicle is even more uncommon. We report a case of a 60-year-old woman diagnosed with endometrial adenocarcinoma found to have isolated metastasis to the clavicle during adjuvant radiotherapy. Following radiation therapy to the clavicle, patient was started on injection zoledronic acid. She was then planned for chemotherapy comprising of paclitaxel and carboplatin for six cycles. Due to lack of compliance, 5 months after the initial diagnosis, she developed severe dyspnea due to disease progression and expired. We hereby discuss the treatment options as well as review the literature of prior published reports on endometrial adenocarcinoma with bone metastasis.

Establishment of Primary Culture of Ovarian Cancer Cells from Ascites and Tumor Tissue to Detect Chemoresistance

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Background: Ovarian cancer is the second most common gynecological malignancy in the world, with very high mortality. Surgery and chemotherapy is the mainstay of treatment, however, recurrence is common as most patients are resistant to first line drugs, namely platinum compounds and taxols. Establishing primary cultures from patient sample and using them for in vitro testing of drug resistance may help us in selecting the best combination for individual patients. **Methodology:** Ascitic fluid along with corresponding primary tumor tissue was collected from ten untreated epithelial ovarian cancer patients. Expression of p53, Survivin, Bcl-2 and Bcl-xl was seen by immunohistochemistry. Five primary cultures were established from ascites and tissues obtained from untreated ovarian cancer patients in MCDB 105 and M199 medium (ratio 1:1). IC50 doses of curcumin, carboplatin and paclitaxel for the five primary cultures were determined by MTT assay. Ovarian cancer cells were treated with graded dose of curcumin, carboplatin and paclitaxel singly and in combinations. Combinations were fixed at three different grade; 1/4th IC50, ½ IC50 and IC50 doses of Curcumin (6.25, 12.5, 25 μM) , carboplatin (12.5, 25, 50 μg/ml) and paclitaxel (1.25, 2.5, 5μg/ml). The percentage of cell survival was determined by MTT. All experiments were done in triplicates. Isobologram analysis was done for the combination treatment. **Result:** Bcl-2 ($p=0.018$), Bcl-xl ($p=0.176$, not significant), Survivin ($p=0.043$) and mutated p53 ($p=0.018$), were overexpressed in ascitic cells as compared to primary tumor tissue. There was a wide variation in response of individual primary cultures to treatment with the chemotherapeutic agents. Curcumin by itself was as good as carboplatin or paclitaxel in inducing apoptosis in the primary

ovarian cancer cells. Combination of curcumin with paclitaxel or carboplatin was found to be synergestic by isobologram analysis. **Conclusion:** Primary cultures of ovarian cancer cells can be used to personalize treatment offered to ovarian cancer patients based on their molecular profile and response to in vitro treatment with chemotherapeutic agents. Curcumin has the potential to increase sensitivity of ovarian cancer cells to paclitaxel

Retro Conversion of Immature Ovarian Teratoma To Mature Teratoma - A Case Report

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Background: Immature teratoma represents 3% of all teratomas, 1% of all ovarian cancers and 20% of malignant ovarian germ cell tumors. It is found either in pure form or as a component of a mixed germ cell tumour. Although testicular germ cell tumors and their association with chemotherapeutic retroconversion have been reported at a substantial rate of 2%-8% in the literature, the retroconversion of immature ovarian teratoma to mature teratoma is quite uncommon. **Case report :** A 24 year , nulliparous woman was evaluated for lower abdominal pain and loss of weight in 2004 and was found to have right tubo ovarian mass with elevated beta HCG and Alfa fetoprotein levels. She underwent laporotomy and mass excision. The histopathological examination of the specimen revealed an immature grade III teratoma. She received six cycles of bleomycin,etoposide,cisplatin adjuvant chemotherapy in 2004. she was not on regular follow up. In September 2015 antenatal scan showed multiple peritoneal deposits, and was further evaluated with CECT abdomen showed multiple peritoneal deposits with calcifications with normal serum markers. She underwent secondary cytoreductive surgery .The histopathological examination revealed mature cystic teratoma with mature glial tissue. Post operative period is un eventful. **Conclusions**: Chemotherapeutic retroconversion is rarely seen in ovarian germ cell tumors. CT appearances of retroconversion of immature ovarian teratoma , which is an important radiological diagnosis to make in order to avoid confusion with advancing malignancy. The phenomenon of maturation seems to be of a good prognosis as compared with those where the teratomas stayed immature.

Clinico-Pathological Characteristics and Prognostic Factors of Synchronous Primary Endometrial and Ovarian Cancers- A Single Institute Review Of 35 Cases

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Introduction: Synchronous primary endometrial and ovarian cancers are uncommon and occur in about 10% of women with ovarian cancers and 5% of women with endometrial cancers. They are often misdiagnosed as stage III of endometrial cancers or stage II of ovarian cancers. Synchronous primaries of endometrium and ovary have a better prognosis than either disease with metastasis. **Objectives:** The purpose of the present study is to describe the clinicopathological characteristics and prognostic factors of women with synchronous endometrial and ovarian cancers. **Material and Methods:** A retrospective study was carried out on 35 case of pathologically proven synchronous endometrial and ovarian cancers diagnosed between January 2008 and December 2015. Uterine sarcomas, carcinosarcomas, borderline ovarian tumors, sex-cord stromal tumors and germ cell tumors of ovary were excluded so were the patients who had received chemotherapy or radiotherapy prior to surgery. 3 year PFS and OS were calculated by Kaplan-Meier method. **Results:** The mean age of patients was 48.5 years (range 27-75 years). The mean BMI was 28.9 (range 21-37). Eleven patients were nulliparous. Co morbidities were present in 16 patients. 13 patients were postmenopausal. The main presenting symptoms were AUB in 14 patients, associated with abdominal pain or mass or distension in another 7 patients, with symptoms in other patients being abdominal mass or pain or distension. All the patients underwent surgical staging with debulking in advanced cases. Both endometrial and ovarian counterparts were stage I in 17 patients, both were grade I in 11 patients and both had Endometrioid histology in 16 patients. Ten patients did not receive adjuvant treatment, 23 patients received adjuvant chemotherapy while 2 patients received CT followed by RT. Over a follow up period of ranging from 3 – 85 months, recurrence developed in 10 patients and 5 patients died of disease. The 3 year DFS in this study is 68.5% and the 3 year OS is 88%. **Conclusions:** Synchronous primaries of endometrium and ovary are uncommon. They usually occur in young, obese, premenopausal women and are usually early stage and low grade at presentation. They have better prognosis compared to stage IIIA endometrial cancer or stage IIA of ovarian cancer.

Case Report of Vaginal Melanoma

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Primary malignant melanoma of vagina is a rare disease with a predilection for local recurrence, distant metastasis and short survival time. Due to the low incidence and lack of reporting in the literature, treatment choices still remain controversial. We describe 2 cases of vaginal malignant melanoma. A 42yr old female presented with complaints of post coital and per vaginal bleed of 1 month duration. Examination findings show growth 6cmx6cm on anterior vaginal wall, another 3x3cm lesion on right lateral vaginal wall. Vaginal biopsy showed malignant melanoma, S-100 and HMB-45 positive while negative for CK and LCA. MRI Whole abdomen showed altered lesion [3.8cm (AP), 6.0cm (TR) and 4.9cm (CC)] in upper 2/3rd of vagina extending into vaginal fornices and abutting right lower cervix superiorly, right paravaginal extension and mesorectal fascia. No significant enlarged lymph nodes were seen. In view of localised disease she underwent Type III Radical hysterectomy with bilateral salpingo-ophorectomy with bilateral pelvic lymphnode dissection with total vaginectomy. Histopathology s/o 2 tumour nodules, one located in the anterior vaginal cuff measuring – 5x5x3.2cm, another located in right lateral vaginal cuff measuring 2.5x3x1.5 cm, malignant melanoma with involvement of the cervix with full thickness stromal invasion (2.8/2.8cm,) invading perivaginal soft tissue, distance of invasive carcinoma from closest stromal margin <0.1cm (12 O' clock), LVI, PNI – not seen, all pelvic LN free(0/25). In view of positive margin and full thickness stromal involvement, she received radiotherapy to pelvis and Inguinal region to a dose of 45 Gy/25# followed by a boost of 16 Gy/8# to the tumour bed till 01/01/16. Another case is a 40yrs female, presented with complaints of bloody discharge per vaginum of 4 months duration. On examination, there was a large growth occupying the vagina till introitus. Cervix normal, para free. MRI Pelvis showed altered lesion involving left lateral uterine cervix and upper 2/3rd of vagina with full thickness stromal involvement with mild left parametrial, anterior and posterior paravaginal extension, measuring 2.9x4.5x5.3cm. Few subcmlymphnodes were seen in bilateral external and internal iliac regions (L>R). Vaginal Biopsy was suggestive of Malignant Melanoma, expressing S-100, HMB 45 and SDX-10. Metastatic work up was negative. She underwent RH with total vaginectomy with bilateral PLND with RPLND. HPR showed exophytic black growth seen involving all quadrants of vagina, extending upwards into both lips of cervix – 7x6x2.5cm, Malignant melanoma, distance of invasive carcinoma from closest margin : <0.1cm (paravaginal soft tissue), 3/8 right Pelvic LN , ECE +, 01/9 Left pelvic LN , ECE absent, 0/6 Right common iliac LN, 0/1 Reperitoneal LN was seen. She received adjuvant radiotherapy to a dose of 50Gy/25# to the pelvis and inguinals→ boost of 6Gy/3# to nodal regions showing ECE & 10Gy/5# to the primary region.

A Rare Case of Esthesioneuroblastoma

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Introduction: Esthesioneuroblastoma (ENB) also known as olfactory neuroblastoma is a rare malignant neuroectodermal tumor (NET) that arises from the olfactory epithelium. ENB accounts for only 1%–5% of intranasal cancers & to the best of our knowledge fewer than 980 cases of ENB have been reported in the world literature. Unlike most other NETs, occurring in childhood, ENB has a bimodal age distribution between 11-20 years and 51-60 years. As such, much about its biology, clinical behavior, and optimal treatment remains poorly understood, patients may present with nasal obstruction, recurrent epistaxis, hyposmia, or anosmia, periorbital edema, frontal headache or proptosis. Its biological activity ranges from indolent growth to local recurrence and rapid widespread metastasis. Treatment options are surgical resection followed by radiation therapy for primary lesions and the addition of chemotherapy for advanced, recurrent, or metastatic lesions. **Objectives:** To sensitize the audience regarding the diagnosis, workup and management of this rare disease. **Material and Methods:** We report the case of a 24 years old male, who presented in May 2013 with features of epistaxis, periorbital edema, lacrimation, blurring of vision & frontal headache. On evaluation, CECT-PNS showed mass in Right ethemoid sinus with intracranial & intraorbital extension. Biopsy revealed neuroblastoma (Hyams gd IV). Pt was managed with anterior craniofacial resection & tumour excision. Post op MRI Brain showed a large residual mass involving both nasal cavities with intra cranial & intraorbital extension. Adjuvant radiotherapy along with concurrent chemotherapy was offered. **Results:** He was managed with surgery followed by adjuvant radiotherapy to a total dose of 50Gy/25# along with Inj Etoposide & Inj Cisplatin concurrently. The patient showed good symptomatic response. Presently on a regular follow up without any residual disease. The details of the case will be presented in poster form. **Conclusions:** The modified Kadish staging system (extent of disease at diagnosis), lymph node status, treatment modality, pathological grading and age are useful predictors of survival in patients who present with esthesioneuroblastoma. Excellent outcomes for esthesioneuroblastoma are achievable. Long-term follow-up is necessary because of the extended interval for recurrent disease; unlike most sinonasal malignancies, surgical salvage is possible. The sole purpose of this case report study is to analyze the history, management and prognosis of this tumor, based on the literature review.

Use Of Uplift Fascialatasling in Reconstruction of Complex Lower Face Defects Following Resection in Ca Oral Cavity.

Sandhya Pandey, Ravi Kumar Chittoria

JIPMER

Background: A 40 year old gentleman who presented with ulceroproliferative growth in the left lower alveolus, skin infiltration and enlarged left submandibular nodes. Almost entire middle and lower face on left side was involved. CECT reported heterogeneously enhancing mass lesion involving body of mandible left side. Biopsy reported Pleomorphic sarcoma. Malignant peripheral nerve sheath tumor with rhabdomyosarcomatous differentiation also known as malignant triton tumor accounting for <10%, is rare in head and neck. **Material and Method:** He was treated with wide local excision with condyle preserving hemimandibulectomy and MRND. Resultant defect was extensive and included full thickness near total cheek and hemi mandible defect. Double free flap was designed with free fibula osteocutaneous and free anterolateral thigh fasciocutaneous flap. Usually after reconstruction of such a complex and big defect using double flap, deviation of angle of mouth and drooping of lower lip is noted post operatively primarily because of bulk of the flap itself. The loss of facial nerve branches also contributes to the final deformity. This is cumbersome for both patient and surgeon with respect to cosmetic and functional results. Although use of static sling is described in literature in lip reconstruction and following facial nerve resection prophylactic use of sling in major facial reconstructions is not reported. **Result:** We used fascia Lata sling before flap insetting to prevent drooping of angle of mouth. Both flaps settled well. No deviation of angle of mouth or drooping of lower lip was noted. Bone scan showed viable condyle and free fibula after 4 weeks. **Conclusion:** We present such rare diagnosis with extensive disease treated with functional and aesthetic reconstruction following oncologically safe resection and by prophylactic use of fascia lata sling to prevent post operative drooping of lip and oral commissure.

Key words: free fibula, free ALT, facial sling.

Excellent Survival in a Paediatric Sinonasal Teratocarcinosarcoma with Multimodality Treatment:a Case Report

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Introduction: Sinonasal teratocarcinosarcoma (SNTCS) is a rare malignant neoplasm consisting of primitive neuroepithelial elements with various malignant epithelial and mesenchymal components.Henfer and Hyams were the first to coin the term "teratocarcinosarcoma" after the clinicopathologic study of 20 patients with sinonasal tract neoplasms. The most common presentation for teratocarcinosarcoma is nasal obstruction and epistaxis with the average duration of symptoms being reported at 3.5 months.Overall, there is a strong male predominance with a 7:1 male to female ratio.Mean survival for this neoplasm has been reported at 1.7 years with a 60% mortality rate within 3 years.Metastasis of SNTCS is rare and has previously only been reported on the spinal axis, cervical lymph nodes, and respiratory tract. **Materials and Methods:** A 9 year old male patient presented with nasal mass and epistaxis.Excision was done once and the hpe report was suggestive of mucoepidermoid carcinoma.The nasal mass recurred after 6 months.Again a biopsy under general anesthesia was done and an immunohistocytochemistry diagnosis of teratocarcinosarcoma was confirmed. CT scan showed a mass lesion in the roof of right nasal cavity extending intracranially. **Treatment:** Craniofacial resection with removal of intracranial tumor excision with frontalis myofascial flap reconstruction was done. The post-operative course was uneventful and patient was discharged on 18th post-opereative day.HPE report was teratocarcinosarcoma and the IHC report was positive for CD-99 ,neuron specific enolase(NSE) and vimentin , thus confirming the diagnosis of teratocarcinosarcoma. Patient took adjuvant radiation of 50grays in 25 fractions over 5 weeks. Patient was followed up every 3 monthly for 2 years and 4 monthly for next 3 years with imaging . There was a disease free survival of 5 years. On follow up in 5th year,MRI showed no evidence of any disease. **Results:** Teratocarcinosarcoma is a rare neoplasm with less than 65 reported cases in the literature. The term teratocarcinosarcoma was first coined by Heffner and Hymans in 1984 after they reviewed 20 cases of sinonasal tract neoplasms with mixed histological features of carcinosarcoma and teratoma.Along with the pathological features of SNTCS, they also observed the treatment and survival rates in their patients. This neoplasm is exclusively seen in adults with a reported age range from 18 to 79 years but in our case the patient's age was 9 years and very few cases have been reported in such young patients as in study by agrawal n et al.SNTCS has a male predominance which has been reported at 7:1 or 8:1. which in our case also holds true. It was determined that the mean survival rate was 1.7 years with a 60% mortality within 3 years but in our case report the patient has already had an excellent disease free survival of more than five years and is on regular follow up. Diagnosis of SNTCS can prove to be difficult if only a biopsy is taken because of the heterogeneity and variegated histological architecture. therefore an IHC confirmation is imperative in confirming the diagnosis. Treatment has relied upon surgery and or radiation therapy. No effective chemotherapeutic regimens have yet been reported for SNTCS in part because of its highly variable histology. our case was also managed with surgery and adjuvant radiotherapy only and giving an excellent survival .However, single modality treatment has proven to be ineffective for locoregional control. Wei et al, in a meta-analysis of 54 cases determined that 67% of patients that had a single surgical resection and 80% of patients treated primarily with radiation had reccurrence, metastasis, or unresponsiveness to treatment. **Conclusion:** SNTCS is a very rare tumor in paediatric age group considered to have a bad prognosis with single

modality treatment.however with multimodal treatment ,the patients can achieve an excellent long term disease free survival .adult patients do not fare that well as compared to paediatric patients however further studies are needed to support this view.

Key words: Sinonasal teratocarcinosarcoma, pediatric, craniofacial resection

Adenoid Cystic Carcinoma of Upper Lip: A Rare Entity

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Background: Adenoid cystic carcinoma is a rare malignant neoplasm most commonly arising from minor salivary glands and accounts for 1% to 2% of all malignant tumors of head and neck. Parotid is the single most common site (25%) of ACC in head and neck. However, majority of ACC (50-60%) arise from the minor salivary glands. The most common intraoral site is the palate. Other less common sites of oral cavity are retromolar region, sublingual gland, buccal mucosa, floor of the mouth and upper and lower lip. Adenoid cystic carcinoma of upper lip is extremely rare and only a few cases have been reported in literature till date. **Case Presentation:** A 50 years old gentleman presented with painless swelling of right upper lip since 3 months. Physical examination revealed approximately 5x4 cm globular swelling involving right upper lip from commisure to midline and extending upto nasolabial fold on cheek. Mucosa of upper lip was fixed to swelling without ulceration; overlying skin was stretched and fixed. Cervical lymph nodes were not palpable. FNAC revealed adenoid cystic carcinoma and CECT scan of thorax was normal. Patient underwent wide local excision of right upper lip and commisure with reconstruction using Abbey-Estlander flap. Final histopathological examination also confirmed diagnosis of adenoid cystic carcinoma of lip. Patient is asymptomatic at one year of follow up. **Conclusion:** Adenoid cystic carcinoma is a malignant neoplasm usually arising from minor salivary glands of palate in oral cavity. Upper lip site for ACC is a very rare occurrence. It may be confused with benign tumors both clinically as well as on fine needle aspiration cytology. There should be high suspicion for minor salivary gland tumors over all mucosal surfaces of head and neck.

Paraganglioma Of Carotid Body: Management by Internal Carotid Artery Excision and Ptfe (Polytetraflouroethylene) Grafting

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Keywords: Carotid body tumor, carotid artery excision, ptfe grafting

Background: Case report and review of literature of a very rare case of carotid body paraganglioma treated by internal carotid artery segmental excision and PTFE grafting in a 20 yr old female. Carotid body paragangliomas are a very rare tumours and can be successfully treated by artery excision and grafting after proper preoperative imaging and workup of the patients. **Methodology:** A 20 yr female patient came with presenting complaint of right upper neck swelling from last 5-6 months.MRI and digital substraction angiography were suggestive of carotid body paraganglioma. She was successfully treated by internal carotid artery segmental excision and PTFE grafting without any postoperative neurological deficits and significant complications. **Results:** Our patient was successfully treated by internal carotid artery segmental excision and PTFE grafting without any postoperative neurological deficits. She recovered well after surgery with slight hypoglossal nerve neuropraxia and slight deviation of the tongue. Patient was discharged after 10th postoperative day. Pathology report and immunohistochemistry report was suggestive of paraganglioma of carotid body. Patient on follow up was alright 3 years after surgery with resolution of neuropraxia and no recurrence. **Conclusions:** Although rare, carotid body tumor still a pathology that we encounter in our experience and it should be kept in mind as a differential diagnosis for painless lateral neck masses. Surgical removal is the treatment of choice and it should be performed early in order to avoid progressive local invasion and decrease the rate of morbidity.

Reconstructive Surgery in Terminally Ill Cancer Patients: A Social Indication

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JIPMER

Background: Patients with advanced cancer experience a complex web of problems, all of which interact. Specialist palliative care services have developed to meet these needs, but their effectiveness should be considered. Though the carcinoma is known for high rates of morbidity and mortality, it is an obligation of a plastic surgeon to help the patient to have a dignified and normal social life for their remaining lifespan. **Material and Method:** A 40 year old female presented with a carcinoma cheek underwent wide local excision and flap cover with free flap, which failed. Subsequently patient underwent a pedicled flap which too failed. On evaluation patient was diagnosed with post op status stage IV carcinoma oral cavity with flap failure. Institution`s tumor board consultation was taken and palliative chemotherapy instituted, though reconstructive surgery was not advised in view of metastasis. But the patient`s psychological and social impact of hindrance and anonymity among family members and society persuaded the patient for repeated request for reconstruction and the psycholosocial impact compelled the reconstructive surgery in this patient. **Result:** Patient was managed according to Society for Wound Care and Research (SWCR) guidelines and in spite end stage disease Successful wound management and improved quality of life was provided to the patient. **Conclusion:** End stage carcinoma should not be considered always to be managed with conservative measures alone. Surgery may be considered to remove this high impact of psycho-social burden on such patients.

Keywords: Carcinoma cheek, free ALT, DP flap, SWCR guidelines.

Post Laryngectomy Stricture Dilatation Leading to Esophageal False Tract- A Rare Complication Managed By A New Endoscopic Technique

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Introduction: Post laryngectomy stricture is usually late sequelae and has been reported in 10-50 % of patients. **Presentation of case:** A 49 year old man with history of T1N0M0 squamous cell carcinoma of larynx treated with radiation therapy. After one year he presented with local recurrence for which underwent salvage laryngectomy, neck dissection, stapled pharyngeal closure, primary tracheoesophageal prosthesis and reconstruction of skin lining with pectoralis major mycutaneous flap were performed. He was then on regular follow up. After 7 years he presented with dysphagia. Oesophagoscopy showed cricopharyngeal stricture for which multiple balloon dilatation were done. In view of persistent dysphagia, LASER assisted stricturoplasty with dilatation under microscopic guidance were performed. In immediate postoperative period he had complains of chest pain with dyspnea. On evaluation CT scan showed contained cervical esophageal perforation with dissection of esophagus. Flexible nasopharyngolaryngoscope (NPL) examination showed two lumens. Then endoscope was passed through tracheo-esophageal puncture (TEP) site retrogradelly and wire guided balloon dilatation were done. Ryle's tube was placed. Foley's catheter was introduced retrogradelly through the TEP site in to true lumen and inflated so as to compress the false lumen. Patient was managed conservatively and improved. Further retrograde dilatation has led to complete obliteration of false tract. Tracheoesophageal prosthesis was reinserted. Patient is tolerating semisolid diet and doing well on follow up. **Discussion:** Only few reported cases of retrograde endoscopy through TEP site for stricture dilation has been described in literature. We used this technique for true lumen identification and subsequent dilation

to compress the false tract. **Conclusion:** This new endoscopic combined antegrade and retrograde dilatation through TEP site is safe and feasible option for false lumen obliteration with simultaneous stricture dilatation for post laryngectomy complex neopharyngeal strictures in expert hands.

Intra-Osseous Adenoid Cystic Carcinoma of Maxilla: Case Report

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Adenoid cystic carcinoma is a form of malignant neoplasm that arises within the secretory glands. Most common site is the major and minor salivary glands of head and neck. Rare sites include the lacrimal gland, external auditory canal, nasopharynx, tracheo-bronchial tree, vulva and breast and even rarer are the intra-osseous primary tumors. The present case illustrates a mixed variant of ACC of right maxilla encroaching the hard palate, maxillary sinus, pterygopalatine fossa, lateral and medial pterygoid muscles, right nasal cavity through sinus ostium and inferior turbinate, middle cranial fossa, right orbital apex and superior orbital fissure and bowing the adjacent cavernous segment of right Internal Carotid artery. The strong neurotropism of ACC had manifested in certain symptoms and signs noticeable since his presentation. Ptosis, anisocoria, drooping of right eyelid, decreased visual acuity, nasal blockade, maxillary fullness, hyposmia, dysgeusia, referred otalgia, hypoesthesia of right side of face, exfoliation of teeth 1-7 and deviation of tongue to right side .His tumor volume was initially 70ml and two months later,at the time of presentation to our Institution, 130 ml. The histopathological features showed tumor tissue arranged in cribriform and solid subtype of ACC. A panel of antibodies was used for immunohistochemical evaluation namely S-100, p63, vimentin, MSA, and Ki-67. Due to a large tumor volume and intracranial extension he was taken up for Neo-adjuvant chemotherapy with Flouro-uracil, Doxorubicin and Mitomycin and Surgery/Radiotherapy relegated to a later date in lieu of his present morbidity status.

Key words: Adenoid cystic carcinoma, intra-osseous tumor, neurotropism, chemotherapy.

Primary Hyperparathyroidism Presenting as Unilateral Ptosis – An Unusual Manifestation With Strange Post-Operative Recovery

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We present a case of young male presenting with sudden onset unilateral ptosis of right eye, evaluated with provisional diagnosis of myasthenia gravis. As the tests were negative for myasthenia, patient was incidentally detected as hypercalcemia without any chronic symptoms of it. On evaluation, found to have left inferior parathyroid adenoma and operated for it although unsuspected as cause for the initial symptoms of ptosis. As an unexpected event, patient had extraordinary recovery of the ptosis on the same post operative day. Unilateral ptosis as the only clinical presentation has not been reported so far in literature, and although the cause for such presentation is unknown, it certainly throws light on the varied molecular mechanisms associated behind it which needs further research.

Fibrosarcoma of Mandible: A Rare Tumor

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Fibro sarcoma of mandible (1%) is a rare entity and associated with high chance of local recurrence and distant metastasis. Biopsy provides definitive diagnosis, IHC analysis helps to rule out other differential diagnosis. Adequate surgical resection is the main stay of treatment. Adjuvant radiotherapy is indicated in high grade, large size (>5cm) lesion. Free bone flap reconstruction provides good functional and cosmetic outcome. Hereby we are reporting a case of fibro sarcoma of left mandible in 38 years old, whose biopsy and IHC analysis confirmed diagnosis of fibrosarcoma. Contrast enhanced computed tomography revealed extent of lesion and bone involvement and lung metastasis ruled out. She underwent posterior segmental mandibulectomy and free fibula bone flap reconstruction. Final histopathology also confirmed the diagnosis of high grade fibro sarcoma and mandible involvement. She received adjuvant radiotherapy. She is in regular follow up, till date no recurrence.

A Rare Occurrence of Ewing's Sarcoma of Maxilla In Adults– Report of a Case And Data Analysis in Indian Population

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A 55 year old patient visited the college with the complaint of swelling on left upper posterior tooth region for the last one and half months. He gave a history of extraction form the same site after which he notice the swelling. A CT scan revealed obliteration of the maxillary sinus with no involvement of nasal cavity. Based on the age, clinical and radiography a provisional diagnosis of Squamous cell carcinoma, Non hodgkin's lymphoma and Mucormycosis was made. But was proven to be Ewing's Sarcoma by histopathology and further immunohistochemical analysis. Ewing's of maxilla is a rare condition and in adults is even rarer. In this paper, the case will be described along with data anlaysis and comparison of similar reported cases from the Indian Sub-continent.

Resection of Salivary Duct Carcinoma Ex Pleomorphic Adenoma of Minor Salivary Gland Of Parapharyngeal Space Without Mandibular Osteotomy – A Case Report

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Background: Salivary duct carcinoma (SDC) is an aggressive histological subtype of salivary gland malignancy. Although majority of these tumours arise de novo in major salivary glands, 10-27% have been found to originate in pre existing pleomorphic adenoma. Salivary duct carcinoma ex pleomorphic adenoma in parapharyngeal space (PPS) has never been documented in English literature. We are reporting one such case which was resected via a transcervical approach while avoiding a mandibular osteotomy. **Case report:** Forty five year old gentleman presented with history of swelling in front of left ear of 3 months duration. MRI of the left parotid region revealed 9 x 7 cm, dumbbell shaped mass in the pre styloid compartment of left PPS. Transverse incision was placed 2 cm below the base of the mandible. Parotid was separated from the underlying mass through blunt and sharp dissection. Styomandibular ligament was cut to lift the mandible superiorly to improve access to the mass. Tumour was separated from the styloid process superiorly and resected en bloc. Intra and post operative recovery was uneventful. Histopathological examination was suggestive of salivary duct carcinoma ex pleomorphic adenoma with resection margins being free. He was given adjuvant radiotherapy. **Discussion:** Surgical excision remains the mainstay of

treatment for PPS tumours. Although mandibular osteotomy improves surgical access, it increases overall morbidity of the procedure. Transection of the stylomandibular ligament was the key in improving the access and avoiding a mandibular osteotomy. **Conclusion:** Parapharyngeal salivary duct carcinoma ex pleomorphic adenomas are rare neoplasm which can be safely resected via trans cervical approach. Precise knowledge of the anatomy as well as clear definition of the relationship of the tumour with surrounding structures on MRI is the key to R0 resection.

Retropharyngeal Lipoma A Case Report

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Lipomas of retropharyngeal region are rare. They attain a large size before producing symptoms like dysponea & dysphagia. A case of lipoma in retropharyngeal space is reported with characteristic radiological findings and surgical management. **Case Report:** Retropharyngeal tumours are relatively rare. Most of these tumours are malignant though benign tumours like lipoma and fibroma also occur rarely. These have to be managed surgically when symptoms are severe. A 70 yr. old female presented with large ill-defined swelling in left side of neck for last 15 yrs. There was sudden respiratory distress for which emergency tracheostomy was done. Direct laryngoscopic examination revealed smooth bulging in entire posterior pharyngeal wall with normal overlying mucosa suspicious of mass in retropharyngeal space.MRI suggestive of fat containing lesion in posterior wall of oropharynx and hypopharynx. Excision of tumour was planned through trans cervical approach. A large lobulated lipomatous mass removed intoto. Final histopathological report was suggestive of pleomorphic lipoma. **Conclusion:** Majority of lipomas are subcutaneous lesion. Approximately 13% of these occur in head and neck. The clinical history of lipoma is that of a slow growing mass and deep lesion may go undiagnosed because of patient getting habituated to symptoms. Retropharyngeal lipomas are often present with progressive dysponea and dysphagia. The patient in present report is having 15 yrs. history before retropharyngeal lipoma was diagnosed. Diagnosis is often made with CT scan which also helps in delineating the extent of lesion. Histopathological examination is confirmatory and surgery is the treatment of choice. Although the malignant potential of lipoma is low these tumors need to be surgically excised if they produce lifethreatening symptoms

An Unusual Presentation of Squamous Cell Carcinoma Over Lower Lip- A Case Report

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Introduction: Malignant labial neoplasms account for approximately 30% of all tumours occurring in the oral cavity. Of these 95% are classified as squamous cell carcinomas (SCC).Though most of the times malignancies present typically with large ulcerative growths, halitosis, anorexia,weight loss and general debilitation , at times they may present unconventionally. **Case report:** A 75 year old male,farmer by occupation, reported with a chief complaint of growth over lower lip since 2 months and pain associated with it since 1 month. Physical examination revealed a large,brownish black growth over right side of lower lip measuring 3.5X 2cm which was crossing the midline.Considering the anatomic location and the occupation of the patient , a provisional diagnosis of basal cell carcinoma was given.However,on performing excisional biopsy,histopathological diagnosis came out to be moderately differentiated squamous cell carcinoma. The growth was excised under general anesthesia and the post operative recovery was uneventful.

Keywords: Squamous cell carcinoma; Lip; Basal cell carcinoma; moderately differentiated squamous cell carcinoma.

Preferred Format of Presentation- Oral

Multiple cutaneous metastasis in a patient of carcinoma tonsil – a rare case report

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Carcinoma tonsil with visceral metastasis is a rare entity, and cutaneous metastasis is seen even more infrequently. We present a case of a 55-years-old male with carcinoma tonsil having received concurrent chemo radiotherapy, presenting with multiple cutaneous metastasis to the scalp and thigh. To the best of our knowledge, till date only two similar cases of carcinoma tonsil with cutaneous metastasis have been reported in the literature.

Dr Gunjesh Kumar Singh, Dr Vikas Yadav, Dr Pragya Singh, Dr K.T Bhowmik

Mixed Medullary-Follicular Carcinoma of Thyroid: Rare Dual Malignancy in a Large Thyroid

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Keywords: Mixed medullary-follicular carcinoma (MMFC), medullary, follicular, calcitonin, thyroglobulin, immunohistochemistry

Introduction: Mixed medullary-follicular carcinomas (MMFCs) are rare tumors of the thyroid that have morphological and immune-histochemical features of both medullary and follicular neoplasms. With less than 50 cases having been reported in the literature till date, it remains a rare tumour with mysterious origin. There is paucity of such case reported from Asia. **Case Summary:** A 40 year old patient presented to our out-patient department with complaints of swelling in the neck from past 20 years with recent increase in size since 1 year. The patient was clinically euthyroid and had no family history of neck swellings. The laboratory investigations including thyroid function tests were within normal range. FNAC showed follicular cells with high N/C ratio. A computed tomography scan showed a large heterogenous enhancing mass lesion in right lobe & isthmus of thyroid gland measuring 8 x 12 x 8 cms with multiple coarse foci of calcifications, reaching up to thoracic inlet posterior to manubrium causing left side displacement of larynx, trachea & oesophagus along with posterolateral displacement of right carotid sheath. No neck nodes were palpable or detected on scan. The patient underwent total thyroidectomy & central lymph node dissection and made an uneventful recovery. Histopathological examination of the specimen revealed a tumour with no extra thyroidal extension and negative neck nodes. It was identified as "Mixed Medullary & Follicular Carcinoma" expressing Calcitonin and Thyroglobulin on immunohistochemistry. Further work up for MEN syndrome was negative. The patient is healthy at one year of follow up. **Discussion:** Mixed medullary follicular carcinomas (MMFC) were defined strictly as tumors showing the morphological features of both a medullary thyroid carcinoma with immunoreactivity for calcitonin and a follicular carcinoma with immunoreactivity for thyroglobulin. MMFC consist of both follicular and parafollicular cells. The histogenetic origin and possible molecular mechanisms leading to MMFCs are still unclear. This rare tumour possess a diagnostic challenge to the pathologists and surgeons as it shows morphological and immune-histochemical features of both medullary and follicular neoplasms. High index of suspicion is of utmost importance to detect such tumours and measurement of serum calcitonin & thyroglobulin levels is helpful. The treatment is essentially surgical with total thyroidectomy and lymph node dissection.

Primitive Neuroectodermal Tumour (PNET) of Thyroid : A Rare Presentation

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Extra skeletal Ewing's sarcoma (EES) is rare. It commonly arises in the soft tissues of trunk or extremities.[1]EES is rare in the head & neck region; most being documented in nasal cavity, paranasal sinuses and neck. Head and neck peripheral PNETs have an intermediate prognosis . We report the case of a 12 year old boy who presented with primary primitive neuroectodermal tumour of the thyroid and is being treated with multimodal treatment (chemotherapy, surgery and radiotherapy). Multimodal treatments yield 5 yr survival rates of about 60%. Major drug regimens use vincristine, doxorubicin, Ifosfamide or cyclophosphamide, dactinomycin and/or etoposide. Complete surgical excision is undertaken whenever possible to improve long-term survival. However, the relative radiosensitivity of tumours of Ewing family, suggest multimodal treatment including adjuvant conformal radiotherapy in case of positive margins or poor response to chemotherapy rather than resection with 2-3 cm margins, which requires laryngeal sacrifice for thyroid tumours.

Keywords: Extra skeletal, Ewing's sarcoma, thyroid

Introduction: Primitive neuroectodermal tumours (PNETs) belong to the Ewing family of tumours and represent 1% of sarcomas.[2-4] Ewing's family of tumour is the second most common primary bone malignancy of childhood, however extra skeletal Ewing's sarcoma is rare. Head and neck PNETs have an intermediate prognosis between abdominopelvic disease and extremities.[5,6] Ewing's thyroid cases mostly occur in patients' ≤ 30 years. **Case History:** A 12 year old boy presented with a short history of cough and intermittent nasal blockage. On examination, the patient had a good performance status with clinically palpable thyroid swelling and no cervical lymphadenopathy. On investigating him, PET CT showed hypermetabolic lesion (SUV max9.3) involving thyroid gland suggestive of primary neoplasm, hypermetabolic bilateral level II nodes and no evidence of metabolically active/ FDG avid lesion elsewhere. CT guided biopsy of thyroid revealed malignant round cell tumour. However, the presence of strong membrane expression of CD 99 and nuclear expression of ERG, suggested that this is a primitive neuroectodermal tumour with a possible EWS/ERG translocation. The possibilities considered were metastatic undifferentiated carcinoma from a possible primary in nasopharynx (in view of strong cytokeratin and p63 positivity and high uptake in the nasopharynx and tonsil on PET) and primitive neuroectodermal tumour/Ewing's sarcoma (in view of MIC2 positivity, although Fli-1 is negative). On FISH test, EWSR1 gene rearrangement was not detected. After a tumour board discussion, the patient received 4 cycles of chemotherapy (Vincristine, Ifosfamide, Doxorubicin and Etoposide) as per EURO-EWING protocol. Post 3 cycles of chemotherapy PET-CT showed good response (SUV max 6.22) in the primary and no new lesions elsewhere in the body. In view of the good response, patient received one more cycle of chemotherapy. He underwent total thyroidectomy with central compartment clearance and bilateral neck dissection (Level II-IV) and tracheal resection. Intraoperatively retrosternal extension was noted and the tumour was infiltrating in to the anterior wall of trachea and encasing the left recurrent laryngeal nerve. Both the recurrent laryngeal nerves and

parathyroids were preserved. Trachea was closed primarily after resection of three rings. Postoperatively the patient developed hypocalcaemia which was managed conservatively. Patient was discharged on post operative day 7 with no hoarseness and no loss of tonality of voice. Histopathology report revealed 60% residual viable PNET involving both lobes of thyroid, LVE +, 1/6 perithyroidal nodes positive and 1/10 right neck nodes positive. Immunohistochemistry studies revealed FLI-1 +/ CD 99 + which confirmed the diagnosis of Primitive Neuroectodermal Tumour (PNET). The patient has been planned for adjuvant chemotherapy and radiotherapy.
Discussion: Ewing and PNET sarcomas share a similar histological appearance of small round blue cell tumour (except for the presence of rosettes), immunohistochemical markers , cytogenetic translocation t(11;22) (q24;q12) and MIC 2 gene expression (both present in more than 90% of cases). An absence of neural differentiation supports a diagnosis of Ewing's sarcoma rather than that of PNET. Primitive neuroectodermal tumour is usually identified as a primary malignancy of the bone affecting children and young adults. In the event of multimodality treatment involving chemotherapy, surgery and radiotherapy Ewing's sarcoma of the bone has a favourable prognosis and often can be considered as a curable malignancy. Extra skeletal Ewing's Sarcoma (EES) is rare. EES commonly arises in the soft tissues of trunk or extremities.[1] Diagnosis is based on immunostaining with atleast 2 neural markers, ultrastructural examinations and evidence of an abnormal t(11;22) (q24;q12). Previous clinical series[9-12] of EES have suggested prognosis either identical or more favourable than osseous Ewing's Sarcoma with treatment modalities of chemotherapy and surgery. Based on a review of Ewing's sarcoma/ PNET (bone or soft tissue, ± head and neck cases), the optimal multimodality therapy of PNETs consists of neoadjuvant chemotherapy, surgery and radiation based both on response to neoadjuvant chemotherapy and tumour site. Complete surgical excision with wide 2-3 cm margins is undertaken whenever possible to improve long term survival.[13] Radiotherapy is indicated in Ewing sarcomas whenever there are close or positive margins or poor response to chemotherapy (necrosis <90%). Adjuvant radiotherapy is associated with improved local control and improves survival when compared to surgery or radiotherapy alone. Additionally, owing to the relative chemosensitivity of tumours of the Ewing sarcoma family chemotherapy (neoadjuvant or sequential) has predominant part in the multimodal treatment. Neoadjuvant chemotherapy aims at targeting occult micro metastases and allowing tumour cytoreduction at the primary site. The type of adjuvant chemotherapy is chosen on the basis of the histological response, namely the percent of necrotic cells to neoadjuvant chemotherapy. Major drug regimens use vincristine, doxorubicin, Ifosfamide or cyclophosphamide, dactinomycin (actinomycin D) and/or etoposide often in alternate VAC/IE derived regimens. The rare case reports of PNET or Ewing head and neck/thyroid location have mostly used Ifosfamide and etoposide. Multimodal treatment yield five year survival rates of about 60% (52-88%) as reviewed in the series including at least one case of Ewing sarcoma/PNET of head and neck.

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Carcinoma Tongue in a Patient with Von Willebrand Disease -Management Challenges: A Case Report

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Introduction: Von Willebrand disease(vWD) is a common , inherited, genetically and clinically heterogenous hemorrhagic disorder caused by a deficiency or dysfunction of von Willebrand Factor(vWF).There are no guidelines available on management of patients with vWD receiving radiotherapy(RT) for head and neck cancers. **Case Report:** Here we present a case of a 34 year old female, a diagnosed case of vWD, who presented with a growth over the right side of the tongue and neck swelling since four months. Clinical examination revealed severe trismus and ankyloglossia, with a diffuse indurated mucosa covered growth involving entire tongue extending to posterior third and floor of mouth. There was no bleeding from the lesion. CT scan neck revealed a heterogeneously enhancing lesion involving the tongue towards right side and enlarged submandibular lymph nodes. FNAC of the submandibular swelling was inconclusive. Hence a biopsy of the tongue lesion was performed under intravenous Factor VIII and von Willebrand Factor(vWF) cover. Histopathology revealed a moderately differentiated squamous cell carcinoma. Subsequent PET scan confirmed a locally advanced tongue cancer involving multiple bilateral cervical lymph nodes. She had multiple bleeding episodes following the biopsy which were controlled with intravenous Factor VIII injections. She was started on radiotherapy with IMRT after consultation with the hematologist. During the course of the treatment, patient had multiple episodes of spontaneous bleeding from mouth which was managed with intravenous Factor VIII and vWF, cryoprecipitates and blood transfusions when required. During the last week of treatment, she required intravenous Factor VIII and vWF daily and it was continued for two weeks post RT. Treatment was completed in 7 weeks and she was discharged in a stable condition, with no bleeding, but persistent trismus. During follow-up, her general condition improved, but there was no improvement in trismus and clinical response evaluation was not possible. Two months post RT she was suggested to undergo an MRI of face and neck, for response evaluation. Meanwhile, she developed uncontrolled bleeding and succumbed to it. **Conclusion:** There is a paucity of guidelines in the management of cases with von Willebrand disease who develop head and neck malignancies making it challenging for both diagnosis and treatment.

Prospective Study on Relationship of Radiation Dose Received by Dysphagia and Aspiration Related Structures (Dars) And Degree Of Dysphagia in Head and Neck Cancers Post Radical Radiation Therapy with or Without Concurrent Chemotherapy'

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Introduction: Radiation Therapy with Concurrent Chemotherapy is now the accepted standard of care for organ preservation in head and neck cancers. Although there is increased local control and overall survival by this method, a substantial percentage of survivors suffer from significant treatment-related adverse effects, both acute and long term. Dysphagia is an important adverse effect of Chemoradiotherapy. Important structures involved in swallowing include the pharyngeal constrictors, supraglottic and glottic larynx and the cervical esophagus. Though there are many factors associated with dysphagia, DARS has gained importance due to most studies showing that a lower dose to it can decrease dysphagia. However, prospective studies are lacking. This study analyses the dosimetric correlates of post-CRT worsening of various measures of dysphagia, up to 6 months post treatment and compares it with the pre-therapy baseline. **Objectives:** To study relationship of radiation dose received by DARS and degree of dysphagia in Head and Neck cancers post Radical Radiation Therapy with or without Chemotherapy. If a positive relationship does exist, to recommend sparing of the DARS (in cases where it is feasible and target dose is not compromised) in future radiotherapy plans in our set-up. To assess other patient-, disease- and treatment- related factors that are associated with post treatment dysphagia. **Material and Methods:** 42 patients of Head and Neck Cancers, satisfying the inclusion criteria were included from April 2014 to May 2015 and were treated with radical Radiotherapy using IMRT with or without Chemotherapy. DARS structures which included superior, middle and inferior constrictors, supraglottic and glottic larynx and cervical esophagus were contoured on the planning CT scan along with other Organs at risk (OARs). Radiation therapy was delivered with IMRT to cover the primary tumor and the cervical lymph nodes. No dose constraints were given to the swallowing structures. Only regular OARs like salivary glands, oral cavity and spinal cord were given constraints. The mean dose (Dmean) and the maximum dose (Dmax) to each of these structures and the partial volumes of each of these structures receiving a specified dose (VDs: V30, V50, V60, V66 and V70) were calculated from the DVHs. Dysphagia was evaluated at baseline (pre-therapy) and at 6 months post treatment using Subjective questionnaires [M.D Anderson Dysphagia Inventory (MDADI) and Performance Status Scale for Head and Neck Cancers (PSSN)] and using Modified Barium Swallow for Objective Scoring of dysphagia [Swallowing Performance Scale (SPS) and Penetration Aspiration Scale (PAS)]. Correlation between dysphagia Scores at baseline & 6 months and doses at various sites was assessed using Spearman's rank Correlation. This and other statistical analyses were used to study patient and treatment related factors that predict dysphagia. **Results:** On applying non-parametric correlation (Spearman's rank correlation coefficient), there's correlation between V30 of Superior Constrictor and the PSSN Score at 6 months follow up and Dmax of superior constrictor and PSSN score at 6 months. For MDADI scores, there's a positive relationship of Dmax of superior constrictor and 6 month MDADI score. There's correlation between V30, V50, V60, V66, V70, Mean doses of middle constrictor and the PSSN Score at 6 months follow up. For MDADI scores, there's a positive relationship of V30, V50, V60, V66 and V70 of middle constrictor and 6 months MDADI. There's correlation between V30, V50 and Dmax of inferior constrictor and MDADI Score at 6 months follow up. There's correlation between V30, V50, V60, V66, V70, Mean doses of supraglottic larynx and the PSSN Score at 6 months follow up. For MDADI scores, there's a positive relationship of V30, V50, V60, V66, V70 and Mean of supraglottic larynx and 6 month MDADI score. But there is no relationship between any of these doses or volumes and dysphagia scores when baseline dysphagia is considered. There is no significant correlation between doses to Glottic Larynx and Cervical Esophagus (Vd's and Mean and Dmax) and PSSN or MDADI Scores. None of the patient related factors like stage of disease, location of tumour, age of the patient showed any relationship with dysphagia after treatment. Treatment related factor like Concurrent Chemotherapy also showed no significant relationship with dysphagia post treatment. **Conclusions:** Thus, the dose to DARS showed strong correlation of different volumes (Vd's) and Mean and Max doses of superior, middle, inferior constrictor, supraglottic larynx with dysphagia and aspiration scores (subjective and objective) at 6 months follow up. But on taking into account baseline dysphagia, there was no correlation between doses and dysphagia. Though dysphagia improved in a significant proportion of patients due to shrinkage of the tumour mass as a response to radiation, many showed deterioration. This maybe due a wide range of possible causes like xerostomia, mucositis, fibrosis, dose to DARS, Ryle's tube or PEG dependency etc. An important pattern of observation was that while nearly 80% of patients showed significant dysphagia on subjective assessment, only 62% showed significant dysphagia on objective tests. It was noted from our pattern of observation that the cases which had the poor grades and scores in assessment tests were the ones with maximum baseline dysphagia, and these in turn were the locally advanced cases. The findings of this study motivate further efforts to reduce the dose to the swallowing structures, especially to the pharyngeal constrictor muscles and the larynx when planning concurrent Chemoradiotherapy for locally advanced head-and-neck Squamous cell Carcinoma in cases where the planning target volume does not overlap with DARS. Pre-treatment dysphagia must be considered in all future prospective studies to find true correlation between DARS and dysphagia. Also, a single gold standard assessment test that takes into account all confounding factors must be devised.

A Rare Case of Papillary Carcinoma Thyroid with Anaplastic Transformation- Case Report

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Introduction Anaplastic thyroid carcinoma is one of the most aggressive malignancies wit h poor prognosis. Anaplastic thyroid carcinoma may occur in synchrony with other thyroid malignancies including papillary, follicular and HCC leading to the question about development of anaplastic thyroid cancer through dedifferentiation of these well differentiated cancers, possibly through activating mutations of BRAF and RAS. Approximately 50% of patients with ATC will have prior or coexisting differentiated carcinoma. We report a rare case of papillary thyroid carcinoma with anaplastic transformation in neck nodes **Case Report:** We report a rare case of papillary thyroid carcinoma with anaplastic transformation in neck nodes. Patient presented with large bosselated swelling in the neck . Further examination and investigations revealed it to be a secondary deposit from anaplastic carcinoma of thyroid. After ruling out metastasis, Total thyroidectomy and bilateral functional neck node dissection done including the large neck nodal mass. Post operative histopathology revealed papillary carcinoma of thyroid in the thyroidectomy specimen with anaplastic carcinoma in neck nodal mas. Postoperative Radio Iodine Scan has revealed a single skull metastasis. Usually Papillary carcinoma thyroid metastatic sites behave as their primary. In this case, primary papillary carcinoma thyroid has undergone dedifferentiation in the neck node and at the same time skull metastasis is behaving like primary. Patient developed recurrence at the operated site and is receiving palliative care now. **Discussion:** Our patient has a Papillary carcinoma thyroid which metastasized to both lymph nodes and the skull.

An unusual case of metastatic thyroid carcinoma with diagnostic and therapeutic challenges.

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Background: Pituitary/sellar metastasis in differentiated thyroid cancer (DTC) is rare. Diagnosis and treatment of this rare entity is challenging in the face of hypopituitarism. **Case Report**: A Lady aged 80 yrs, diagnosed with

follicular carcinoma of thyroid with skeletal and lung metastasis underwent total thyroidectomy. Postoperatively, TSH was persistently low at 4 weeks. Several diagnostic possibilities were entertained like contrast interference, functioning metastasis etc. Detailed workup revealed a sellar mass with evidence of hypopituitarism. Thus, she was treated with radioiodine ablation after a course of recombinant TSH(rTSH). **Discussion:**This case showed that unusual presentation of seemingly usual disease may pose dilemma in management. Thus, a high degree of clinical suspicion and thorough workup will help solve the clinical conundrum and contribute to better patient care.

Keywords: DTC, sellar metastasis

Extracranial Meningioma Presenting as a Nasal Polyp: Rare Case Report

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Introduction: Meningiomas are tumors developed from arachnoid meningeal cells which are derived from neuroectodermal cells. Its primary onset from extracranial and extravertebral site is a rarity, making fewer than 2% of all the meningiomas, arising more frequently in the scalp and orbit. Its primary origin in nasal fossae is considered exceptional. Common extracranial anatomical sites include head and neck region, mediastinum, skin and soft tissues. **Objective:** To report a rare case of nasal meningioma. **Material and Methods:** A 57 years old female presented with episodes of left nasal cavity epistaxis and bilateral nasal obstruction. On examination, a polypoidal soft tissue growth was identified in the nasal cavity. On CECT paranasal sinus, a left side nasal expansile polypoidal soft tissue mass was observed and differentials of inverted papilloma/ mitotic mass/ hemangioma were suggested. Biopsy was taken and sent to the department of Pathology. **Results:** On histomorphological and immunohistochemical examination, the diagnosis of meningioma was made which is extremely rare at this site. Various histomorphological forms have been identified which typically arise in proximity to the meninges. Extracranial meningiomas of the head and neck region are rare, the majority being the secondaries from a primary intracranial tumour. **Conclusion:** The histopathologic diagnosis of meningioma is usually straightforward; however, a high index of suspicion is needed for diagnosis when they present in unexpected locations (extracranial) especially in view of a variety of differentials ranging from benign to malignant conditions. The clinical and radiological features of these tumors are unspecified in literature and so, an accurate diagnosis requires histologic evaluation. Complete surgical removal of the sinonasal tract meningiomas has an overall good prognosis.

Woldenstrom Macroglobulinemia a rare case report

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Introduction: Lymphoplasmacytic lymphoma (LPL) is a neoplasm of B lymphocytes & plasma cells, usually involve bone marrow (BM), sometimes lymphnodes & spleen, which doesn't fulfill the criteria for any other B cell neoplasm that may have plasmacytic differentiation. Waldenstrom Macroglobulinemia (WM) is defined as LPL with BM involvement (>10% infiltration) & IgM monoclonal gammopathy (IgM-MG) in blood. [WM= LPL + BM involvement+ IgM-MG]. It is a rare entity. Median age is 70 years with slight male predominance. 20% cases are familial (1, 2). **Short clinical history:** A 64 year male, presented with low back pain, headache & early fatigue 2-3 yrs. History of hypertension, diabetes mellitus with a healed H. zoster lesion in right T10 dermatome was present. Patient was moderate to heavy alcoholic for last 30 years. There was bilateral axillary lymphadenopathy with no organomegaly, Hb 96 gm/L & beta 2 microglobulin 2.49 mg/L (0.8-2.1). Occult blood in stool was present. BM aspirate smear showed 5 % plasma cells. M band was seen on Protein electrophoresis (serum & urine), immunofixation showed IgM lambda. There was raised twenty four hours urinary protein, serum IgM 1588 (40-230) & IgG 1895 (70-1600). Skeltal survey showed patchy osteopenia in ribs. Final diagnosis Waldenstrom Macroglobulinemia was made. Patient is on Chlorambucil +Prednisolone therapy. **Discussion:** The term "macroglobulinemia"(IgM-MG) refers to excess of monoclonal IgM. It includes MG of undetermined significance, Smoldering WM, WM, chronic lymphocytic leukemia, lymphoma variants and primary amyloidosis (2).There may be hyperviscosity syndrome (causing CNS signs and symptoms), neuropathy (IgM reactivity to myelin sheath antigen), cryoglobulinemia or paraprotein deposition. IgM deposition may occur in skin & GIT to cause diarrhea (1). Bone or kidneys involvement is uncommon. Tortuous retinal veins (sausage link) is characteristic. Asymptomatic WM is called SWM. Plasmacytic component will be CD138+, CD38+ and CD45- or dim.

Key words: Lymphoplasmacytic lymphoma, Waldenstrom Macroglobulinemia, IgM monoclonal gammopathy

A Rare Case of a Diffuse Large B-Cell Lymphoma Arising From The Parotid Gland in a Patient With Sjogren's Syndrome

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Introduction: Primary lymphoma of the salivary gland is rare. Most are low grade lymphomas with MALT lymphomas being the most common. DLBCL lymphomas are uncommon with most thought to be due to transformation from underlying low-grade lymphomas, postulated to arise in sialedinitis and Sjogren's syndrome. We report a rare case of DLBCL in a patient of Sjogren's syndrome. **Case report -** A 63 Year old female, a case of Sjogren's Syndrome on treatment presented with complaints of fever and painful swelling over her left parotid gland for 2 months duration. There was a 10*8 cm swelling of her left parotid. Systemic examination was unremarkable. Investigations– showed a normal CBC, biochemistry with negative viral markers. The biopsy from the parotid was reported as a malignant lymphoma and the IHC – positive for CD20 with a high Ki-67, suggestive of a Diffuse large B-cell lymphoma. The CT imaging done – revealed a mutiloculated heterogeneously enhancing lesion in both the superficial and deep lobes of the left parotid, predominantly in the superficial lobe, with infiltration of surrounding structures and cervical lymphadenopathy. The thoracic and abdominal & pelvic imaging was unremarkable. The bone marrow examination showed no involvement. She was diagnosed as a case of stage II EAX DLBCL and received 3 cycles of chemotherapy- with standard doses of the CHOP regimen. Reassessment CT scan of the neck revealed a residual lesion. She was continued on CHOP chemotherapy and is doing well with complete regression of the parotid swelling at the end of 5 cycles of chemotherapy. **Conclusions :** Whether the extranodal origin, probable de novo origin of the tumour, lack of persistent enlargement of the parotid glands prior to development of the lymphoma and LMP-1 negativity portend a better outcome in our patient will be known in due course.

Key words: Sjogren's syndrome, extranodal DLBCL, parotid

Complete Metabolic Remission with Crizotinib in ALK positive Diffuse Large B cell Lymphoma (ALK Positive DLBCL) -Case Report and Literature review

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Introduction: We report a rare diagnosis of ALK positive DLBCL(CD 20 negative) with rapid massive progression post conventional CHOP based chemotherapy regimen, is reversed with targeted therapy crizotinib(ALK inhibitor) with complete metabolic response.Literature review with previous published reports of crizotinib in ALK positive DLBCL is discussed. **Case**: A 43 yr old male has presented to us with large palpable abdominal mass in the epigastric and umbilical region with jaundice and significant weight loss of 15 kg over last 2 month.Both Liver and spleen are enlarged(5 cm and 8 cm from costal margin respectively)and palpable separtely from mass.Initial CT scan done outside revealed a large pancreato-duodenal mass of size 12.6 * 6.3 *4.5 cm encasing the superior mesenteric & portal vein with dilated common bile duct and satellite mass in mesentry (largest measuring 5.4 *5.3 *4.2 cm) along with massive splenomegaly.Clinical differential diagnosis at presentation included either a pancreatic carcinoma with obstructive jaundice or lymphomatous process involving the pancreatico-duodenal region with obstructive jaundice , hepatosplenomegaly and B symptom.PET CT done revealed predominantly bulky abdominal disease and osteolytic lesion in right humerus.Upper Gastro-esophageal endoscopy showed duodenal infiltration and biopsy done.The biopsy is suggestive of Large B cell lymphoma which is lambda chain restricted, LCA & ALK positive and is negative for CD 3,CD 5,CD 7 & CD 20.BMA &BM biopsy was normal.So a diagnosis of primary pancreatic Large B cell Lymphoma ALK positive ,stage 4 has been made and initiated on steroids only for first 1 week till his jaundice gradually came down to normal.Then he received CHOP based chemotherapy for 4 cycles after which PET CT showed metabolic CR.As the residual abdominal mass caused persistent abdominal pain he received local radiation therapy to the mass and subsequently received 2 more cycle of CHOPReevaluation with PET CT showed progressive right humeral lesion and new active peritoneal disease along with stable primary abdominal mass.As patient was symptomatic regarding right upper arm pain ,the plan was to give pain palliative radiation to right humerus followed by salvage chemotherapy.Immediately after the receipt of pain palliative RT he developed progressive symptomatic large hepatomegaly measuring 10 cm below costal margin with multifocal lymphomatous liver involvement in PET CT along with parenchymal disease related deranged live function abnormality.As the ECOG PS is 2 along with deranged LFT,immediate secondline salvage chemotherapy could not be started.As his condition deteriorated,we discussed with patient and family members about the use of crizotinib as targetted therapy since ALK was positive.After consent from family,crizotinib 250 mg twice a day has been started.The performanace status and jaundice improved dramatically.After 3 months of crizotinib,his PET CT shows complete metabolic remission. **Discussion**: ALK positive DLBCL (classically CD20 negative,ALK cytoplasmic positive, B cell light chain restricted and positive for plasma cell markers CD 38 & CD 138) is a rare variant of aggressive Large B cell Lymphoma which needs to be differentiated from other CD 20 negative lymphoma including plasmablastic lymphoma,primary effusion lymphoma and lymphoma associated with multicentric castlemans disease.Also it needs to differentiaed from anaplastic DLBCL (CD 20 + and ALK negative) and ALK positive Anaplastic Large Cell Lymphoma(ALCL; T cell origin,CD 30 positive).High index of suspicion and battery of IHC needs to done prior to accurate diagnosis and management.Outcome of ALK positive DLBCL is poor when compared to CD 20 positive DLBCL where rituximab is used along with chemotherapy or ALK positive ALCL to conventional CHOP based therapy.Targeting ALK with ALK inhibitor such as crizotinib has been reported in ALK positive Lung adenocarcinoma,ALK positive ALCL,ALK positive neuroblastoma and ALK positive inflamatory myofibroblastic tumour.More data of crizotinib with good outcome is available for ALK positive ALCL in refractory setting .But only two cases of ALK positive DLBCL has been treated with crizotinib where it has been used as 3rd or 4th line refractory setting with short duration response and both the reported patients has died within 30 and 60 days crizotinib treatment(Table 1).In our case we have used crizotinib as firstline salvage therapy as a stand alone therapy , achieved complete metabolic remission in 3 months and is still continuing crizotinib.

Mantle Cell Lymphoma of the Rectum: A Rare Scenario

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Introduction: Primary lymphomas of the gastrointestinal tract constitute only 5% of all lymphomas. Colorectal lymphomas account for 10- 20% of all gastrointestinal tract lymphomas. Primary rectal lymphoma accounts for 0.1-0.6% of colonic malignancies and 0.05% of primary rectal tumours. Diffuse large B cell lymphomas are the most common histological subtype. We report a rare case of primary rectal lymphoma of intermediate grade Mantle cell type. **Case report:** A 50 year old male presented with complaints of bleeding per rectum , incomplete evacuation of stools, mucous diarrhea and constipation of four months duration . Clinical evaluation revealed a wide based polypoid growth on the Lt lateral wall of the rectum, three cms from the anal verge. Colonoscopy showed an ulceroproliferative lesion occupying 2/3rd of lumen 3 cm above anal verge which was biopsied .

Table 1: Crizotinib in ALK positive DLBCL

Authour	Patient (n) Age/Sex	Stage	Chemotherapy Exposed (Firstline & Salvage chemotherapy)	Crizotinib	Duration of Crizotinib	Outcome
Wass M et al,(2014)	n=1 27/ F	IV	CHOP *6 +RT DHAP*2 ICE* 2 Auto -HSCT	Crizotinib used post transplant	30 days	Died 30 days after crizotinib treatment
Li J et al,(2015)	n=1 24/ M	III A	CHOP *5 ICE * 5 GEMOX+ Dexamethasone	Crizotinib combined with GEMOX+ Dexamethasone	60 days	Short term relief Patiend died 60 days after massive progression
This study	n=1 43/M	IV	CHOP*6 RT	Crizotinib u sed as s alvage therapy alone	90 days and counting	Complete metabolic CR Alive on crizotinib

MDCT of the Abdomen revealed an eccentric polypoidal mass lesion measuring 5 x 4.1 x 5 cm in the anterior and left lateral wall of the rectum causing marked luminal compromise .There was no obvious extension into para rectal fat. Significantly enlarged lymphnodes were seen in left perirectal , internal iliac and left inguinal region. Biopsy taken from the lesion reported as Mantle cell Lymphoma . Lymphoma workup was negative . With final diagnosis of stage IIA NHL rectum he received 6 cycles of chemotherapy with CHOP and Pelvic radiotherapy to a total dose of 2400cgy in 12 fractions. Follow-up at 4 years showed no evidence of tumor recurrence. **Discussion.** Rectum is an uncommon site for lymphomas to occur . Helicobacter pylori infection ,immunosuppression ,celiac disease ,inflammatory bowel disease and human immunodeficiency virus infection are considered risk factors . Our patient did not have any of the mentioned risk factors. Diffuse Large B cell lymphoma is the most common histological type in rectal NHL. Our patient however had Mantle cell histology , which is an extremely rare occurrence. Treatment of primary Rectal NHL remains controversial as the case numbers are limited. In the literature , treatment varies from chemotherapy alone to multimodal therapies combining surgery, chemotherapy and radiotherapy. **Conclusion:** The optimal management of primary lymphoma rectum is uncertain and yet to be determined. Due to rarity of cases , so far there is no prospective randomized trials

Key words: Mantle cell Lymphoma , Rectum

Primary Cardiac Lymphoma - A rare case report

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Background: Primary Cardiac Lymphoma (PCL) is a very rare variant of extra nodal non-Hodgkin's lymphoma. PCL accounts for 1.3% of primary cardiac tumors and only 0.5% of extra nodal lymphomas. Clinically patients present with cardiac symptoms depending its location in heart. Surgical removal of intra cardiac mass (palliative to remove the obstructive lesion) followed by combination of chemotherapy and radiation therapy is considered as the treatment of choice. **Case Report**: A 31 year old male presented with complaints of increasing dyspnea on exertion since 3 months duration and history of one episode of syncope while playing football. Echocardigraphy showed a mass in the right atrium measuring 5.2 X 4.6cm, suggestive of cardiac myxoma or thrombus. Patient was taken for surgery. Intraoperatively there was hard mass originating from anterior free wall of right atrium near tricuspid valve with partial obstruction of the valve orifice. The tumor was excised in toto with excision of part of right atrial wall. The postoperative period was uneventful. The mass was measured 6.5 x 5.5 x 4 cm. The outer surface was greyish-white and the cut-surface was solid grayish-white in color with multiple areas of hemorrhage. Histopatholopgical examination showed monotonous large sized cells with enlarged nucleus, raised N:C ratio, coarse chromatin, prominent nucleoli and moderate amount of cytoplasm. There were 20-50 mitotic figures per high power field. Background showed interspersed inflammatory cells, consisting of mostly reactive plasma cells. Immunohistochemical examination showed diffuse positivity for LCA and CD 20, and aberrant positivity for MPO and sprinkling positivity for CD 68 in histiocytes and dendritic cells. Tumor cells were negative for CD 3, CD117, CD 34 and synaptophysin. Finally a diagnosis of Non-Hodgkins lymphoma in favour of diffuse large B-cell lymphoma was made. Further postoperative evaluation with contrast Computed Tomography of neck, thorax and abdomen showed no lymphadenopathy. Presently the patient is undergoing chemotherapy with cyclophosphamide, doxorubicin (hydroxydaunomycin), vincristine (Oncovin), prednisolone regimn. **Conclusion:** Lymphomas presenting as primary cardiac tumors are rare, especially among immunocompetent individuals and about 80% of these are B-cell lymphomas. They usually involve the right chambers and pericardium. The diagnosis is suspected when patients present with a cardiac mass or an unexplained refractory pericardial effusion. A thorough workup should include transthoracic and transesophageal echocardiography, computed tomography, and magnetic resonance imaging. Transvenous biopsy is a controversial procedure because of the risk of pulmonary embolism. Treatment options include chemotherapy and radiotherapy. Surgical treatment is palliative (for relieving obstruction).

Key words: Primary cardiac lymphoma, Non-Hodgkins lymphoma, Diffuse large B-cell lymphoma.

Renal Non-Hodgkin Lymphoma confused with Renal Cell Carcinoma: Case Report

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Background: Kidney is a rare site for lymphoma and the diagnosis is often confused with renal cell carcinoma. In earlier instances, diagnosis of renal Non-Hodgkins lymphoma have been made from biopsy specimen after surgery. In our case, the diagnosis was based upon the clinical suspicion followed by biopsy. **Case Report:** A 64 year old female presented with one month history of right flank pain, weight loss and decreased appetite. Her examination revealed ballottable mass which was confirmed on ultrasound examination as right renal mass. A working diagnosis of renal cell carcinoma was made and the patient underwent further tests including a PET-MRI examination which showed metabolically active right renal mass with active cervical, retroperitoeal and mesenteric lymph nodes. Imaging did not show any involvement of inferior vena cava .This type of presentation with presence of non-contiguous lymph nodes necessitated a biopsy which was taken from supraclavicular node which confirmed CD 20 positive Diffuse Large B-Cell Lymphoma. She was then started on chemotherapy with Rituximab, Cyclophosphamide ,Vincristine , Adriamycin and Prednisolone (R-CHOP) regimen of which she has completed two cycles so far. Her pain has subsided with improvement in her general condition. **Conclusion:** Renal cell carcinoma may sometimes be mimicked by Lymphoma and a cytological analysis, if not a biopsy must be taken to rule out lymphoma and to avoid nephrectomy.

Keywords: Renal cell carcinoma, Non-Hodgkin lymphoma

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Orbital Diffuse Large B-Cell Lymphoma with Leptomeningeal Spread and Spinal Deposits

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Introduction: Orbital lymphoma accounts for only 2% of lymphomas, and 10% of extra nodal lymphomas. They are mostly low grade and the commonest subtype is extra nodal marginal zone B cell lymphoma, followed by follicular, lymphoplasmocytic and diffuse large B-cell lymphoma (DLBCL). DLBCL accounts for only 15% of orbital lymphomas **Case Report:** : A 65 year old female presented with back pain of 3 months duration. She was evaluated with MRI lumbar spine which showed diffuse thickening of cauda equina nerve roots and diffuse effacement of epidural space from L3 to S4. CSF cytology showed atypical lymphoid cells and CSF flow cytometry shows clonal B cell population. PET CT showed FDG avid irregular enhancing soft tissue density lesion in bilateral retrobulbar region and in spinal canal surrounding cauda equina. During evaluation, she developed proptosis of the left eye. Spiral CT scan of the orbits showed soft tissue density lesion in bilateral retro-bulbar regions. Biopsy from right

retro-bulbar mass showed poorly differentiated malignancy with features of Non-Hodgkins lymphoma. IHC was positive for CD20, CD 138 and negative for CD3, CD5, CD23 and BCL-6. Ki-67 proliferative index was 30-40%. Final diagnosis was diffuse large B-cell lymphoma with focal plasmablastic differentiation. Bone marrow biopsy showed normal cellular marrow with focal atypical lymphoid cell clusters. MRI brain and orbits showed T1-isointense, T2-hyperintense masses in bilateral retro-bulbar regions with nodular enhancing leptomeningeal deposits. She received nine cycles of chemotherapy with R-MVP regimen following which there was a reduction in left orbital and leptomeningeal lesions with stable disease in other locations. She was further treated with craniospinal irradiation 23.4Gy, followed by 21.6 Gy boost to right orbital and spinal deposits following which there was symptomatic improvement. **Discussion**: Orbital DLBCL is unusual and presentation with diffuse CNS involvement and spinal deposits is extremely rare. The optimal management remains unclear. Our patient responded poorly to chemotherapy and had partial response with symptomatic improvement after craniospinal radiation.

Oro-Nasal Fistula, a Complication of Invasive Oral Aspergillosis in a Child With Acute Myeloid Leukaemia

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Background: Prolonged neutropenia secondary to chemotherapeutic agents enables the spread of invasive aspergillosis, which is unaffected by anatomical barriers. Reports of invasive oral aspergillosis in pediatric AML are limited. **Summary:** we are reporting a case of invasive aspergillosis resulting into oro-nasal fistula in a 6 year male having acute myeloid leukemia. The child was admitted for induction chemotherapy (week 12) comprising of cytosine arabinoside and daunorubicin. On day 5 of admission child developed febrile neutropenia for which empirical broad spectrum antibiotics (pipracillin + tazobactum and amikacin) were started. On examination no focus for fever could be identified. In view of no response antibiotics were upgraded after three days to meropenem and vancomycin. Blood and urine culture reports were noncontributory. Neutropenia persisted on 5th day post antibiotics so amphotericin –B was also added empirically. On day 10th of admission on routine examination we observed a black colored necrotic lesion of size 0.5*0.5 approximately on the hard palate. In view of suspected Aspergillosis voriconazole was added and a detailed fungal work up was sent, including fungal blood cultures and swabs from the index lesion. Two days later child complaints of nasal regurgitation of fluids while eating. On examination there was a fistula on the hard palate at the site of previous lesion. Child responded clinically on 15th day and neutropenia also starts improving alongwith. Patient received total of 3 weeks of antibiotics and 6 weeks of antifungal. Currently the child had completed the chemotherapy successfully but the fistulae is still persisting and corrective surgery is planned in follow up. **Conclusion:** Thus this is a rare case of AML where oro-nasal fistula has been reported due to invasive oral Aspergillosis.

Key words: Acute myeloid leukaemia, invasive oral Aspergillosis, oro-nasal fistula

Bortezomib Induced Sweet Syndrome in a Case of Multiple Myeloma

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Introduction: Sweet's syndrome (SS) was first described in 1964 by Dr Robert Douglas Sweet. It is etiologically classified as classical (idiopathic SS), malignancy-associated (Paraneoplasic SS) and drug-induced SS. Idiopathic SS is the most common accounting for more than 70% of cases. The Paraneoplasic variant accounts for 10 to 20% predominantly attributed to haematological malignancies like acute myelogenous leukemia, myelodysplastic syndromes and lymphoma. Association with multiple myeloma (MM) is very rare with only fourteen cases reported in literature so far. **Objectives:** To report occurrence of sweet syndrome in a 65 years old patient who was diagnosed with MM three years back and was on bortezomib. **Material and Methods:** Elderly patient who developed SS three years after being diagnosed with MM and was on bortezomib. **Results:** A 65 years old male patient, a known case of Multiple Myeloma (IgG type) since three years presented with complaints of multiple red raised painful lesions on his face of three days duration. Lesions over his face coalesced within one day of their appearance and subsequently similar lesions appeared on his extremities with associated history of fever. Patient was on Injection Bortezomib 2mg IV weekly since last six months. Dermatological examination revealed multiple erythematous papules and nodules coalescing to form plaques on forehead, malar region, arms and thighs. No mucosal lesions were found. Skin biopsy showed neutrophilic infiltration of dermis. A diagnosis of Sweets syndrome secondary to multiple myeloma was made and he was managed with a tapering dose of oral prednisolone starting at 40 mg per day. Topically he was prescribed 0.05 % Fluticasone cream to be applied twice. Patient had an excellent clinical response to oral steroids and his lesions cleared off and he became afebrile within one week. **Conclusions:** SS is an acute febrile neutrophilic dermatosis. Diagnostic criteria for Sweet's syndrome consist of major and minor criteria. Both the major criteria plus 2 out of 4 minor criteria are essential to establish the diagnosis. The major criteria include acute onset of typical lesions in skin and histopathological correlation without evidence of vasculitis. Minor criteria include fever > 38 degrees, associations (malignancy, inflammatory disorders or pregnancy), excellent response to oral corticosteroids and abnormal laboratory values (ESR >20 mm, leukocytes >8000, neutrophils >70% and positive C-reactive protein). Our patient fulfilled both the major criteria as well as three minor criteria. The secretory status in MM may influence occurrence of SS. Among 14 associated cases of SS with MM reported in literature, seven cases were IgG, four IgA, one was free kappa, and two had unknown immunoglobulin secretion. Our patient expressed the IgG type. Medications that have been incriminated in Sweet's syndrome includes granulocyte colony stimulating factor (GCSF), all-trans retinoic acid, carbemazepine, celecoxib, diazepam, diclofenac, hydralazine, levonorgestrel/ethinyl estradiol, minocycline, nitrofurantoin, propylthiouracil, and trimethoprim-sulfamethoxazole. Bortezomib has also been reported to cause Sweet syndrome. Differential diagnoses include mainly erythema multiforme, erythema elevatum diutinum, erythema nodosum, and pyoderma gangrenosum. The first line treatment of SS is Systemic glucocorticoids. Systemic symptoms and skin manifestations rapidly respond to therapy. Localized lesions may respond to topical or intralesional corticosteroids. Our patient was treated with Oral corticosteroids with a good response within one week. Many other treatments reported to be successful in treating SS include potassium iodide, colchicine, dapsone, indomethacin, cyclosporine, cyclophosphamide, chlorambucil, doxyxycline and clofazimine. Spontaneous resolution may occur but only after several weeks or months. High Index of suspicion and promp

Primary Lymhoma Thyroid: A Diagnostic Dilemma

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Introduction: Primary Lymphoma of Thyroid is a rarely encountered clinical entity that occurs in late age intrinsically associated with Hashimotos thyroiditis. It is very rare constituting 5% of all thyroid malignancies and 3% of all Non Hodgkin Lymphomas. Typically it presents in seventh decade of life with female to male ratio of 3:1. Primary thyroid lymphoma is associated with poor prognosis and divided in two groups: pure mucosa associated lymphoid tissue (MALT) lymphoma and diffuses large B cell lymphoma (DLBCL) or mixed subtype. DLBCL is more aggressive and survival outcome are highest with multimodal therapy incorporating monoclonal antibodies, chemotherapy and radiotherapy. The importance of recognizing PLT lies in the fact that this disease is quite curable without need for extensive surgery if recognized early and treated appropriately. Primary thyroid lymphoma is rare disease and continues to produce diagnostic and therapeutic dilemmas. **Material and methods:** A 60 years

old female with thyroid swelling with mild odynophagia was reffered to department of pathology with no other systemic complaints or swelling elsewhere in the body. Patient was subjected to FNAC. Later on after three months cervical lymph node biopsy was also received in the department. **Result:** FNAC smears show degenerate and intact follicular cells and large number of lymphoid cells with prominent immature component. A diagnosis of florid lymphocytic thyroiditis with suspected lymphomatous transformation was rendered. Histopathological examination of cervical biopsy received after three months show Diffuse Large B Cell (DLBCL) Type of NHL. **Conclusion:** FNAC smears from thyroid with immature/ atypical lymphoid cells should raise suspicion of lymphoma and patient should be subjected to intense scrutiny for possibility of NHL. Our report emphasizes the need for clinical awareness in such perplexing cases which require multidisciplinary approach for early diagnosis of such lesions and preventing delay and unnecessary surgery.

Keywords: Thyroid Lymphomas, FNAC, Clinical Awareness

Philadelphia Positive Chronic Myelogenous Leukemia (Cml) in Pediatric Patients

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Background: Incidence of CML in children is very rare, clinical presentation being similar to that of adults. Blood picture shows leucocytosis and shift to left. Cytogenetic studies confirm the diagnosis. **Materials and method:** The following two cases were examined and investigated at AIIMS. **Results:** Both cases were diagnosed to be Philadelphia positive CML. They are being followed up, and have shown different progression. Case1 has progressed to blast crisis probably due to noncompliance of treatment and lack of follow up, whereas case 2 has improved clinically and hematologically. **Conclusion:** One requires high sense of suspicion when leucocytosis is found even in pediatric age, as CML could be one of the differential diagnosis.When differential count is also suggestive of CML, for confirming, cytogenetic tests are essential.

Key words: Chronic myelogenous leukemia, pediatric, leucocytosis

Cardiac Myxoma- a Benign Tumour of Heart- Managed At Sskm Hospital Kolkata, India

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Background: Cardiac myxoma is the commonest benign intra-cardiac tumour. **Methods:** Near about 6000 cardiac cases were operated at cardio-thoracic and vascular surgery department of SSKM hospital, IPGMER Kolkata, India. 38 cases of cardiac myxoma were operated over a period from October 2002 to October 2011. Preoperative diagnosis was made with clinical presentation and preoperative echocardiography. Complete tumour excision was done and all patients were followed up for recurrence and complications. **Result:** Cardiac myxoma constituted about 0.6% of all cardiac cases operated at our institute. This most commonly presented at 5th decade of life. 35 cases were left atrial and 2 cases were right atrial and 1 case was having both atrial involvements. The Left atrial myxoma mostly presented as mitral stenosis and very few presented with embolic and constitutional symptoms. No death or recurrence was observed during the follow up period. **Conclusion:** Cardiac myxomas form a very small percentage of the cardiac cases. Echocardiography is the ideal diagnostic tool. Immediate surgical treatment is indicated in all patients to prevent complications. Cardiac myxomas can be excised with a low rate of mortality and morbidity.

Case details	Case 1		Case2
Age/ Sex	**6years / Female**		**14years/ Male**
Complaints of	Low grade fever, increasing pallor, left sided mass per abdomen X 4 months		Low grade fever, left sided lump in abdomen X 2 months
On examination	Pallor Inguinal, axillary lymphadenopathy Hepatosplenomegaly		Pallor Splenomegaly
Hemoglobin (gm %)	8.3		14.9
Total Leukocyte count (cells/cumm)	1,08,000		70,700
Differential Leukocyte count (%)	*Blast*	1	1
	Promyelocyte	4	-
	Myelocyte	15	4
	Metamyelocytes	20	2
	Neutrophil	39	80
	Lymphocytes	6	8
	Monocyte	-	-
	Eosinophil	6	2
	Basophils	5	3
NRBC (cells/100 WBC)	2		0
Platelet count (cells/cumm)	2,60,000		2,68,000
Philadelphia chromosome (RT-PCR)	POSITIVE		POSITIVE

High Total Leukocyte Count in Down syndrome infant: Transient Abnormal Myelopoiesis (TAM) or myeloid leukemia associated with Down syndrome (ML of DS).

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Background: TAM and ML of DS have morphologically indistinguishable blasts. TAM usually presents and regresses within the first three months of life. In a subset of patients, myelopoiesis remains abnormal, and the persistence of elevated blasts after 6 months is considered ML of DS. **Case Details:** Two neonates referred to our institute in view of marked increase in total Leukocyte count (TLC) and features suggestive of Down Syndrome (broad flat face with small nose, upward slanting of eyes, epicanthal folds, single palmar crease) present. Down syndrome confirmed on Cytogenetic study. Per abdomen: massive spleenomegaly present. **Result:** One of the patient turned out to have AML-M7 while other TAM. **Conclusion:** Careful and detailed investigation

should be carried out with high index of suspicion for Acute Leukemia. As out of these two cases one turned out to be Acute Megakaryocytic Leukemia, which requires chemotherapy and other turned out to be Transient abnormal myelopoiesis in which the role of chemotherapy is not yet established.

	Baby no.1	Baby no.2
Age	**8 days**	**27 days**
Haemoglobin %	15.1	16.0
Total Leukocyte Count (per cumm)	1,61,000	1,01,600
Differential Leukocyte count	Blast 96% Neutrophil 2% Lymphocyte 2%	Blast 70% Neutrophil 10% Lymphocyte 20%
Platelet count (per cumm)	37,000	59,000
Flow cytometry	AML-M7	TAM

Primary Adenoid Cystic Carcinoma of Lung. A Case Report

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Background: Adenoid cystic carcinoma (ACC) is a distinctive salivary gland-type malignant neoplasm that arises rarely as a primary tumor in the lung. **Case report:** A 45 year old male presented with persistent dry cough for last 6 months. Chest radiograph showed consolidation in the left mid zone. Fibreoptic bronchoscopy revealed an endoluminal growth in the left mid lobe bronchus, which was diagnosed on histology to be poorly differentiated carcinoma. Metastatic workup showed no other disease. He underwent right pneumonectomy for the same. Histopathological examination of the specimen confirmed adenoid cystic carcinoma on immunohistochemistry. The patient was kept on follow up uneventfully for 7 years, when he showed multiple suspicious opacities in right lung on chest X-ray. On metastatic workup, he was found to have multiple small right metatsases. The patient was then started on palliative chemotherapy. **Conclusion:** Primary adenoid cystic carcinoma of lung is a rare entity, with scarcity of literature regarding treatment. Surgical treatment remains the cornerstone of management in localised disease, however there are no standard guidelines regarding management of metastatic disease.

Keywords: lung cancer; adenoid cystic carcinoma; pneumonectomy

Primitive Neuroectodermal Tumours/Extra Osseous Ewing Sarcoma of Lung Masquerading As Hydatid Cyst: An Unusual Case

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Introduction: Primitive neuroectodermal tumors (PNETs) arising directly from the lung are extremely rare but particularly aggressive neoplasm. Although thoracic PNET usually develops on the chest wall, there have been reports of primary Ewing sarcoma/PNET of the lung. **Methods**: In the current study, the authors describe a patient with PNET/Extra-osseous Ewing's Sarcoma mimicking as Hydatid cyst of right middle lobe of Lung. **Results:** We present the case of a 35-year-old female presented to us as hydatid cyst of Right middle lobe of Lung which on Right posterolateral thoracotomy followed by right middle lobectomy was diagnosed following histology and immunohistochemistry as PNET/extra osseous Ewing's Sarcoma. Patient has received four cycles of chemotherapy and is in regular follow up. **Conclusions:**. PNETs arising from the lung parenchyma without pleural or chest wall involvement are extremely rare. Moreover, this tumour mimicking hydatid cyst of Lung is unparalleled. Although uncommon, if the pathological features are similar to Ewing sarcoma, PNETs should be kept in mind, and the target therapy may be a potent treatment for this disease. Although clinical course in most of the patient does not carry a favorable response few patients may respond well to surgical excision followed by chemotherapy.

Key words: Ewing, Hydatid , PNET

Asymmetric Secondary Hypertrophic Osteoarthropathy with Monoparesis

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Case description 43 y male factory worker heavy smoker from Uttar Pradesh who had receive five months of treatment for Pulmonary tuberculosis presented with symptoms of cough, haemoptysis, pleuritic type of chest pain and solitary non fluctuating weakness in the left arm since the past 15 days. Examination revealed pallor, cachexia, poor built, left supraclavicular lymphadenopathy with drumstick appearance of the digits in the right hand along with parrot beaking in the left hand with signs of proximal muscle weakness with swelling of digits of both the hands. Decreased air entry was noted in the right mammary and inframammary areas along with motor deficit, absence of overhead abduction, inability to form a fist and absence of deep tendon reflexes with no sensory deficit in the left upper extremity. No tenderness was elicited in bilateral wrist joints. Acrosteolysis was present on X ray of the Left hand however no acrometastasis was documented. CT Thorax was suggestive of a mass in the right upper lobe following which a biopsy was obtained and following appropriate staging and metastatic workup ,he was planned for one cycle of chemotherapy with Pemetrexed plus Cisplatin which was subsequently discontinued in view of grade four Thrombocytopenia. He was being being planned for targeted therapy after ALK testing. The differential diagnosis for this presentation includes Assymetric HOA , ATT induced Peripheral neuropathy ,Paraneoplastic syndrome, Chemotherapy induced Peripheral neuropathy. He was provided medical management for his symptoms.

Discussion Hypertrophic osteoarthropathy is seen in 10 – 20 percent of Adenocarcinomas. It is usually bilateral. Large megakaryocytes or platelets release TGF B1 which increases accumulation of extracellular matrix proteins. Increase in levels of VEGF, PDGF, and HIF 1 attributible to platelet impaction and subsequent hypoxia have also been implicated in the pathogenesis. Assymetrical involvement of the digits associated with acroosteolysis is usually present in pseudoclubbing which can be associated with acrometastasis. Unilateral Clubbing is seen in the hemiplegic arm however Monoparesis and asymmetrical Clubbing in advanced Adenocarcinoma has been rarely reported.

Response of Crizotinib in brain metastasis in ALK positive Non-Small cell Lung Carcinoma

Ullas Batra

Rajiv Gandhi Cancer Institute and Research Center

Background: Brain is an important site of progression in non-small cell lung carcinoma. Anaplastic lymphoma kinase inhibitor, Crizotinib, shows systemic and intracranial control of disease. **Case Presentation:** 68 years old non-smoker female presented with breathlessness. Pleural fluid cytology was suggestive of adenocarcinoma. PET-CT showed lesion in the anterior segment of left upper lobe, irregular nodular left pleural thickening, and mediastinal lymph nodes with moderate left

pleural lesion. MRI brain showed right parietal lesion, though patient was asymptomatic. CT guided biopsy was done and subjected to mutational analysis for ALK and EGFR. Patient was diagnosed ALK positive NSCLC with brain metastasis and prescribed Crizotinib. Breathlessness resolved quickly. Follow up scan after 8 months showed inactive brain lesion along with systemic control. **Conclusions:** Crizotinib shows clinical activity in brain metastasis.

Keywords: Brain metastasis, Crizotinib, clinical response

Rapid Complete Response of Crizotinib in ALK positive Non-Small cell Lung Carcinoma

Ajay Sharma

Rajiv Gandhi Cancer Institute and Research Center

Background: Crizotinib, a tyrosine kinase inhibitor (TKI) for anaplastic lymphoma kinase (ALK), shown to have remarkable efficacy in patient harboring ALK mutated gene in non-small cell lung cancer. **Case Presentation:** A patient was presented with cough and hemoptysis. He was diagnosed with adenocarcinoma lung. He was given 3 cycles of chemotherapy (pemetrexed and cisplatin). PET –CT showed partial response after chemotherapy. Patient underwent diagnostic thoracoscopy and VATS biopsy of pleural and diaphragmatic nodule. IHC for ALK gene mutation was positive. Crizotinib was prescribed in dose of 250 mg BD. Patient tolerated Crizotinib well and showed rapid improvement. A follow up PET CT after 3 months of initiation Crizotinib showed complete response. **Conclusions:** A case study of rapid complete response achieved by Crizotinib in ALK positive non-small cell lung cancer.

Keywords: Complete response, Crizotinib, ALK positive non-small cell lung cancer

Malignant Pleural Mesothelioma- A Case Report

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Malignant mesothelioma is most common primary neoplasm of pleura. It is found in both diffused and localized forms. Malignant mesothlioma arises from mesothelial cells lining the visceral cavity. It has a etiological correlation with asbestos exposure. It has non-specific clinical presentation requires high degree of clinical suspicion before final diagnosis. Malignant mesothelioma is usually a fatal neoplasm for which operation has been the main stay of treatment because chemotherapy and radiotherapy are relatively ineffective. The choice of operation for malignant mesothelioma remains controversial.Reducing the bulk of tumor with cytoreductive surgery is key to extending survival. Two surgeries have been developed, extrapleural pneumonectomy and pleurectomy.Extrapleural pneumonectomy has been advocated because it allows complete removal of gross tumor and can be associated with long term survival. Extrapleural pneumonectomy is associated good local control of disease with greater likelyhood of relapse in distant sites We report a new case of diffuse malignant mesothelioma involving left lung without any distant metastasis. Patient had no history of asbestos exposure. Patient underwent extrapleural pneumonectomy with excision of left hemidiaphragm. A complete en-block resection was performed. Final histopathology and immunohistochemistry confirmed the diagnosis as malignant epithelial mesothelioma. Rarety of disease poor outcomes and limited treatment options prompted us to report this case. **Introduction:** Malignant mesothelioma is a rare neoplasm of pleura. They presents with vague symptoms and pose difficulty in diagnosis and treatment. Effective treatment is limited for most patients. Multimodality treatment approach is required for optimal outcome. In this article we report a case of malignant mesothelioma to underwent complete en-block resection of tumour. Also included discussion of clinical features diagnostic dilemmas and therapeutic options.

Primary Synovial Sarcoma of the Mediastinum: A Rare Case Report

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Introduction: Synovial sarcoma is a malignant mesenchymal neoplasm predominantly affecting soft tissues of the extremities of adolescents and young adults accounting for up to 10% of all histological types of soft tissue sarcoma. It has no relation to the synovium and may arise in any part of the body. Its' occurrence as a primary tumour in the mediastinum is very rare (0.02% of all soft tissue sarcoma), only few cases can be found in the literature. Treatment protocols include surgery, radiation and chemotherapy. Only a few cases have been reported over the last years; here we are reporting a new case of this entity. **Objectives:** To present a rare case and to assess treatment outcome and toxicities in primary mediastinal synovial sarcoma. **Material and Methods:** A 62 year old female normotensive, non-diabetic with a pleasant personality presented with complaints of shortness of breath and chest pain since last 1 month. CECT THORAX which showed a heterogenous mass of size 15 x 10 x 8 cms in mediastinum. Biopsy from lesion was suggestive of malignant spindle and round cell neoplasm. PET-CT scan showed a large heterogeneously enhancing soft tissue mass involving almost the entitre upper lobe of left lung, measuring 12.3 (AP) x 10.7 (TR)x 16.0 (CC) cms. Patient underwent near total excision of tumor, followed by radiotherapy. IHC tumor cells were negative for SMA and S100. Focal positivity was seen for bcl2 and CD99. Occasional EMA positive focus was seen. **Results:** Patient is disease-free, in good health after 1 month of radiotherapy. **Conclusions:** In summary, though mediastinal sarcoma is a rare entity, if aggressively treated with complete resection and or multimodal therapy with intensive follow-up, the survival of such patients can improve.

Inflammatory Myofibroblastic Tumor Requiring Intrapericardial Pneumonectomy via Sternotomy: A Rare Case Report

A G Ahangar

North East Indira Gandhi Regional Institute of Health and Medical Science

Background: We are reporting an uncommon case of large pulmonary inflammatory myofibroblastic tumor (PIMT) of left upper lobe of lung, which had local invasion in to the left bronchus and left pulmonary artery. The patient had to undergo intrapericardial pneumonectomy via sternotomy in view of bronchovascular infiltration to both left main bronchus and proximal left pulmonary artery. Inflammatory myofibroblastic tumor (IMT) is a rare tumor of lung and it is unclear whether these lesions represent a primary inflammatory process versus a low-grade malignancy with inflammatory response. Histologically they show spindle cell proliferation with a distinctive fibroinflammatory and even appearance of a pseudosarcoma. These tumors are often a diagnostic dilemma for the surgeon and the pathologist since biopsy reveals only inflammatory cells. **Case Report:** This 25 years old lady had presented with cough and occasional fever for six months duration. Routine evaluation showed a large left upper lobe lung mass and repeat fine needle aspiration cytology (FNAC) was inconclusive. There was no mediastinal lymphadenopathy in contrast compute topography (CT) scan of thorax. Although there were no constitutional features of malignancy, no mediastinal lymphadenopathy and inconclusive preoperative FNAC, but in view of young age of the patient along with large mass lesion of left upper lobe and its bronchovascular infiltration to both left main bronchus and proximal left pulmonary artery, we had planned for a curative resection through midline sternotomy. The

intrapericardial approach of pneumonectomy for complete resection of the tumour had to be done. Her postoperative period was uneventful and she has been asymptomatic at last follow up at one year. **Conclusion:** IMT is generally a benign lesion; however it has potential for local invasion and recurrence. The diagnosis and prognosis depend on complete resection. To pronounce a tumour "irresectable" depends on the experience, skill and local conditions of the surgical team.

Key words: Inflammatory myofibroblastic tumor; Pulmonary Tumour; Therapy.

EGFR mutation- a commonly neglected mutation in squamous cell lung carcinoma.

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Introduction: Advances in molecular biology have led to the identification of mutations within the epidermal growth factor receptor (EGFR), and the finding that these mutations make tumors exquisitely sensitive to EGFR tyrosine kinase inhibitors (TKIs), has revolutionized treatment of non-small-cell lung cancer (NSCLC). EGFR mutations are more common in never-smokers, in patients with Asian ethnicity, and in patients with adenocarcinoma histology.. We present two cases of squamous cell lung cancer diagnosed on small biopsy in non smoker females with EGFR mutations who benefitted with oral tyrosine kinase inhibitors. **Objectives:** To aware the oncologists of the fact that even in patients of lung cancer with squamous histology , EGFR testing should be done in selected group especially in never smokers, female gender, asian ethnicity and those in whom diagnosis were made on small biopsy specimen. **Material and Methods:** Two cases of squamous cell lung cancer diagnosed on small biopsy in non smoker females with EGFR mutations presented to our hospital who benefitted with oral tyrosine kinase inhibitors. A 56 years old female, diabetic, hypertensive, non smoker presented with history of cough, weight loss and right sided weakness. MRI brain showed two hypodense lesions in left frontal lobe. PET CT revealed right lung mass with mediastinal lymph nodes, brain, adrenal, pancreatic and bone lesions. A core needle biopsy from lung mass revealed squamous cell carcinoma, p40 positive and thyroid transcription factor (TTF) negative. In view of symptomatic brain metastasis, she was treated with whole brain radiotherapy followed by two cycles of gemcitabine and carboplatin based chemotherapy. However, in view of poor tolerability due to grade 4 neutropenia and poor performance status, chemotherapy could not be given. Her biopsy was reassessed for EGFR mutational analysis and showed L858R mutation positive. She was started on erlotinib and imaging studies after 2 months of therapy demonstrated significant tumor response in the pulmonary lesions and in the metastatic sites. A 44 years old female, diabetic, hypertensive, non smoker presented with history of breathlessness. Bronchoscopy showed malignant intermediate bronchus obstruction. Bronchial biopsy revealed squamous cell carcinoma expresses p40 (Figure 2) but negative for TTF1. In view of her being non smoker EGFR mutation was tested and was positive for exon 21L858R mutation. After 3 cycles of gemcitabine and cisplatin based chemotherapy there was partial response and now she was on maintenance erlotinib with good disease control. **Results:** Both patients were females, non smokers, of asian ethnicity and were diagnosed on small biopsy, found to have EGFR mutation when tested for its presence and benefitted with oral TKI's therapy.

Adenocarcinoma Lung Presenting as Metastasis to Breast; A Rare Presentation: A Case Report

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Introduction: Lung cancer is the most common cancer worldwide and it is the most common cause of cancer related death. The principal histologic types of lung cancer are squamous cell carcinoma,adeno carcinoma,large cell carcinoma and small cell carcinoma. The first three are commonly referred as non small cell lung cancer. Common metastatic sites for carcinoma lung are mediastinal and supraclavicular lymph nodes,liver,lungs,adrenal glands,brain,pleura and pericardium. Lung cancer can also presents as Para neoplastic syndromes. Metastasis to breast is extremely rare. In this case report we present a case of adenocarcinoma lung presenting with metastatic deposit in breast in a premenopausal lady. **Case report:** 43 year old lady with no co morbidities living with husband and children presented to a hospital with increasing cough over 4 months, chest pain and upper back ache of 2 weeks duration. She was evaluated with MRI scan of spine and screening of chest and it showed narrowing of right upper lobe bronchus at around 2 cm from origin. Soft tissue density of 7.8* 4.6 cm in right upper lobe, reaching up to the right hilum. Right sided pleural effusion was also there. With the suspicion of lung cancer she was referred to Regional Cancer Centre Trivandrum for further management. On clinical examination she was having ECOG performance status 2,pale,grade 1 clubbing, bilateral small scalene nodes, air entry was decreased in Right upper and lower lobes. There was a 3*3 cm firm to hard tender swelling in medial lower quadrant of right breast and few tiny axillary nodes on same side. CT scan of chest and abdomen done which showed right upper lobe mass with focal lymphangitic infiltration, and right pleural effusion.Bronchoscopic biopsy was done and it showed adenocarcinoma cells which are ck7+ve,TTF1+ve,synaptophysin –ve and 34BE12 –VE.Morphological and immunohistochemistry picture was suggestive of adenocarcinoma lung. Pleural fluid cytology and cell block also showed same picture.Tru cut biopsy from right breast lump showed the same picture with the same IHC picture suggestive of adenocarcinoma lung deposit in breast tissue.EGFR study results are awaited and patient is started on palliative chemo with pemetrexed and carboplatin. She is symptomatically better after chemotherapy and pleural fluid aspiration. **Conclusion:** This case reports shows a very rare presentation of non small cell carcinoma lung as metastatic deposit in braest.

Giant Solitary fibrous tumour of pleura – a rare case

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Solitary fibrous tumour of the pleura is a rarely encountered clinical entity which may have different clinical pictures. The majority of these neoplasms have a benign course, however it is important to identify it so that curative treatment may be offered to the patient. We herein describe a case of a 43 year old labourer, presenting with progressive breathlessness and cough with expectoration. The diagnostic workup including chest X- ray and CT scan, which revealed a large tumour in the right hemithorax. Radical surgical resection of the mass was performed through a right lateral thoracotomy. Histological examination of the surgical specimen showed a mass measuring 27x17x18 cm and weighing 7.5kgs consistent with features of a benign giant solitary fibrous tumour of the pleura. Its surgical removal definitely resolved the symptoms. The patient had no postoperative complications. This case is being presented for its large size and rarity.

Contralateral Haemothorax Caused Due to Chemoport Catheter Malposition: A Rare Case Report

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Introduction: Chemoport, a central venous infusion system is commonly used in cancer patients for administration of chemotherapy. Malposition of chemoport catheter into contralateral pleura, which cause massive haemothorax, is very rare, but potentially catastrophic complication. We report a case presented as sudden catastrophe, massive haemothorax caused due to chemoport catheter tip malposition into contralateral pleura through SVC. **Case report:** A 53 yrs old female, a diagnosed case of carcinoma right breast. After all workup patient planned for right MRM and contralateral Chemoport insertion in same sitting. We routinely practice chemoport insertion on unaffected site followed by definitive surgery. During left sided subclavian vein chemoport insertion with Seldinger's technique without image guidance, after introducing dilator sheath patient developed sudden hypotension and fall in O^2 saturation. Left sided pneumothorax was suspected and left sided ICD was inserted immediately in operating room and further surgery deferred and patient shifted to ICU for ventilatory support. Chest x-ray suggestive of massive Right sided haemothorax and abnormal position of catheter tip. Immediate right sided ICD inserted and patient stabilized with multiple blood transfusions. After resuscitation CT thorax done to confirm the position of catheter. Further definite management done. **Discussion:** Malposition is one of the most common complication after catheter placement. Catheter tip may lie in IJV, contralateral jugular, axillary or azygous vein. If the catheter is too long, the tip may coil in right atrium or inferior vena cava. Usually, fluoroscopic guidance prevents these complications. Malposition increases the risk of thrombosis and perforation. Therefore, an incorrect tip position must be corrected as soon as possible. Besides simply exchanging the malpositioned catheter, there are interventional methods which may facilitate correct cathter positioning. Here, we report an interesting case of malposition of chemoport cathter tip in contralateral pleura through SVC. **Conclusions:** During Chemoport insertion, if patient suddenly goes into hypotension and falling of O^2 saturation, it can be caused due to malposition of catheter into contralateral pleural cavity through SVC, instead of suspicision of only ipsilateral pneumothorax or haemothorax.

Tetanus Infection from Cancer Lesions

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Introduction: Tetanus is an acute, often fatal disease manifested by skeletal muscle spasms and autonomic nervous system disturbances. It is uncommon but present with a high fatality rate; it can occur from cancer lesions. **Material and Methods:** Adult tetanus patients admitted at the Philippine General Hospital between January 2010 and July 2015 were included in this retrospective case report. Patients in remission and those with tetanus points of entry other than the tumor site, and those whose charts could not be retrieved were excluded. Tetanus was clinically diagnosed based on the presence of trismus, muscle spasms and/or abdominal rigidity, not attributable to other aetiologies. **Results:** There were 3 cancer cases where the tumor lesion was the suspected tetanus site of entry. Case 1 was with an ulcerating sarcoma, wherein a core needle biopsy was done. Case 2 was a poorly healing biopsy site of a phylloides tumor; case 3 was a recurrent nasopharyngeal cancer, with no repeat biopsy. All patients presented with trismus and muscle spasms, with two patients developing the symptoms post biopsy, and no tetanus prophylaxis given. None had a known vaccination history. All patients' required mechanical ventilation and the patients with open wounds expired from complications. **Conclusions:** Tetanus can occur in cancer patients with ulcerating tumors, in those undergoing biopsies and even those with no evidence of a break in the skin. A poorer prognosis is associated with open skin lesions and biopsies. It leads to delays in management of the cancer and significant morbidity and mortality. High index of suspicion should be maintained in these patients. A vaccination or booster dose against tetanus infection for patients with ulcerating tumors and undergoing biopsies is recommended.

Role of VEGF Blockade in Malignant Ascites due to Solid tumours

Rahul D Arora

Tata Memorial Hospital Tata Memorial Centre

Case description A 50 year oldfemale a known case of Carcinoma Cervix stage 3 b post radiotherapy ,a known case of HIV on HAART(ZLN) with lower limb DVT on Tab Warfarin 5 mg once daily developed generalised distension of the abdomen with difficulty in breathing and early satiety. Generalized abdominal distension, tenderness and diffusedull note on Percussion. No accompanying fluid thrill.No renal or hepatic impairment. Planned to insert a pigtail catheter for continuous drainage however procedure deferred. Point of maximum fluctuation for ascites marked for therapeutic tap,gross fluid collection with multiple internal echoes documented, diagnosed to have loculated ascites with multiple organised septations. Therapeutic paracentesis attempted,80-90 ml of bloody fluid removed. Fluid Cytology suggestive of malignant adenocarcinoma. In view of anaemia and deranged coagulation profile (INR 16.5), ZLN stopped, TLE initiated .Therapeutic paracentesis, peritoneo venous shunt,and tenkhoff catheter insertion not indicated. Hyponatremia ,Hypokalemia and elevated Serum Creatinine ruled out. Started on Inj Octreotide 100 ug sc stat followed by 300 ug continuous intravenous infusion over 24 hours. Daily weight monitoring and daily abdominal girth monitoring instituted. Octreotide discontinued in view of lack of level 1a or 1b level of evidence of its utility. This neccesitated a literature review where pubmed database was searched with the words "octreotide" "malignant ascites" and "solid tumors". DiscussionAnecdotal evidence exists regarding the role of Octreotide however trials have not shown a consistent benefit.A pilot study done reports an improvement in symptoms .Role of VEGF Blockade by somatostatin analogues in malignant ascites and frequency of administration (single dose versus continuous infusion), dosage, and Route of administration (Role of intraperitoneal installation) needs to be defined further.

Keywords: VEGF Blockade Malignant Ascites Octreotide

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Silent Extra-Adrenal Retroperitoneal Paraganglioma:an Unusual Presentation

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Introduction: Extra-adrenal Retroperitoneal Paragangliomas (PGLs)tend to arise from dispersed paraganglia symmetrically distributed in close relation to the aorta and sympathetic nervous system. Extra-adrenal retroperitoneal paragangliomas are rare tumors causing considerable difficulty in both, diagnosis and treatment. **Case presentation-**A 60 yrs old male presented with a lump in the left hypochondrium and lumbar region .On routine workup pt was normotensive ,with normal echocardiogram and chest x ray without any complaints of headache,sweating and palpitations.CT scan of whole abdomen demonstrated inhomogeneously enhancing mass lesion in retoperitoneum(left para-aortic region) with areas of necrosis and hemorrhage with loss of fat planes with psoas muscle . With presumptive diagnosisof retroperitoneal sarcoma patient was worked up for surgery and CECT thorax was normal .Urinary catecholamines levels were not done as pt was asymptomatic and normotensive.Pt underwent laprotomy showing tumor in left infrarenal region with prominent surface veins and tumor was shaved of inferior venacava ,renal vein and aorta.Intraoperatively wild Bp fluctuations were seen during tumor dissection (130/90 to 250/150),which was controlled by intravenous vasodilators. After tumor extirpation there was sudden fall in the blood pressure to 60/40 which was managed with vasopressors. .After 3 days in ICU patient recovered, blood pressure was maintained without vasopressors .Final histopathology report was Retroperitoneal Paraganglioma showing IHC positive for vimentin and synaptophysin. **Discussion-**Retroperitoneal extra-adrenal PGLs are neoplasia of the chromaffin cells commonly located in the para-aortic sympathetic chain. They often manifest themselves by symptoms of episodic freeing of catecholamines, such as high blood pressure, migraines, sweating and palpitations. Incidence of extra-adrenal PGLs is only 2–8 per million, which occur either sporadically or as part of a hereditary syndrome. Extra-adrenal retroperitoneal PGLs have a more aggressive course and the prognosis of PGLs can be very difficult to predict. Approximately 20–42% of PGLs metastasize.Distant metastasis to bones, lymph nodes and lungs has been reported as a unique feature of the metastatic spread of extra-adrenal retroperitoneal PGLs. Diagnosis of malignant PGLs is based on evidence of extensive local invasion , or more reliably on documentation of metastasis. Owing to their hyper-vascularization, these tumors usually exhibit intense enhancement with central necrosis or hemorrhage on CT imaging. 131I-MIBG and octreotide have high sensitivity and accuracy in diagnosing silent extra-adrenal PGL.Urinary metanephrines have a higher specificity. Surgery remains the mainstay of treatment of extra-adrenal PGLs of retroperitoneum once the correct diagnosis is acquired.Surgical treatment should be carried out after using alpha-adrenergic blockade for 2–4 weeks with attentive intraoperative monitoring to achieve the safest and most successful outcome with operative mortality to <1%. Preoperatively "silent" extra-adrenal PGLs of retroperitoneum may induce hypertensive crisis secondary to anaesthestic drugs or during tumor handling. Resection is often challenging as these highly vascular tumors are located near major vital blood vessels. Therefore it is very difficult to differentiate retroperitoneal sarcoma from retroperitoneal paraganglioma and any lesion in this location needs to be properly evaluated before any surgical intervention is attempted.

"Simultaneous resection of tumour following cardiovascular surgery"

Atul Samaiya

Navodaya Cancer Hospital

Background: Coexistence cardiac disease with cancer and both requiring surgical treatment at the same time is rare. For patients requiring open-heart surgery, this raises concern that the use of cardiopulmonary bypass (CPB) may cause a transient immunosuppression with the potential to promote the spread and growth of coexisting cancer cells. feasibility of the simultaneous cardiac surgery with tumor excision in patients suffering from tumor combined with coronary artery disease(CAD). **Methods:** From May 2013 to Aug 2015, 4 patients suffering from (2- endometrial, 1 – colon and one tongue) cancer and cardiovascular disease (3 coronary artery disease, 1 Aortic stenosis) were successfully treated by simultaneous surgeries. Cardiovascular surgeries were carried out first followed by tumour resection. Postoperative recovery was uneventful, and patients were discharged in stable condition. Cardiovascular surgeries coronary artery bypass grafting (CABG) in 3 patients, aortic valve replacement in 1 patient. **Results:** The combined operations were satisfied. There was no in-hospital mortality, no postoperative hemorrhage, no myocardial ischemia or infarction, with few complications. Postoperative in-hospital stay was 07-12 days, average 10 days. All discharged in cure. **Conclusion:** In accordance with the majority of the data published in the literature, combined procedures did not negatively influence hospital morbidity and mortality. Simultaneous operations eliminate the necessity of a second operation and do not delay the postoperative oncological therapy. No patient died in hospital. Mean blood loss, duration of intubation and length of hospital stay were not different from other patients who underwent cardiac operation only.

Keywords: CABG ; Cardiac surgery, Carcinoma; Cancer surgery, Simultaneous surgery

Primary Visceral Primitive Neuroectodermal Tumor (Pnet) : A Series of Two Cases

Suman Tomer

Pt.B.D.Sharma PGIMS Rohtak

Background: Primitive neuroectodermal tumors (PNETs) are small, round-cell tumors of neural crest origin classically found in the central nervous system (CNS) but more recently characterized in the periphery. Peripherally located PNETs (pPNETs) are members of the Ewing's sarcoma family of tumors (EFTs). Occurrence of this type of tumor in the kidney and liver is considered as unusual and few cases have been reported so far. We present here two cases of PNET occurring in kidney and liver with an unusual presentation. **Material and methods:** Case 1. An enbloc specimen of kidney with spleen and omentum with embolectomy specimen from inferior vena cava of a 19 years old female was received for histopatholgical examination who presented with left flank pain and swelling since 15 days. There was no complaint of fever, vomiting or hematuria. On examination a hard lump of size20x15 cm was present in epigastrium extending towards the right, not moving with respiration. Ultrasonography (USG) showed a large heterogenic mass with central cystic area arising from upper pole of the left kidney, invading the liver, concerning for malignancy. A staging CT scan of the abdomen was then performed revealing a large heterogeneously enhancing mass with large central non enhancing necrotic area noted with in it arising from upper pole of left kidney extending up to midline. There is also enhacing thrombus extension in to left renal vein and infrahepatic IVC. Case 2. Viscera including heart, lung, liver and kidney of a 56 years old chronic alcoholic deceased male were received for histopathological examination. The surgical specimens were formalin-fixed and paraffin embedded. The sections were stained with routine Hematoxylin and Eosin. Immunohistochemistry was performed. **Results:** Case 1.Cut surface of kidney was replaced by grey white tumor area with haemorrhage with some focal areas of normal renal tissue. Microscopic sections revealed malignant round cell tumor. On immunohistochemical examination, the round tumor cells were positive for CD 99, focally positive for vimentin and negative for cytokeratin, CD5, CD20, TdT, synaptophysin, chromogranin and S-100. Based on the morphological and immunohistochemical profile diagnosis

of primary primitive neuroectodermal tumor was given. Embolectomy specimen from IVC was also positive for tumor. Case 2. Grossly the external surface of the liver was multinodular with nodules varying in size from 0.2 to 0.8 cms. The cut surface was also multinodular along with a solid grey white area of 4x3 cm. Microscopic sections from the grey white area revealed a neoplastic lesion composed of sheets or lobules of small round cells, with little cytoplasm and darkly staining round to oval nuclei. Coexistant with the above findings, areas of cirrhosis consisting of lobules of liver parenchyma separated by broad fibrous septa were observed. On immunohistochemical examination, the small round blue tumor cells were positive for CD 99 and negative for LCA, cytokeratin, smooth muscle actin, desmin, vimentin, S-100, HMB-45 and synaptophysin. Further, other investigations like CT scan of chest, MRI of brain and whole body scan were looked for and found to be normal. Based on the morphological and immunohistochemical profile diagnosis of primary primitive neuroectodermal tumor with cirrhosis was given. Microsections from heart, lung and kidney revealed no significant pathological change. **Conclusion:** PNET is an infrequent differential diagnosis in visceral malignancies. The distinction from other primary malignancies is crucial for prognosis. The CT and MRI findings are nonspecific, but they are useful methods for local assessment of resectability and detection of metastasis. The diagnosis is based on.

Extra-ventricular Ependymoma involving Thalamus: A case report

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We report an extremely rare and unusual case of Ependymoma located in the right thalamic region in a 61 years old male in this presentation. **Background:** Extra-ventricular Ependymomas are extremely rare. They can originate from the Ependymal rests. Only a few cases of Extra-ventricular Ependymoma occurring in the cerebral hemisphere mainly involving frontal, parietal, temporal lobes of the brain have been reported in the literature. So far, no case of occurrence of Thalamic Ependymoma in human beings has been reported. Furthermore, an extensive review of the literature showed that a case of thalamic Ependymoma has been reported in a white tailed deer in Veterinary Pathology journal. **Materials and Methods:** A 61 years old male Pakistani presented with 2 months history of patchy altered sensation on the left side of face and left half of body. He did not have any focal signs of any neurological deficit. CT scan of the brain showed a low density mass lesion occupying right thalamus. MRI of the brain showed a vaguely hyper-intense mass lesion with post contrast enhancement after Gadolinium, representing possibility of a low grade glioma involving almost whole of right thalamic region. No features of ventricular obstructions or mid line shift noted. MRI spectroscopy revealed increased choline and creatinine levels & decrease in NAA levels . An endoscopic biopsy of the thalamic lesion was performed, which on microscopic examination revealed mildly cellular lesion with mild to moderate pleomorphism, peri-vascular pseudo-rosseting , focal calcification and intra and extracellular yellowish brown pigment . The Ki -67 proliferative index was low(<1%). The overall picture favored a low grade Ependymoma (grade II) and it was further confirmed by histo-chemical and immunohisto-chemical stains .The intracellular pigment suggested the possibility of a pigmented variant of Ependymoma. MRI of the spine did not show any drop metastases. The patient was treated with primary external beam radiotherapy using 3-Dimentional conformal radiotherapy (3-DCRT). A dose of 54 Gy/27 fractions delivered . He tolerated radiation very well. The patient remain neurologically in a stable status for about 6 months when he developed weakness over the left side of body and gait disturbances. MRI of the Brain showed progression of the disease. He was referred to Medical Oncology for chemotherapy. Currently, the patient is under going chemotherapy and his neurological status is stable. **Conclusions:** To the best of our knowledge , this is the first case report on an Ependymoma occurring in the region of thalamus in human beings. Because of the difficult location of the tumour, surgery was not contemplated, thus a course of primary radical Radiotherapy has been delivered.

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Glioblastoma multiforme with small cell variant arising from low grade-glioma with extracerebral metastases: A case report highlighting pathological features and molecular analysis

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Background: Extracerebral spread of glial neoplasms is rare and refractory to treatment (Templeton A, Hofer S 2008; Picirrilli M 2008). The small cell variant is a uncommon subgroup with unfavorable prognosis; preliminary data suggest universal absence of both IDH1 mutation and codeletion1p19q (Takeuchi H 2016). We are reporting a patient initially presenting with a low grade glioma which transformed into a glioblastoma multiforme (GBM) and subsequently developed extracerebral metastases. **Methods:** Histology was reviewed by three neuro-pathologists from two institutions (A.H.;I.B.;E.R.). EGFRvIII and BRAF mutations were analyzed by PCR; immunohistochemical (IHC) staining was performed for mismatch repair deficiency (MMR) (HMC: A.H.), c-KIT, and PDGFR alpha/beta (Molecular Pathology (D.Z.; USZ). Further analyses performed with a commercially available platform (MI profile; CARIS) comprised immunohistochemistry, epigenetic alterations, FISH and new-generation sequencing. **Clinical Presentation:** A 30-year old female patient from Jordan underwent surgery for a diffuse fibrillary astrocytoma G2 in the right temporal lobe. Upon tumor progression one year later the tumor was re-resected. 4 months later new a MRI revealed recurrent disease progression. Pending elective surgery the patient developed an acute tumor-related hemorrhage with mass effect requiring emergency surgery. Histopathologic analysis established GBM with two different cell populations including small-cell type variant. After recovery, the patient received radiochemotherapy with Temozolomide followed by Temozolomide alone. Prior to starting the second cycle the patient developped a painless swelling in the right submandibular area as well as pain in the right parotid gland. A surgical biopsy of the submandibular lymphnode confirmed an extracerebral metastasis of the underlying GBM comprising solely the small cell variant. Presence of the codeletion 1p19q (FISH), IDH1 mutation (IHC) and loss of ATRX suggested a mixed origin (astrocytoma/oligodendroglioma); MGMT status was methylated. The patient received locoregional radiotherapy. PCR analysis of BRAF and EGFRvIII did not reveal an alteration; immunohistochemical analyses were negative for PDGFR alpha/beta and c-kit(CD117) overexpression; MMR expression is maintained. The patient is alive eight months after diagnosis of GBM and three months after recurrence outside the brain; quality of life is acceptable. **Conclusion:** Selected analysis of established actionable targets

such as BRAF or EGFRvIII as well c-kit and PDGFR alpha / beta were negative. The observed codeletion 1p19q may be explained by the composite histology. A larger dataset of genetic alterations will be presented which has the potential to individualize treatment in a data-poor environment

Giant Cystic Pheochromocytoma: A 'Silent' Growing Catastrophe

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Introduction: Pheochromocytoma is a catecholamine secreting tumor that originate from chromaffin cells. Usually, it is solid neoplasm of the adrenal medulla, however cystic pheochromocytoma is a rare neuro-endocrine tumour that is frequently asymptomatic and often diagnosed incidentally on imaging or intra-operatively. Only a few cases of cystic pheochromocytomas have been reported in the world literature. We present a case giant cystic pheochromocytoma in a 65 year old lady who presented with a large retroperitoneal lump, which is probably the world's third largest pheochromocytoma as per the available indexed literature. **Case Summary:** A 65 year old female presented to us with complaints of progressively increasing left upper abdominal lump for the last 6 months. She had no history of pain, hypertension, headache and flushing. On examination, her pulse was 76/min and blood pressure of 126/84 mmHg with a large non tender lump predominantly in left upper abdomen. Laboratory investigations were normal except hemoglobin of 9.6 g %. Computed tomography revealed a large retroperitoneal mass which was predominantly multi-loculated cystic lesion with punctate calcifications. The pancreas and kidney were normal. The patient was taken up for exploration. Intra-operatively a giant cystic mass was arising from the upper pole of left kidney which was densely adherent to left renal pedicle and aorta; manipulation of this mass resulted in extreme blood pressure fluctuations. Patient underwent excision of this adrenal tumor with left nephrectomy. The resected specimen measured 25 × 17 × 15 cms containing areas of hemorrhage and cysts of varying sizes, 0.5 to 20 cm in diameter. Histopathological examination confirmed the tumor to be pheochromocytoma arising from the left adrenal and the immunohistochemistry was positive for neuron specific enolase, synaptophysin and chromogranin. Patient was discharged on 7th post operative day with uneventful hospital stay and is doing well up to five month of follow up. **Conclusion:** Giant pheochromocytoma with prominent cystic change is a rare entity and is mostly asymptomatic. Silent pheochromocytoma is one of the exceptions that does not exhibit classic symptoms and therefore, silent pheochromocytoma often remains undiagnosed until surgical excision occurs and the anesthesia teams face a greater challenge. It should be considered in retroperitoneal tumor of patients with nonspecific symptoms and given adequate treatment to promote the perioperative safety. Surgical resection is the only curative treatment for pheochromocytoma.

Keywords: pheochromocytoma, giant, cystic, immunohistochemistry

Comparison of Continuous Versus Interrupted Abdominal Fascia Closure in Patients of Perforation Peritonitis Using Polydioxanone (Pds) Suture: A Prospective Study Of 50 Case

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Introduction: Laparotomy wounds have been closed in a variety of ways in terms of continuous versus interrupted closure, single layer versus mass closure and absorbable versus non absorbable sutures. The continuous suture has an advantage of an evenly distributed tension across the suture line and being more expedient. It has the disadvantage of being a single suture holding the fascia together. The multiple interrupted suture method has been used successfully for many years, but has the disadvantage of being time consuming to perform and of isolating the tension to each individual stitch. **Objectives:** Comparison of closure of midline laparotomy fascia using interrupted PDS v/s continuous PDS in emergency settings in terms of wound infection, wound dehiscence, incisional hernia and suture sinus. **Material and Methods:** The present prospective study was conducted in Department of General Surgery, Pt. B. D. Sharma Institute of Medical Sciences, Rohtak. A total of 50 patients were enrolled who were operated in emergency operation theatre. These patients were grouped in two groups of 25 each. Alternate patient was allocated to Group I and Group II. Group I (study group) patients underwent interrupted closure of abdominal wall using polydioxanone No 1 suture. Group II (control group) underwent continuous closure of abdominal wall using polydioxanone No 1 suture. **Results:** The mean age in Group I was 39.16 and 41.4 in Group II. Majority of the patients were male (88%). Mean length of incision in both the groups were comparable i.e. 20.64 in group I and 20.56 in group II. The mean time taken for closure of rectus sheath in Group I was 39.56 mins and 19.8 mins in Group II. Mean duration of hospital stay in Group I was 12.84 days and 12.2 days in Group II. Also, 6 patients (28%) in Group I underwent wound infection as compared to 4 patients (16%) in Group II. Two patients (8%) belonged to Group I both of which had localised fascial burst and 1 patient (4%) was from Group II who had complete fascial burst. All 3 patients of fascial wound dehiscence were patients of peptic perforation. Further management of this complication in interrupted group only required regular aseptic dressing and secondary suturing while continuous group patient had to undergo a Bagota Bag application under general anaesthesia. One case (4%) of incisional hernia was observed in both the groups at the 3rd month of follow up. Three (12%) patients in interrupted group and one (4%) in continuous developed suture sinus. **Conclusions:** In a patient with peritonitis, midline abdominal fascial clos

Inguinoscrotal Swelling with Acute Abdomen: A Rare Presentation of Burst Amebic Liver Abscess

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Introduction: Amoebic liver abscess is the most common inflammatory space occupying lesion of liver with high mortality and morbidity [1]. It is the third most common parasitic infestation in world having increased incidence in tropical countries [2]. Amoebic liver abscess has highly variable presentation having diagnostic difficulty. Rupture into peritoneal and pleural cavity are common complications but rupture into abdominal wall and presenting as a tender inguinoscrotal swelling with acute abdomen is very rare. We report an extremely rare case of acute abdomen along with tender inguinoscrotal swelling following ruptured amoebic liver abscess. **Case Report:** A 32 year old male was brought to surgical emergency department with complaints of pain in the right upper abdomen for one month, respiratory difficulty and swelling in right inguinoscrotal region for three days. He also had history of intermittent fever and cough with expectoration. On general physical examination patient was afebrile, dehydrated with pulse rate of 96/minute, blood pressure of 92/60 mm Hg and respiratory rate of 28/min. On abdominal examination, there was tenderness and guarding present over right hypochondrium, lumbar and right inguinoscrotal region along with a tender inguinoscrotal swelling of size 6x3 cm with inflamed overlying skin. Swelling was fluctuant but transillumination was negative. Systemic examination revealed significantly decreased air entry on right side of chest. The laboratory studies revealed haemoglobin 6.5 gm/ dL and total leukocyte count of 18000/mm3 with increased polymorphs. Liver function test showed serum bilirubin was 2.5 mg/dL with mildly raised SGOT/PT and renal functions were normal. On chest X-ray, there was pleural effusion on right side. Ultrasonography revealed two hypoechoic lesions of size 10.7x10 cm and 10x7.7 cm in right lobe communicating with peritoneal cavity with right

side pleural effusion. Chest drain was put on right side and 500 cc anchovy sauce pus was drained which was sent for microscopic examination and culture sensitivity of pus. The first abscess was drained by right intercostal drainage while the second one was drained by an inguinal incision and putting a negative drain in the inguinal area, which drained the abscess from parieties as well as scrotal area. He was given intravenous antibiotics in form of ceftriaxone and high dose metrogyl. Patient started improving with the treatment, abscess sizes were reduced on subsequent ultrasounds, right lung expanded and chest tube was removed. The inguinal drain was removed after 21 days and patient was discharged in a stable condition from the ward. **Results:** Amoebiasis has a worldwide distribution and is more common in tropical countries with areas having poor sanitation. Fortunately, hepatic liver abscess occurs only in 3%-7% of all patients with intestinal amoebiasis. Amoebic liver abscesses are more commonly located in right liver lobe. The abscess cavity can vary in size from 1-25 cms and if the condition remains untreated, it can rupture into adjacent organs/cavities. The reported incidence of complications of amoebic liver abscesses vary from 20%-35% in earlier and 12%-20% in more recent series. Most common complications are related to rupture of the abscess into an organ or adjacent space. Common complications are those involving lung and pleura leading to empyema or pneumonitis and rupture of abscess into peritoneum leading to generalised or localised peritonitis. Apart from these relatively common complications, rare complications include rupture of the abscess into stomach, intestines and pericardium. Ultrasound abdomen is the investigation of choice for an uncomplicated liver abscess, but for complicated abscesses, CECT abdomen should be carried out before any intervention is made. CECT was diagnostic in the present case where patient was having two large abscesses, one of which was communicating with pleural cavity while the other had ruptured into the abdominal wall reaching upto inguinoscrotal area. Since we could locate the exact sites of perforations, the patient was managed only by intercostal drainage and incision and drainage of inguinal abscess. We could safely defer the exploratory laparotomy and the morbidities associated with it despite presence of abdominal.

Isolated Trichobezoar of Ileum

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Introduction: The term bezoar refers to accumulation/impaction of foreign material in the gastrointestinal tract and is known to occur in human and animals for centuries. Bezoars from the intestine of animals were originally worn as charms and promoted as remedies to prevent disease. Bezoars can be classified in four types: phytobezoar (vegetable), trichobezoar (hair), lactobezoar (milk/curd) and miscellaneous (fungus, sand, paper). The most common type of bezoar in adults is phytobezoar, while trichobezoars are more often found in children and teenage girls. Trichobezoars typically occur in the stomach and rarely affect the small intestine causing small bowel obstruction. Primary small bowel bezoars without any associated gastric bezoars are uncommon. The most common sites of trichobezoars are the gastric outlet or duodenum whereas obstruction of distal parts of the small bowel or the large bowel without is extremely rare. Here we report an extremely rare case of trichobezoar of the ileum not associated with a trichobezoar in stomach. **Case Report:** A fifteen year old girl had abdominal pain for four months. She presented to the emergency department with various symptoms of abdominal distension, vomiting and non-passage of flatus and stools for last seven days. On general physical examination patient was thin built, afebrile, dehydrated, pulse rate of 96/minute and blood pressure of 106/72 mm Hg. The abdomen was distended with peritoneal signs. The laboratory assessment revealed marked leukocytosis of 15000/mm3. Other laboratory data including electrolytes, liver function tests, blood urea, serum creatinine, and serum amylase were all within normal range. Plain abdominal radiograph showed multiple air-fluid levels without any free gas under the diaphragm. Abdominal ultrasound revealed telescoping of one gut loop into another (intussusception). Laparotomy was done with a midline incision, which revealed significantly dilated and distended small bowel loop with a bowel mass in the ileum measuring around 20 cm in length and 5 cm in width situated at 30 cm from the ileo-cecal junction. Enterotomy was performed and an unclean foul smelling mass of hairs in the form of a bunch was found. The mass was removed and the enterotomy was sutured. There were no bezoars, neither in the stomach nor in the duodenum and proximal jejunum. **Results:** Trichobezoars, although rare, are most common in children and young women. DeBakey and Ochsner studied 311 cases of trichobezoar and found that almost 90% occurred in teenage females. There is an association with mental retardation and psychiatric conditions; almost half of patients present with trichophagiaThe diagnosis is based on a combination of good history taking as well as physical findings to look for a family history of psychiatric disorders, previous bezoars, a palpable mass, patchy hair loss and halitosis. Decreased intestinal motility is the most quoted factor in intestinal bezoar formation. X-ray abdomen in a case of intestinal trichobezoar is generally suggestive of multiple air fluid levels. CT scan is the most useful diagnostic tool in patients with bezoars because it reveals the localization of bowel obstruction; it shows also a well-defined intraluminal mass in the transitional zone of the obstruction. A mottled gas pattern in the mass is reported characterizing the bezoar, and it is supposed to be air bubbles retained within the bezoar. Surgical management is the mainstay of treatment in a case of intestinal bezoar. The bezoar plus its tail can be removed via gastrotomy and sometimes multiple enterotomies to reduce risk of gut perforation, as long bezoar tails are often extremely adherent to the side of the gut wall. The treatment for isolated ileal trichobezoar consists of removing the mass by a single enterotomy or resection of the bowel if not feasible. Duncan et al. recommended bezoar extraction by multiple enterotomies in the Rapunzel syndrome. It is mandatory to perform a thorough exploration of all the small intestine and the stomach searching for retained bezoars. The patient should be followed up in psychiatry OPD after discharge from the hospital.

Sebaceous Gland Carcinoma of Upper Eyelid: Resection and Reconstruction

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Background: Sebaceous gland carcinomas (SGC) are rare malignancies of eyelid which are challenging to diagnose and treat. Surgical resection should be wide enough to ensure complete resection with adequate margins, at the same time not too wide to ensure a functional eyelid. Objective of reconstruction is to ensure a movable eyelid, good corneal protection and acceptable aesthesis. We are presenting a case of SGC of the upper eyelid which was resected and using lid switch along with the facial rotation flap. **Case report:** An 80 year old gentleman presented with a growth over right upper eyelid of 6 months duration. Biopsy of the growth revealed it as sebaceous gland carcinoma. Tumor was resected with adequate margins all around. Lower eyelid was mobilized taking the entire thickness and about 50% of the length of the defect of the upper eyelid. Lateral canthus was re created with facial rotation flap. Three weeks after the primary surgery, flap division was performed under local anesthesia. At 6 weeks follow up, patient was disease free with normal vision and no evidence of exposure keratitis. **Discussion:** Sebaceous gland carcinoma is a high grade malignant neoplasm which accounts for 0.2-4.7% of the malignant tumors of the eyelid. Eyelid defects can lead to corneal irritation, exposure keratopathy and even loss of vision. Z-plasty, the V-Y glbellar flap, median forehead flap and the Cutler-Beard technique are some of the common techniques adopted for reconstruction of anterior lamella. Labial mucosa, hard palate mucoperiosteum, auricular and nasoseptal cartilage are some of the common techniques adopted for reconstruction of posterior lamella. However, each technique has its advantages and disadvantages. **Conclusion:** The purpose of presenting this case is to highlight the rarity of the sebaceous gland carcinoma of the eyelid, importance of early diagnosis and need for thorough understanding of the anatomy to ensure proper reconstruction.

Case report of Homozygous MTHFR-a1298c mutation in precursor B ALL

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Introduction: Thrombotic events are well recognized during treatment for acute lymphoblastic leukemia. Evaluation for thrombophilia is usually not recommended in view of known risks with certain specific drugs. We report a case of recurrent thrombosis off asparaginase wherein thrombophilia evaluation yielded specific etiology. **Case Report**: A 14 year old boy with precursor B cell ALL (high risk) presented with generalized tonic clonic seizures on Day+22 of induction chemotherapy without any focal neurological deficit.Asparaginase associated thrombotic event was suspected. MRI brain with MRV doneshowed right frontal lobe infarct and superior sagittal sinus thrombosis with reduced blood flow in left transverse sinus. Enoxaparin was commenced. Follow-up MRI after 6 weeks showed near total resolution with complete clinical recovery. Enoxaparin had to be discontinued at this point because of thrombocytopenia post cyclophosphamide. The plan was to re-initiate enoxaparin during reinduction.However, after the first dose of systemic methotrexate (5 gm/sqm) therapy he presented with right sided hemiparesis. He was restarted on inj Enoxaparin and supportive care. MRI brain with contrast and MRV showed left cortical venous thrombosis. In view of his recurrent episode thrombosis in the absence of asparaginase, thrombophilia workup was done which showed homozygousity for MTHFR-a1298c mutation. He was continued on further chemotherapy including methotrexate and L-Asparaginase on Folate supplementation along with Enoxaparin. **Conclusion:** MTHFR mutation is a rare cause of thrombophilia which was found in a case of precursor B cell ALL as a cause of recurrent venous thrombosis precipitated by Methotrexate therapy.

Unusual Presentations of Paediatric Teratoma

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Background: Benign Teratomas are the most common germ cell tumours accounting for 70 %of germ cell tumours in childhood. Half of them are asymptomatic. Here we report two rare cases of Teratomas. One was a left parotid swelling and other was anterior mediastinal mass which was invading into bronchus and causing bronchiectasis of lingual lobe of left lung. **Case 1:** Three months old female infant presented with asymptomatic left parotid mass. CECT showed a large round cystic lesion with enhancing cystic wall with areas of fat density and ossification in left parotid gland .Patient was managed with left total parotidectomy with histopathology report suggestive of matured Teratoma. **Case 2:** 10-year-old female patient presented with cough, haemoptysis and fever. CECT thorax revealed anterior mediastinal mass with air foci and lingual lobe bronchiectasis. Exploration and histopathology revealed anterior mediastinal Teratoma invading lingular lobe bronchus and causing bronchiectasis. **Conclusion:** clinicians should be aware of these unusual presentations of Teratoma.

Keywords: mediastinal teratoma , parotid gland teratoma , germ cell tumor

Complete Response to Single Agent Crizotinib in Alk Positive Relapsed, Refractory Neuroblastoma: A Case Report

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Background: Treatment of relapsed neuroblastoma remains a challenge, as the survival is dismal with current therapeutic options. Hence novel treatment strategies are warranted for this subgroup of patients. **Material and Methods:** We share our experience with crizotinib in a patient with relapsed refractory neuroblastoma. **Results:** A 2-year old girl was diagnosed with high risk, adrenal neuroblastoma, stage IV, involving, retroperitoneal lymph nodes and bone marrow. Histopathological examination revealed Shimada favourable histology and n-myc was non-amplified. She received treatment as per HR-NBL-1/ESIOP protocol that included chemotherapy, surgery autologous stem cell transplant, radiotherapy and cis-retinoic acid differentiation therapy. After a disease free period of 22 months she sustained relapse in the bone marrow and pulmonary parenchyma. She received cyclophosphamide-topotecan alternate with ICE (ifosphamide, carboplatin, etoposide) based salvage chemotherapy. Reassessment after 6 cycles revealed persistent marrow and pulmonary lesions. Immunohistochemistry evaluation for ALK protein using D5F3 antibody showed strong expression. Hence she was started on Crizotinib (@ 265mg/m2) monotherapy as palliation with monitoring for side effects. She tolerated the drug well with no significant side effects apart from mild nausea. Clinical response was observed in 4 weeks and work-up after 4 cycles (16wks) revealed complete response of disease in marrow and lung. Parents declined 2nd autologous SCT and opted for continuation of crizotinib monotherapy. She remained in remission for 32 wks after which she sustained a second marrow relapse. Activating mutation or amplification of anaplastic lymphoma kinase gene (ALK) was discovered as the most common genetic mutation associated with familial neuroblastoma and also in about 10-15% of sporadic neuroblastoma cases. Safety and efficacy of crizotinib in pediatric neuroblastoma patients is now well established in recent clinical trials. Owing to unsatisfactory outcome in high risk, relapsed and refractory neuroblastoma, crizotinib may be a useful adjunct to contemporary treatment both in frontline and salvage regimens in selected patients. As development of resistance is well known due to selection pressure in TKIs, therefore monotherapy may not be useful in the long term. **Conclusion:** Remarkable response to Crizotinib monotherapy in relapsed neuroblastoma that had failed two lines of salvage chemotherapy suggests its emerging role in ALK positive refractory disease.

Gastric Adenocarcinoma: Rare Cause of Gastric Outlet Obstruction in Children

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Background: Gastric adenocarcinoma is a rare malignancy in children. It has rarely been described as a cause of gastric outlet obstruction in children. **Case Study:** We describe a child who presented with abdominal pain and vomiting and was eventually diagnosed with gastric adenocarcinoma. A 13-year-old male child presented to us with intermittent abdominal pain for 3 months associated with vomiting and constipation for 4-5 days. The pain was initially managed with antacids and since no obvious cause was identified, it was regarded as functional. Past and family histories were insignificant. The child was further evaluated when the pain intensity increased significantly with associated weight loss. Ultrasonography and CECT abdomen were done, and both were reported normal. At our centre, the films were reviewed, which revealed the presence of a 3.5x2.8 cm mass in the pylorus and first part of duodenum with multiple necrotic abdominal lymph nodes. On examination, a nodular mass was palpable in the epigastric region; the rest of the systems were normal. FNAC of the mass was initially done followed by ultrasound-guided core biopsy. Both revealed poorly differentiated adenocarcinoma with tumour cells strongly positive for cytokeratin and epithelial membrane antigen and focally for alpha-fetoprotein and carcinoembryonic antigen. They were negative for vimentin, CD30, LCA, PLAP, glypican, synaptophysin and beta-catenin with no loss of INI-1. Serum tumour markers like CEA(49.49ng/ml) and CA-125 (52.1 U/ml) were elevated whereas CA19–9, beta-HCG and alpha-

fetoprotein were negative. FDG-PET revealed a lobulated heterogeneously enhancing mass lesion (3.2 x 2.8 x3.5cm) in relation to the antropyloric region of stomach and first and second part of duodenum with multiple FDG-avid discrete and coalescent left supraclavicular, infraclavicular, mediastinal, bilateral retracrural, abdominal and retroperitoneal lymphadenopathy, likely metastatic. There was no significant family history of cancer predisposition syndromes. Upper and lower gastrointestinal endoscopies were done, which revealed multiple polyps. The severe abdominal pain he had could be attributed to the infiltration of celiac plexus and was managed with transdermal fentanyl. A diagnosis of metastatic gastric adenocarcinoma with unresectable primary was determined and he was started on chemotherapy with cisplatin and 5FU. In view of poor oral intake, nasojejunal tube was inserted and enteral feeds were started as a continuous infusion, which he tolerated well. We had planned to continue 2 cycles of chemotherapy and local resection if metastatic disease cleared. The patient continued treatment at another centre subsequently. **Conclusion:** Gastric adenocarcinoma is a rare malignancy in children and can have non-specific presentation. Abdominal pain in children should be evaluated especially when associated with weight loss before labelling as functional.

Mucoepidermoid Carcinoma of Parotid in children- A Rare case Report

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Introduction: Mucoepidermoid carcinoma of the parotid arises from the pleuripotent cells of the gland. It accounts for 5% of all salivary gland tumors. About 45% of mucoepidermoid carcinomas occur in the parotid gland. They usually appear in 5th decade of life but it is very rarely found in pediatric age group. Usually such tumors are low grade and present without nodal metastasis, so surgery is the treatment of choice. Here we report a case of mucoepidermoid carcinoma in a young patient. **Case Report:** Seven year old girl presented with painless swelling over right cheek and right upper neck since 7 months. MRI Parotid and Neck showed a focal lesion involving superficial and deep lobe of right parotid along with multiple bilateral submandibular (Ib & IIa) and posterior cervical (V) lymph nodes, FNAC was s/o pleomorphic adenoma She was treated with right total parotidectomy (Nerve Sparing Surgery) & right selective neck dissection. Histopathology revealed low grade mucoepidermoid carcinoma with one positive node. Post operative radiation therapy was given to the tumor bed and ipsilateral neck nodes. At her last follow up, she has completed 5 months and she is asymptomatic without any evidence of recurrence. **Conclusion:** Mucoepidermoid carcinoma of parotid is very rare in children. Clinical stage and histological grade are the main prognostic factors. Complete excision with preservation of facial nerve is the treatment of choice. Neck dissection is considered when there is clinical evidence of regional metastasis, high TNM stage, high histological grade and involvement of regional nodes. Because of the possibility of long term adverse effects in pediatric patients, radiotherapy should be used only in selected cases. Long term follow up is essential to rule out late recurrence and to see the side effects of therapy. Although rare, it should be suspected in pediatric patients with asymptomatic parotid mass

Keywords: Mucoepidermoid Carcinoma, Parotid, Radiation Therapy

Lymphoepitheliomalike carcinoma Thymic carcinoma, in an 11-year-old boy: A case report

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Background: Primary thymic epithelial tumors are rare in children and constitute less than 1% of all childhood neoplasms. Lymphoepitheliomalike carcinoma (LELC), a variant thymic carcinoma, is even more uncommon in children, with around fourteen cases reported in literature. We herein report a pediatric case of thymic LELC who presented to our clinic. **Case report:** A 11-year-old boy presented with cough, respiratory distress, and chest pain for 1 week. The child had Chest Xray revealed a mediastinal mass and CT chest revealed a space occupying lesion at anterior mediastinum with extensive mediastinal adenopathy with nodular deposits in lung parenchyma. The mass was histologically confirmed to be LELC arising from thymus by computed tomography-guided biopsy. The tumour cells showed strong nuclear signal for EBER (Epstein-Barr virus early RNA) by in-situ hybridization. Immuno-histochemical analysis demonstrated positive staining for keratin (AE1/AE3), epithelial membrane antigen. MRI also confirmed vertebral metastasis to D3 vertebral body. Thus, the patient was diagnosed with metastatic thymic LELC. The tumour was found inoperable at presentation and the child was advised chemotherapy. But the family was lost to follow-up after the initial investigations. **Conclusions:** Thymic LELC is a highly malignant mediastinal tumor often with extensive metastases at diagnosis, most commonly to the lung, liver, and bone. Most thymic tumors in pediatric patients are inoperable at diagnosis, which results in poor prognosis. Pediatric patients with thymic LELC continue to have a poor prognosis despite chemotherapy. More research is needed to optimise chemotherapy approaches to improve outcomes.

Differentiated Adamantinoma of Tibia with Lung Metastases. A Case Report

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Background: Adamantinoma of the long bones is an uncommon, slow growing tumor, constituting less than 1% of all primary bone tumors. Osteofibrous dysplasia-like adamantinoma or differentiated adamantinoma is a rare variant, which shares some microscopic and cytogenetic features with both osteofibrous dysplasia and classic adamantinoma. Classic adamantinoma behaves as a malignant tumor, and may metastasise to distant sites, most commonly to lungs. However, differentiated adamantinoma is considered to be an essentially benign lesion. There are no reported cases of differentiated adamantinoma with lung metastases in literature. **Case report:** A 20 year old male presented with pain in left leg since 2-3 months. X-ray of the leg showed a lytic expansile lesion in left tibia in the mid-shaft region, associated with adjacent fracture. An FNAC done at some private clinic suggested a diagnosis of adamantinoma of tibia. Metastatic workup showed bilateral lung metastases and no other bony lesion. The patient underwent curettage of the tumor and bone cementing with V-nail fixation for fracture tibia. Histopathology and immunohistochemistry of the curettage specimen suggested differentiated adamantinoma as the final diagnosis. The patient has been now started on chemotherapy for metastatic disease. **Conclusion:** Differentiated adamantinoma of long bone is a rare variety of adamantinoma. It is usually considered a relatively benign lesion, and this is the first reported case of metastasis from a differentiated adamantinoma of long bone.

Keywords: differentiated adamantinoma, tibia, lung metastases.

Primary Chest Wall Rhabdomyosarcoma in an Adult: an Unusual Presentation Of Rare Malignancy

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Introduction: : Rhabdomyosarcoma (RMS) is a malignant tumor of mesenchymal origin and is the third most common extra-cranial malignant solid tumor in children and adolescents. RMS is a rare malignancy in adults representing <1% of all solid tumor malignancies. Approximately <20% arise in diverse sites including the chest wall and retro-peritoneum. Chest wall RMS is a relatively rare finding with a reported incidence of 3.7% in the IRS II and IRS III studies with pleomorphic subtype being extremely rare. Adults with rhabdomyosarcoma have significantly worse

outcome than children (5-year overall survival rates 27% Vs 61% in children). Multimodality therapy that includes surgery and chemotherapy with or without radiation therapy is the mainstay of treatment for RMS. **Objectives:** The purpose is to report a case of rare adult malignancy (RMS), its diagnosis, clinical management as a metastatic disease, while highlighting certain aspects that are relevant in literature. **Material and Methods:** Here we report an unusual case of chest wall rhabdomyosarcoma in an elderly male who presented with acute onset dyspnoea on exertion, chest pain and chest tightness. Baseline investigations including ECG were normal. CECT chest showed a large solid mass in anterior mediastinum originating from chest wall, few precarinal & hilar lymph node, multiple pleural based nodules and pleural effusion highly suspicious of metastasis. Trucut biopsy was taken, as the mass was unresectable radiologically. Histopathological examination revealed fibrocollagenous tissue having cells with mild nuclear pleomorphism, IHC of cells display variable immunoreactivity for EMA, Myogenin, SMA & desmin, while being immunonegative for LCA, S-100, CA-125, CK7, CK2 favouring rhabdomyosarcoma. **Results:** In view of advanced metastatic disease and histopathology patient was planned for chemotherapy based on Doxorubicin and Ifosfamide. He is tolerating chemotherapy well and is showing good partial response. There is no role of surgery or radiotherapy presently and has been reserved for palliation. **Conclusions:** In view of the absence of standardized protocols for adult patients, rarity of disease and low inclusion in trials for adolescents and young adults; the optimum treatment of adult RMS remains uncertain. Though the treatment is essentially multimodal, decision regarding management of the case is individually tailored depending upon the site, resectability, medical co-morbid conditions and patient's preference.

Re Recurrent Dermatofibrosarcoma protuberans of the chest wall and its management.

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Introduction: Dermatofibrosarcomaprotuberans (DFSP) is an uncommon soft tissue tumour that tends to recur. It is a locally aggressive neoplasm with a high rate of recurrence despite rarely metastasising. It most commonly occurs on the trunk (42-72%), followed by the proximal extremities (16-30%) and rarely occurs above the neck (10-16%). DFSP comprises of 6% of all soft tissue sarcomas and less than 0.1% of all cutaneous malignancies. We describe the case of a 30 year old female who presented with re-recurrent DFSP of the chest wall. **Objectives:** The objective of this presentation is to emphasise on the aggressiveness of the the tumour biology and the various modalitites useful in management including the reconstruction options. **Material and Methods:** A 30year old female came to the hospital with a painless mass in the sternal region since 1 year. She had a past history of a similar mass twice before, once in 2010 and then in 2014, both times the mass was excised in other non oncologic setup.A histological biopsy of wide excision taken in 2014 revealed DFSP with margins less than 2cms.There was a recurrence and the present MRI scan report revealed multilobulated,hyperintense mass lesion in subcutaneous plane of midline ,sternal,suprasternal and lower neck which appears isointense on T1W and shows diffusion restriction . Wide local excision with a grossly 3cm tumour free margin all around was done. Pectoralis major myocutaneous flap was used to cover the defect resulting from the excision. Biopsy revealed Dermatofibrosarcomaprotuberans. It also showed the lesion to be 10x7x4.3cms , base of resection was 0.3 cms away with nearest surgical margin being 1.2 cms away .The patient had an uneventful recovery and is on regular follow up. **Results:** This is an illustration of a case of re recurrent DFSP which was previously treated twice by surgical excision in a non oncologic set up .The patient presented to our Oncosurgical opd and after work up was subjected to wide local excision with adequate margins and reconstruction done using Pectoralis major myocutaneous flap. The patient was subjected to adjuvant radiotherapy. The patient is on a regular follow up with a disease free survival of more than a year. Conclusions: As dermatofibrosarcoma is a locally aggressive neoplasm with high rate of recurrence, wide local excision with at least 3cms tumour free margin at the time of first surgery and adjuvant therapy if needed will prevent further recurrence.

Mediastinal Tumours – The good which became the bad and then ugly

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Germ cell tumours represent a diverse group of neoplasm containing variable amounts of different tumour types. Rarely they differentiate into other somatic tumours. However, teratoma with malignant transformation (TMT) is a very rare and above all TMTs occurring in the mediastinum are known to be extremely rare. 28 year old male presented with chronic cough and weight loss. Imaging revealed left sided mediastinal mass. Biopsy revealed it to be poorly differentiated carcinoma. Tumour markers like AFP, BHCG and LDH were raised. He was treated as a case of Primary mediastinal germ cell tumour . He was given three chemotherapy and local resection. Post protocol treatment patient the tumour finally differented to Leiomyosarcoma. Due to the rarity of the cases and the diversity of malignant components of TMTs, there is no widely accepted treatment strategy. It is our endeavour to present a rare case of primary mediastinal germ cell tumour differentiating to mature teratoma and then to teratoma with malignant transformation

Presacral schwannoma resected via anterior trans peritoneal approach: A case report

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Background: Presacral schwannomas are rare tumors which offer significant surgical challenge because of the narrow working space available and proximity to the vital structures including external iliac vessels as well as ureter. In addition, abundant vascularity of the presacral plexus of vessels can lead to significant blood loss. We are presenting a case of presacral schwannoma resected via an open, intraperitoneal approach. **Case report:** A 40 year old gentleman presented with pain in the lower abdomen of 1 year duration. MRI of the pelvis demonstrated a dumb-bell shaped tumor in presacral area with no intra spinal extension representing a nerve sheath tumour. Intra operatively, right ureter was mobilized first and the tumor was dissected from right external iliac artery and vein. Tumor was then separated from the sacrum by sharp and blunt dissection. Excision of the tumor was completed after clipping the 5th lumbar nerve root on the right side. There was 100 ml of blood loss. Post operative course was uneventful. Histopathological examination of the resected tumor confirmed it as a benign schwannoma. **Discussion:** Klimo et al classified presacral tumors into 3 categories: Type 1 tumors are confined to the sacrum. Type 2 tumors originate within the sacrum but erode the wall of the sacrum and extend into the adjacent spaces. Type 3 tumors are located predominantly in the presacral or retro peritoneal area. Posterior approach for type 1 tumors, anterior approach is for type 3 tumors and combined anterior and posterior approach for type 1 tumors is preferable. **Conclusion:** Presacral schwannoma are rare nerve sheath tumours. MRI is the most preferred imaging modality. Complete surgical resection can be performed safely via anterior transabdominal approach.

Chondrosarcoma of Scapula – A Rare Case Presentation

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Introduction: Scapular tumors constitute 3% of the bone tumors. Chondrosarcoma is a primary bone tumor which often develops within flat bones such as pelvis, ribs, and scapula. Patient presents late due to deep seated location of the scapula. **Objectives:** Here we are presenting a rare case of chondrosarcoma of scapula- its workup and how it was managed. **Material and Methods:** A case of 81 years old male patient got admitted with the complaints of swelling in the left back of the chest of 1 month duration. No significant medical or surgical history. On examination a 13*12 cm swelling in the left scapular region was present and was not tender. Restriction of shoulder joint was present . Routine investigations done. Trucut biosy was done and came out as grade II chondrosarcoma. MRI chest showed a ~ 12 cm sized solid soft tissue lesion arising from left scapula mainly involving lateral margin and inferior angle extending into the intermuscular plane of the left lateral chest wall, ring and arc calcifications were present. Other investigations were within normal limits. So we planned for Partial scapulectomy and proceeded. patient recovered well and discharged. Patient is on regular follow up and 30 degress of abduction of arm present and is doing well. **Conclusion:** Chondrosarcomas represent a diverse spectrum of diseases. They are tumors that should be treated with definitive and complete surgical resection if local control is to be achieved. Although grade 1 lesions in the extremity can be managed with curettage, incomplete surgical resection of intermediate and high-grade lesions puts the patient at risk for local failure, metastases, and eventual death.

Chondrosarcoma of the Phalanx : A Rare locally aggressive lesion

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Introduction: Enchondromas are the most common benign cartilaginous tumours arising from the medullary cavity of the small bones of the hand. In contrast, Chondrosarcomas, commonly arise in the pelvis and the proximal femur and the humerus are very uncommon at this site. We report a rare case of chondrosarcoma of the Left Ring finger with its radiological and histological features. **Method and Material:** A 75 year old male patient presented with a history of a swelling in the proximal part of the Left Ring finger following trauma. Excision of what was considered a sebaceous cyst was done elsewhere under local anaesthesia. He presented to us with an ulcer on the dorsum of his left ring finger. **Results:** He underwent a through work up with local imaging. As his initial reports were highly suggestive of a chondroid neoplasm a decision to ampute his Left ring finger was taken. His final histopathological report revealed a low grade chonrdosarcoma of the finger. **Discussion:** Chondrosarcomas of the hand have only sporadically reported. They usually occur in the flat bones of the pelvis and the shoulder girdle and very rarely in the small bones of the hand or the foot. They are usually locally aggressive tumours and need to be treated promptly to avoid a local recurrence or distant metastasis. **Conclusion:** Chondrosarcoma of the hand requires a prompt and more radical treatment than enchondroma. Amputation is recommended as wide local excision fails to achieve local control thus reducing local recurrences and metastasis.

Mesenchymal chondrosarcoma of upper alveolus: a rare case report

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Mesenchymal chondrosarcoma is one of the most unusual high grade aggressive variant of chondrosarcoma affecting bone and soft tissues. It mainly affects young adults. These patients need to be treated with radical local surgery. Risk of late recurrences and distant metastasis is high. The present case is a 21years old male with upper anterior alveolar proliferative mass. Patient underwent extended partial maxillectomy. Histopathology revealed mesenchymal chondrosarcoma. It should be considered in differential diagnosis of maxillofacial neoplasms to prevent misdiagnosis and mismanagment. Review of literature revealed only few case reports of upper alveolar mesenchymal chondrosarcoma. Thus we present this report to discuss the management of this rare case.

Keywords: mesenchymal chondrosarcoma, upper alveolus, maxillectomy.

Primary Mediastinal Epithelial Osteosarcoma Rare Case Report

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Common tumours presenting as mediastinal mass are thymoma, germ cell tumours, lymphoma. Primary osteosarcoma arising from the mediastinum is an extremely rare malignant tumor. We present the case of a 40-year-old woman who presented with a backache since 1 month. Imaging studies revealed a huge posterior mediastinal mass with extensive calcification and extension into spinal canal. Gross total excision was successfully performed, and histologically the tumor contained osteoid formation consisting of round atypical cells. Immunohistichemistry showed AE1 positive in few cells and Viamentin strong positive. Extensive review of literature was done and revealed this is one of very rare tumours at this location. Tumour recurred after 1 month of operation then treated with palliative radiotherapy for symptomatic pain relief. Then after patient was treated with palliative chemotherapy consisting of doxorubicin and cisplatin.

A Cytohistological Correlation of a Soft Tissue Tumour with Emphasis on the Importance of Immunohistochemical Marker in Making the Final Diagnosis

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Objective: Soft tissue sarcomas that develop in the axial area, even with early diagnosis those that are treated adequately, have a moderate 5-year survival rate.We present a case of 80 year old male who presented with a large inguinoscrotal swelling measuring 23x9x6 cm for 2 months duration associated with aggravation of pain since 20 days. **Materials and Method:** The specimen was received in formalin fixed state in the Dept. of Pathology. After routine processing, regular H & E stained sections were studied followed by confirmation by Immunohistochemistry. **Result and Conclusion:** Cytological diagnosis of malignant soft tissue tumour was given followed by histopathological examination that revealed differential diagnosis of Malignant Fibrous Histiocytoma , Synovial sarcoma and Malignant transformation in a neurofibroma. Immunohistochemistry revealed positivity for cytokeratin (CK 7 and CK19). Final diagnosis of Synovial sarcoma was given. This case shows the importance IHC in diagnosis of difficult cases of soft tissue tumors and hence merits mention.

IACR 2016
35th Annual Convention Of Indian Association For Cancer Research
April 8 -10, 2016 | The Ashok, Chanakyapuri, New Delhi
Pre-conference Workshop : April 7, 2016 at AIIMS, New Delhi
Theme : Cancer In Asia: Bridging The Gaps

Journal of Carcinogenesis

IACR-BEST POSTER AWARDS

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PO 1: Corr Net Map: tool for correlation map and network

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Correlation in expression of multiple molecules gives clue about their functional and organizational relations. Biologists often measure changes in expression of multiple molecules at different time points and under different experimental conditions. Visualization of such data, in a meaningful way, is a challenge; particularly when number of targets is large and data is multidimensional. Tools have been developed for co-expression analysis and visualization, particularly for large-scale microarray data. However, most of such tools are for only one dimensional data and are usually embedded in microaarray analysis software. Here we report CorrNetMap, a ready-made, easy-to-use tool that calculates correlations in expression of multiple molecules and display the data as a heatmap and coexpression network. CorrNetMap calculates the correlations and creates network map for one-dimensional data (e.g time or dose dependent data) as well for multi-dimensional data (e.g where time and dose of treatment are varied). It can even consider temporal/phase lag in expression of molecules. CorrNetMap is a standalone tool and work in the freely available statistical software environment R. It reads data from simple text file and is designed primarily for data generated through small scale experiments like quantitative PCR or Western Blots. Though developed for co-expression analysis, CorrNetMap can be used, without any modification, to calculate and visualize correlations in any other type of data.

PO 2: Studying the expression of CR1 in specific colon cancer cell lines in vitro

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Introduction: Cripto-1 (CR1) is regulatory gene involved in embryogenesis and promotes carcinogenesis by modulating cancer cell proliferation, migration and EMT transition. Metformin is an anti-diabetic drug which has been found to exhibit anti-neoplastic effect. Since cancer stem cells are believed to be a major driving force for the aggressiveness nature of cancer, we want to study how treatment with Metformin affect changes in CR1 expression. **Method:** Colon cancer (HT29) cell lines were cultured in vitro. Dose of Metformin used was determined using MTT. HCT116 and HT29 cells were treated with Metformin for different time periods and CR1 expression was studied. To further validate the regulation of expression, CR1 cDNA was amplified and the product was ligated to 1013 vector. Transfected cells were analyzed for CR1 and other related parameters. **Result:** Changes in expression of CR1 were observed on treatment of cells (HCT116, HT29) with Metformin. Specific bands for CR1 were aligned completely to human gene reference sequence in NCBI database. Increased expression of human CR1 were observed in transfected cells. Modulation of gene expression was validated using QPCR. **Discussion:** Initial results indicate an inverse correlation between Metformin doses and CR1 expression patterns. Signals from various growth factors cascade through cardinal signaling pathways like PI3K/Akt and MAPK. We are currently studying the molecular cross-talking between these pathways and their regulatory role in controlling the action of CR1 and their link with the genesis and modulation of cancer

PO 3: Role of WNT canonical signaling pathway and cancer stem cell genes genetic variants on gallbladder cancer susceptibility, prognosis and survival

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Objectives: Gallbladder cancer (GBC) is the most common malignancy of the biliary tract with adverse prognosis and poor survival. **Methods:** In this study, we assessed the effect of genetic variants in CSC genes CD44, ALCAM, EpCAM, CD133, NANOG, SOX-2, LIN-28A, ALDH1A1, OCT-4 and Wnt signaling pathway genes (SFRP2, SFRP4, DKK2, DKK3, WISP3, APC, AXIN-2, B-Catenin, GLI-1) with GBC genetic predisposition, treatment

outcomes and survival. Total 564 GBC patients and 250 controls were genotyped. Grade 2–4 chemothareuptic drug toxicity was noted in 200 patients and tumor response was recorded in 140 patients undergoing non-adjuvent chemotherapy (NACT). **Results:** Single locus analysis showed statistically significant association of SFRP4 rs1802073G>T, DKK2 rs17037102C>T, DKK3 rs3206824C>T, APC rs4595552 A>T, APC rs11954856G>T, AXIN-2 rs4791171C>T, B-catenin rs4135385A>G and GLI-1 rs222826C>G with increased risk of GBC. In GMDR analysis, ALCAM rs1157G>A, EpCAM rs1126497T>C and APC rs11954856, AXIN2 rs4791171 emerged as best significant interaction model with GBC susceptibility and ALDH1A1 rs13959T>G with increased risk of 3-4 grade hematological toxicity. SOX-2 rs11915160A>C, OCT-4 rs3130932T>G and NANOG rs11055786T>C were found best gene-gene interaction model for predicting response to NACT. In both Cox-proportional and recursive partitioning ALCAM rs1157GA+AA, GLI-1 rs2228226 CG/GG and AXIN-2 rs4791171 TT genotype showed higher mortality and hazard ratio. **Conclusion(s):** ALCAM rs1157G>A, EpCAM rs1126497T>C, APC rs11954856, GLI-1 rs2228226 and AXIN-2 rs4791171 emerged as major effective genetic variants, responsible for poor survival in advanced gallbladder cancer.

PO 4:Enhancement of the therapeutic index of carboplatin by adjuvant use of a novel coumarin based organoselenocyanate (MUS)

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Introduction: Platinum-based drugs are at the mainstay of cancer chemotherapy. New Platinum derivatives like carboplatin, oxaliplatin, nedaplatin and lobaplatin are in clinical use and lots of others are under clinical trials in search of better therapeutic index. The second generation platinum drug, carboplatin, although less toxic than its precursor, cisplatin but do not possess substantial efficacy against broad range of neoplasm. Hence we hypothesise that molecules, like organoselenocyanates, those can deliberately reduce the tumor progression without effecting the anticancer mechanism of carboplatin may have the potential to act as novel adjuvant during carboplatin therapy. **Objectives:** To evaluate the efficacy of MUS in chemoprotection and chemoenhancement of carboplatin In Vivo. **Material and Methods**: MUS was synthesized in a two-step procedure, purified by column chromatography and characterized by spectral analysis. Carboplatin was given intraperitoneally. MUS was given orally alone and in combination with carboplatin in Swiss albino mice bearing EAC cells, **Results:** Administration of MUS along with carboplatin resulted in significant DNA damage and subsequent apoptosis towards tumor cells which ultimately increased the survivability of the host along with reduction in the tumor burden. **Conclusions:** MUS has the potential to open a new therapeutic profile for anti-cancer treatment when used as adjuvant along with carboplatin.

PO 5: Investigating Novel Interactors of a Tumor Virus Oncoprotein – Using Dual Tag labeling and Immunoprecipitation System

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Introduction: Several studies have contributed to the understanding of Polyomaviridae family of viruses and its potential role in viral oncogenesis and cancer biology. Among all the discovered viruses, Merkel Cell Polyomavirus (MCV) is the only human polyomavirus with convincing data supporting its classification as a direct causative agent of a human skin malignancy called Merkel Cell Carcinoma (MCC). MCC is a rare and aggressive neuro-endocrine carcinoma, which arises from the transformation of mechanoreceptor Merkel cells. MCV has been found to be clonally integrated into the genome of more than 80% MCC and occurs primarily in immunosuppressed individuals. Its genome is 5.4Kb and expresses variably spliced viral T antigen transcripts and proteins. The MCV large T antigen contains MCC tumorspecific truncation mutations that inhibits its C-terminal replication capacity but preserves its N-terminal oncogenic functions, such as the RB binding LXCXE motif. **Objectives**: We aim to identify novel interactors of MCV Large T that possibly participate in oncogenic transformation of the cell. **Material and Methods**: We are using a dual tag (biotin and flag) labeling and immunoprecipitation system for finding these interactors. We have cloned a codon-optimized version of MCV LT into a pFbek plasmid (gift from Dr. Chandrashekhar, CCMB) thereby tagging it with both a biotag and a flag tag at its N terminus. Following an overexpression in a cell line we performed several immunoprecipitation reactions. After validation we will send these precipitates for mass-spectrometric analysis to identify the interacting proteins. **Results:** We are expecting to identify yet-unknown interactors of Large T antigens that are relevant to MCV LT induced tumorigenesis. Data defining the MCV LT interactome will be presented during the meeting. **Conclusions:** The identification of its interactors will provide opportunities to expand knowledge of virus- host interactions and also to translate them into new targeted therapies for this disease, which are currently dismal. This knowledge can also be extrapolated to other cancers to identify new nodes and targets to understand the disease better.

PO 6: In silico search of putative molecular marker in esophageal Cancer from north east Indian population

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Introduction: Esophageal cancer is sixth leading Gastro-Intestina malignancy, cause of death in worldwide with an estimated around 4 lakhs newly diagnosed cases and deaths in 2012. Highest incidence of this cancer has been reported from North east (NE) region of India. Three studies had reported from our lab with high alteration number genes in which 78 downregulated and 32 upregulated genes was from nonfamilial expression, 287 downregulated upregulated 24 and genes was from familial and copy number study revealed 187 genes form deleted region and 139 genes from amplified regions datasets. These studies prompted us to explore unique molecular markers. **Objectives:** To identify putative molecular signature genes from NE datasets of esophageal squamous cell carcinoma. **Material and Methods:** A combined bioinformatics analysis which includes DAVID tool for ontology, Network of Cancer gene (NCG 5.0) for cancer gene analysis, Oncomine was applied for differential expression analysis for putative candidate genes resulted from NCG. Further Cancer cell line encyclopedia (CCLE) demonstrated mRNA level among the 21 cancer types to find putative molecular marker. Gene enrichment analysis was also executed by Integrative Genomics Viewer to validate the putative genes. **Results:** In siilico analysis was showed eight putative molecular genes i.e., CD14, PAK1, FGF12 (upregulated and amplified region), FGF18, MAPT, PPP3CC (deleted region) and CAPN2, COL4A4 (functionally downregulated).

PO 7: FAT1 modulates the expression of molecular regulators of hypoxia and stemness in glioma

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Introduction: Glioblastoma (GBM), arising from supporting glial cells, are the most common and most aggressive form of brain tumors with patient survival of 12–15 months after diagnosis. FAT1 gene, encoding a transmembrane protein, is an ortholog of the Drosophila tumor suppressor gene „fat". FAT1 is reported to have dual role, it may function as oncogene or tumor suppressor in different human cancers. Our lab previously identified the oncogenic role of FAT1 in human glioma where knockdown of FAT1 was found to inhibit migration/invasion of glioma cells and downregulate the expression of pro-inflammatory molecules. Hypoxia is one of the most pervasive micro-environmental stresses in GBM. **Objectives:** Here, we analyzed the functional role of FAT1 gene in regulating the expression of hypoxia and stemness markers in GBM under hypoxia. **Material and Methods:** FAT1 and the markers of hypoxia and stemness were analyzed at mRNA level in 31 GBM tissue samples. Correlation and cluster analysis were done using SPSS 11.5 and Cluster 3.0 softwares. U87MG and A172 glioma cell lines were used for in-vitro analysis. Cells were transfected with FAT1 specific siRNA or control siRNA, maintained under normoxic (20% O2) and severe hypoxic (0.2% O2) conditions and expression of hypoxia and stemness markers was analyzed 72hrs post-siRNA transfection. **Results:** In GBM tissue samples, a positive correlation of FAT1 expression with hypoxia (HIF1α, VEGF, PGK1 and CA9) and the stemness marker (SOX2) was observed. These correlations were also validated using heat map analysis Cluster 3.0. Kaplan-Meier analysis showed an inverse relationship of GBM patient"s survival with FAT1 and SOX2 expression. In U87MG & A172 cell lines, increased FAT1 expression along with the expression of hypoxia and stemness markers was observed on treatment with severe hypoxia (0.2% O2) as compared to their normoxic (20% O2) controls. Upon transfection with FAT1 siRNA, we observed decreased mRNA expression of hypoxia markers (HIF1α, VEGF, PGK1 and CA9) and stemness markers (SOX2, OCT4, Nestin and REST) in cells maintained under severe hypoxia. **Conclusions:** Therapeutic targeting of pathways operative in GBM has had limited success so far and thus new targets are needed to be identified for therapeutic intervention. Our **Results** suggest FAT1 to be a novel molecule regulating the expression of hypoxia and stemness markers in GBM and FAT1 may emerge as a target for therapeutic intervention.

PO 8: A-Kinase Anchor Protein 4 (AKAP4) is a Potential Biomarker for Breast Cancer

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Introduction: Breast cancer is the second leading cause of cancer related deaths in women worldwide. Early diagnosis of breast cancer can improved clinical outcome and overall survival rate in patients and better cancer management. **Objectives:** To study the role of association of cancer testis antigen, A-Kinase anchor protein 4 (AKAP4) with breast carcinoma. **Material and Methods:** We first compared the AKAP4 gene and protein expression in four breast cancer cells (MCF7, MDAMB-231, SK-BR3 and BT474) and normal human mammary epithelial cells. In addition, 91 clinical specimens of breast cancer patients of various histotypes and 83 available matched adjacent non-cancerous tissues were examined for AKAP4 gene and protein expression by in situ RNA hybridization and immunohistochemistry respectively and humoral response by employing ELISA. **Results:** Our in vitro studies in all breast cancer cells revealed AKAP4 gene and protein expression whereas, normal human mammary epithelial cells failed to show any expression. Using in situ RNA hybridization and immunohistochemistry, 85% (77/91) tissue specimens irrespective of histotypes, stages and grades of breast cancer clinical specimens revealed AKAP4 gene and protein expression but not in ANCT. Furthermore, humoral response was observed in 79% (72/91) of total breast cancer patients. Interestingly, 94% (72/77) of breast cancer patients positive for AKAP4 protein expression generated humoral response against AKAP4 protein. **Conclusions:** Collectively, our data suggests that AKAP4 might be a potential marker for an early detection and diagnosis of breast cancer for improving mother and child health care program.

PO 9: Tumor Associated Macrophages and their Association with Drug Resistance in Cancer

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Introduction: Tumor Associated Macrophages (TAMs) are reported to regulate the tumor microenvironment. While working with drug induced acquisition of chemoresitance by cancer, we identified Galectin-3, a TAM specific β-galactoside binding lectin, as a potential target. **Objectives:** To study the important molecular alterations in drug induced, drug resistant cancer cells using in vitro and in vivo models. To study the key functional role of altered proteins in the tumour progression/resistance. **Material and Methods:** In vitro studies were conducted using colon cancer cell line DLD-1 and its paclitaxel-resistant and camptothecin-resistant variants, and lung cancer cell line A549 and its doxorubicinresistant and podophyllotoxin-resistant variants. Selected drug resistant cells were used for in vivo study in SCID mice. Infiltration of TAMs was analysed in primary and metastatic sites. Galectin-3 expression was analysed in vitro and in vivo. Western blotting and Immunohistochemistry were the main techniques employed for the study. **Results:** Increased infiltration of TAMs and increased expression of galectin-3 were seen to be associated with drug resistance. Differential intracellular localization of galectin 3 was seen in the primary tumour, tumour emboli and metastatic sites. A shift from nuclear to cytoplasmic localization of galectin-3 was seen to be associated with tumour progression. **Conclusion:** Galectin-3 overexpression and its differential localisation are associated with tumour progression and drug resistance. Hence, it could be a potential therapeutic target.

PO 10: Cardiovascular disease in metabolic syndrome associated with metabolic induction of a hypoxic response

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Introduction: The risk of cardiovascular disease (CVD), asthma, non-alcoholic fatty liver disease (NAFLD)as well as common cancers is increased in subjects with metabolic syndrome (MetS). Interleukin4 (IL-4), a marker of Th2 immune response, is often upregulated in these contexts and may potentiate aberrant arginine metabolism. Altered arginine/nitric oxide metabolism and mitochondrial dysfunction represent putative common molecular pathways that may connect these diseases, possibly via oxidativestress driven induction of the cellular hypoxic response. The importance of this pathway is not well studied in MetS associated vascular dysfunction. **Objectives**: To investigate how altered arginine/methyl arginine balance, oxo-nitrative stress, hypoxic response, and mitochondrial dysfunction may cause vascular dysfunction in metabolic syndrome. **Material and Methods**: MetSmice (C57BL/6) were fed chow-diet (CN), high-fat-diet (HFA), or highfructose-diet (HR) for 6 months.HFR and HFA diets induce MetS. Arginine/methyl arginine balance and oxo-nitrative stress were determined in aortic tissue by measuring the levels of ADMA, iNOS and 3nitrotyrosine. Estimation of hypoxic response was done by checking

levels of HIF1α and resultant mitochondrial dysfunction by measuring levels of cytochrome c, TFAM and mitochondrial membrane potential. **Results**: IL-4 and ADMA were increased in HFA and HFR mice with MetS, compared to normal controls (CN). Vascular endothelial cells of both these groups also showed an increase in oxo-nitrative stress. IL-4 and ADMA led to potent induction of the cellular hypoxic response (HIF1α), despite normoxic conditions. The hypoxic response was associated with increased levels of the hypoxamir-210 that targets mitochondria, reduced mitochondrial membrane potential,decreased TFAM (mitochondrial biogenesis factor) levels,and leak of cytochrome-c to cytosol. **Conclusion:**IL-4 and ADMA are increased in MetS, leading to mitochondrial dysfunction through oxonitrative stress and hypoxic response. This has broad applicability to multiple diseases influenced by the hypoxic response, including cancer.

PO 11:A novel bioactive carbonyl pyridine from Tinospora cordifolia down regulates HSF-1 in triple negative breast cancer cells and inhibits tumor angiogenesis

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Introduction: Heat shock proteins (HSP) are critical for proper folding, assembly, stabilization of cellular proteins and are involved in tumor cell proliferation, differentiation angiogenesis and migration. The master regulator of the heat shock response is HSF-1, a multifaceted transcription factor is over expressed in a variety of human tumors including metastatic cancer cells. Hence down-regulating HSF-1 is an effective strategy for treatment of Triple negative breast cancer (TNBC). **Objectives:** We purified and characterized a small molecule carbonyl pyridine (TCCP) from leaves of Tinospora cordifolia, investigated its ability to inhibit heat shock response in MDA MB 231 cells through HSF-1 down-regulation and thereby inhibiting tumor cell proliferation, migration and tumor angiogenesis. **Material and Methods:** Purified butanolic extract was analyzed for homogeneity by LC MS and MALDITOF-MS, structure established by 1 and 2D NMR spectroscopy. Cytotoxicity and metabolic response of TCCP on MDA-MB-231 cells assessed by MTT and LDH assays, migration by wound healing assay. HSF1 regulation was ascertained by immunolocalization, expression of regulatory kinases, HSP 90, 70 and phosphorylation of HSF-1 were studied by immunoblotting. In vivo studies on anti-HSP and antiangiogenic properties were evaluated in EAT model, Rat cornea micro-pocket assay. **Results:** Molecule isolated was Carbonyl pyridine (C23H41NO3), IC50 of 125μM. LDH and TCCP inhibited MDA-MB-231 cell proliferation, metabolic activity, VEGF induced cell migration, tumor angiogenesis and corneal neovascularization through the downregulation of HSF-1 via AKT and PLK1 down-regulation and ERK1 upregulation. The HSP90 and 70 expressions were simultaneously decreased. **Conclusions:** TCCP may serve as a novel anticancer small molecule in targeting tumor growth via inhibiting HSF1.

PO 12: Activation and regulation of matrix metalloproteinases (MMP-2) induced by transcription factor snail in human oral tumour progression

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Introduction: Oral squamous cell carcinoma (OSCC) remains a major public health problem in Indian subcontinent. Epithelial-mesenchymal transition (EMT) leading to the invasiveness and metastasis is the main cause of morbidity and mortality. On the other hand, Matrix metalloproteinases like MMP-2, Snail are important regulators of EMT. However their expression and regulation is incompletely understood in OSCC invasion and metastasis. **Objectives**: To evaluate the expression and regulation of MMP-2 induced by Snail in various stages of human oral cancer progression and invasion. **Material and Methods**: Overexpression of MMP-2 and Snail were assessed in invasive oral cancer tissue samples, primary oral tumours, apparently normal adjacent tissue and premalignant lesions by using various methods: Western blot analysis, immunohistochemistry, gelatin zymography and RT-PCR. **Results**: The protein expression of activated MMP-2 was significantly higher in invasive cancer samples than adjacent non- cancerous tissue. A positive correlation of MMP-2 and Snail was observed ($r = 0.432$, $p < 0.012$). **Conclusions**: Our present results provide evidences of increased expression of MMP-2 and Snail in invasiveness of oral cancer. The positive correlation of MMP-2 activation and Snail expression may be exploited for efficient targeting of OSCC in future.

PO 13: EWS-FLI1 DERIVED POLYPEPTIDE INHIBITS EWING's SARCOMA CELLS IN-VITRO AND INTERACTS WITH EWS-FLI1 PROTEIN.

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Introduction: Our previous studies indicated that the Junction region (aa 251–343) in the EWS-FLI1, when ectopically expressed in Ewing's sarcoma cells displayed a dominant negative effect. In the present study, the effect of a peptide (TAT/NLS/EWS-PEP) derived from the junction region (a.a. 251-280) of EWS-FLI1 in combination with NLS and HIV1-TAT sequence was analyzed. Monoclonal antibodies were raised against CD99, a surface antigen highly expressed in Ewing's sarcoma cells. **Objectives**: Efficacy studies and functional characterization of a peptide derived from the junction region, on the oncogenic properties of Ewing's sarcoma cells. Raising monoclonal antibodies against CD99 for targeting the peptide to Ewing's Sarcoma cells in vivo. **Material and Methods**: FACS analysis and Fluorescence imaging, Cell proliferation and Colony formation assays, Cell cycle and BrdU incorporation assay, Matrigel invasion assay, Quantitative RealTime PCR, Electrophoretic Mobility Shift Assay, Immunoprecipitation and western blotting, cloning, expression and purification of recombinant protein and ELISA. **Results**: The peptide TAT/NLS/EWS-PEP induced inhibition of cell proliferation, clonogenicity, cell cycle and invasive properties of Ewing's sarcoma cells. Gene expression analysis of EMT markers and target genes of EWS-FLI1 in the peptide treated cells, showed a reversal in target genes and E-Cadherin levels relative to the control. Immunoprecipitation and EMSA assays showed that the peptide interacts with wildtype EWS-FLI1 protein and with EWS-FLI1-DNA complex. Serum half life analysis of the peptide revealed a stability of ~13 minutes indicating it to be unstable. Various clones of hybridomas, secreting antibodies against CD99 were screened and found to be specific for CD99. **Conclusions**: The peptide could potentially be applied in targeting EWS-FLI1 with modification in the delivery mechanisms to improve its stability.

PO 14: Structural and Genomic Analysis of the Mitochondrial DNA Displacement-Loop Region in Human Retinoblastoma with Patient Survival

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Introduction: Alteration in mitochondrial DNA plays an important role in the development and progression of cancer. The Displacement Loop (D-loop) region of mitochondrial DNA is the regulatory region for

its replication and transcription. **Objectives**: We aimed to characterize mutations in the D-loop region along with the structural changes of mitochondrial DNA and their impact on survival in retinoblastoma patients. **Material and Methods**: The entire D-loop region of mtDNA was amplified in polymerase chain reaction and mutations were evaluated in 60 retinoblastoma patients by DNA sequencing. Transmission electron microscopy was performed on 5 retinoblastoma specimens. Mutations were correlated with clinical, histopathological parameters and patient survival. **Results**: D-loop mutations were found in total of 52/60 (86.6%) patients. The most common mutations were T to C and C to T followed by A to G. There was 5.81% novel mutations observed on comparison with the MITOMAP database. A73G (83.33%) were the most frequent mutations found in our cases. However, there was no significant association between mutations and overall survival of patients. In addition, this study was expanded by analysis of morphological changes in retinoblastoma that has disorganized, swollen and less numbers of mitochondria on electron microscopy. **Conclusions**: This is the first study showing high frequency of mtDNA mutation which might be due to abnormal morphology of mitochondria in retinoblastoma. Our results strongly indicate that pathogenic mtDNA mutations may be a potential prognostic marker for retinoblastoma. Furthermore, dysfunctional mitochondria may play an active role in cancer development and the patient"s response to radiotherapy/chemo-radiotherapy.

PO 15: Regulation of Bcl-xL, Bax and p53 in human oral squamous cell carcinoma progression and chemo-resistance

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Introduction: Oral squamous cell carcinoma (OSCC) is one of the major causes of cancer related death in Indian subcontinent. Failure of apoptotic machinery is frequently disrupted leading to tumour progression including OSCC. Lack of proper understanding of molecular pathways and their crosstalk resulted in frequent treatment failure in oral cancer. Here, the expression and regulation of Bcl-xL, Bax and p53 were analysed in tissue samples of OSCC progression and chemo-resistance. **Objective:** The aim of this study to evaluate the expression of Bcl-xL, Bax and p53 in oral cancer progression and chemo-resistance. **Material and Methods**: Expression of Bcl-xl, Bax and p53 were assessed in chemo-resistance oral tumours (n=12), primary oral tumours (n=15) and primary tumour adjacent normal samples (n=21) by using various methods like Immunohistochemistry, Western blot analysis and RT-PCR analysis. **Results**: The protein expression of Bcl-xL and p53 were observed significantly higher in chemo-resistance tumours than primary tumours and adjacent normal tissues. The protein expression of Bax was observed higher in normal tissues than primary tumour tissues and chemo-resistance tumour tissues. The expression of Bcl-xL mRNA was observed more in chemo-resistance tumour tissues than normal tissues. The expression of Bax mRNA was observed higher in normal tissues than primary tumour tissues and chemoresistance tumour tissues. **Conclusions**: Deregulation of these apoptotic molecules found associated with human oral tumour for drug resistance. Targeting these molecules may be useful for therapeutic success for human oral cancer.

PO 16:Association of Clinicopathological Parameters with NF-κB/p65 Expression in Uveal Melanoma

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Introduction: Uveal melanoma is the most common primary malignant intraocular tumour in adults. NFkappa-B/p65 is a transcription factor which is present in almost all cell types and is involved in many biological processed such as inflammation, immunity, differentiation, cell growth, tumorigenesis and apoptosis. Numerous studies have investigated the correlation between NF-κB expression and prognosis in solid tumors. **Objective:** Therefore, the aim of our study was to investigate the immunohistochemical expression of NFκB/p65 and correlation with clinicopathological parameters. **Methods:** Immunohistochemical expression of NF-κB/p65 protein was analyzed in 20 prospective cases of uveal melanoma specimens. Cytoplasmic staining was considered as positive and graded as weak/negative (1+), moderate (2+) and strong (3+). Expressions of this protein were correlated with clinical parameters, tumor cell type, necrosis and histopathological invasion. **Results**: There were 20 cases of uveal melanoma. Tumour cell type was classified as spindle (>90% spindle cells), epithelioid (>90% epithelioid cells), or mixed. Expression of NF-κB /p65 was found in 12/20 (60%) cases of uveal melanoma. Expression of NF- κB /p65 was statistically significant with tumor cell type and cell size ($p<0.005$). **Conclusions**: This is the first study to show the expression of NF-κB /p65 in uveal melanoma cases. Investigating NF-κB /p65 pathway might be helpful for developing biomarkers in the management of uveal melanoma patients.

PO 17: Anticancer activity of novel limonoid against triple negative breast cancer

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Introduction: Triple negative breast cancer (TNBC) is the aggressive subtype of the breast cancer commonly occurring in females with high rates of tumor recurrence and poor overall survival. It was estimated that around 25% of people with breast cancer are triple negative. Currently, there are no effective standard chemotherapeutic agents being used in the treatment of TNBC.Therefore, there is an urgent need to develop highly efficacious and safe chemotherapeutic agents. Azadiradione, isolated from Azadiracta indica, is believed to be one such agent that could serve as a safe and efficacious agent for the treatment of this disease. **Objectives**:The present study aims to determine the anticancer potential of azadiradione against TNBC and its mechanism of action. **Material and Methods**:The antiproliferative and apoptotic effect of azadiradione was determined by MTT and FACS analysis. Wound healing assay was employed to assess the effect azadiradione on the TNBC migration. Underlying mechanism for its anti-cancer activity was studied by western blot. **Results**: Our Results showed that, Azadiradione inhibited the proliferation of TNBC cells in a dose dependent and time dependent manner with an IC50 of 36μM at 72 hr. FACS analysis showed that with increase in concentration of azadiradione, an increase in cell death was observed. Azadiradione inhibited the migratory potential of TNBC cells at 30μM. Further azadiradione inhibited the proteins responsible for cell proliferation, survival and metastasis of TNBC, and induced apoptosis which shows that this compound has potential in treatment of TNBC. **Conclusions**:Altogether, these results indicate that this compound possesses high potential in the treatment of TNBC. Further in vivo studies are required to validate the in vitro findings.

PO 18: A Translational perspective: Gene copy number variations and their control of Imatinib response in Chronic Myeloid Leukaemia

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Introduction: Imatinib Mesylate (IM) induces clinical remission in chronic phase chronic myeloid leukaemia (CML) patients, but IM resistance in later stages of CML still remains a challenge. There is a high degree of variability in drug response to Imatinib treatment within CML patients. The variation in the copy number of genes mapped near the BCR-ABL breakpoint region leads to differential response to Imatinib in CML patients. The molecular basis of differential prognosis is extremely important for the management of CML and for the better refinement of treatment. **Objectives**: The purpose of this study is to draw an association of Copy Number Variations (CNV"s) within genes associated with BCR-ABL translocation leading to differential response to IM. **Material and Methods**: Real-time quantitative PCR analysis was done on mononuclear cells from patients to identify CNV"s in five genes. Gene fold changes were analysed using independent t-test and pearsons coefficient of correlation. **Results**: CNV for SHGC142433, SHGC143988, SHGC106816 and AP0I.II was analysed in responders and non-responders of IM. We found that there was a significant difference between the two groups SHGC142433 ($p<0.01$), SHGC143988 ($p<0.01$) SHGC106816 ($p<0.001$) and APO1.11 ($p<0.05$).The level of correlation was also analysed for the four genes. SHGC cluster show a strong positive correlation (0.01 level of significance), SHGC142433 and SHGC106816 show a positive correlation with AP0I.II (0.01 and 0.05 level of significance).**Conclusions**: The presence of hemizygous deletions in the selected genes showed a co-relation with poor response to IM, while duplication suggests a good response to IM.

PO 19: Antitumour effects of amygdalin, a natural compound in the heterogeneous tumour microenvironment

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Introduction: Cancer is a leading cause of mortality around the world. The adverse side effect of conventional chemotherapy and radiotherapy has intensified the use of natural compound as complementary and alternative medicine (CAM) for cancer treatment. Amygdalin, a cyanogenic diglucoside present in the pits of many fruits and in numerous plants belonging to the Rosaceae family owns antitumor activity. Since the evidence based research on amygdalin is sparse, this study was initiated to determine its antitumor potential in lung and glioma cell-lines. **Objectives**: To investigate the effect of amygdalin on cancer cell growth and migration in both normal and low oxygen conditions. **Methods:** Tumor growth and proliferation was studied using MTT and clonogenic assay and cell cycle progression were investigated via flow cytometry. To evaluate the effect of amygdalin on tumor cell migration wound healing assay was done. Molecular analysis was done using Real time PCR and Western blotting. **Results**: Amygdalin reduces the growth and proliferation of cancer cells and caused a significant decrease in migration of cancer cells in both normoxia and hypoxia. It strongly altered the cell cycle progression by causing cells to arrest at G0-G1 phase. **Conclusions**: This in vitro study points to significant growth inhibition and anti-proliferative effect of amygdalin, by inducing a G0-G1 arrest and distinctly reduced tumor cell migration in both normoxia and hypoxia. We are currently deciphering its mechansim of action.

PO 20: Gene editing of Merkel Cell Polyomavirus (MCV) T antigen using CRISPR/Cas system

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Introduction: Merkel cell polyomavirus (MCV) is a human viral pathogen known to cause a skin cancer called Merkel cell carcinoma (MCC). MCC is a rare and aggressive neuro-endocrine carcinoma that arises from the transformation of mechanoreceptor Merkel cells found in the basal layer of the epithelium. MCV is clonally-integrated into the tumor genome in more than 80% of MCC. MCV expresses two oncoporteins, the Large T (LT) and Small T (sT) antigens that promote cancer survival and proliferation. These proteins retain conserved domains that target various tumor suppressor molecules such as Retioblastoma protein. RNAi mediated partial knockdown of the T antigen proteins in MCV positive MCC cell lines Results in cell death. With the advent of the new CRISPR interference (CRISPRi) technology a more efficient knockdown or block of expression is possible. CRISPR, short for Clustered Regularly-interspaced Short Palindromic Sequences, is a gene editing technology which uses a guide RNA mediated targeting for a nuclease called Cas9 to cleave DNA sequences. Homologous recombination in-conjunction with CRISPR can be used to edit gene sequences. We are currently exploring the use of this technology to block T antigen gene expression and edit its RB binding domain to address the importance of the two in the process of carcinogenesis. **Objectives**: A more efficient knockdown on Merkel cell polyomavirus (MCV) T antigen using CRISPRi.Editing the MCV Large T antigen Retinoblastoma(Rb) binding domain (LXCXE) and making the mutant endogenous protein incapable of binding to Rb. **Material and Methods**: We are using MCC cell lines- MS-1 and MKL-1 for our studies. CRISPR plasmids were obtained from Dr. Feng Zhang"s and Dr. Stanley Qi"s laboratory through addgene. We will design and clone guide RNAs for the MCV genome to target the promoter region (for CRIPSRi) and the LXCXE site for the two aims respectively. **Results**: We are expecting to efficiently knockdown MCV T antigen proteins using CRISPRi that regulates gene expression at the transcription level. We will then analyze the phenotype of the cancer cells lacking the viral oncoproteins further. Also, we expect to successfully edit the RB binding motif of MCV large T antigen and address its importance in MCV mediated tumorigenesis. results will be presented in the meeting. **Conclusions**: Newer efficient technologies like CRISPR gene editing are opening new doors for understanding disease. Our efforts to exploit these methods to address several unanswered questions relating to viral mediated tumorigenesis hold great promise. Also, we hope to extend our findings to the understanding and possible therapy of other cancers in the future.

PO 21: Cytokines modulate ionizing radiation induced Smad signaling in breast cancer cells

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Introduction: Exposure to ionizing radiation (IR), in addition to DNA damage responses, activates several pro-survival pathways like PI3K/AKT, EGFR/RAS/RAF/MAPK, TGF-β/Smad etc. Activation of Smad proteins can be mediated by canonical signalling through TGF-β1 or non-canonical pathways like AKT, ERK and SAPK/JNK. **Objectives**: To delineate the role of tumor microenvironment in modulation of IR induced Smad signalling in breast cancer cells. **Material and Methods**: Adherent human breast cancer cells MCF-7, MDA-MB-231, and mouse fibrosarcoma WEHI-164 cells were serum deprived (0.1%) overnight. Next day, cells were exposed to 1-10 Gy IR, or treated with SB451342 (TGF-β1 receptor inhibitor). BALB/c mice bearing WEHI-164 fibrosarcoma were exposed to localized irradiation. For tumor microenvironment studies, cells were treated with M1 or M2 specific cytokines followed by exposure to IR. Migration assays were carried out in 8 μM transwell inserts. Smad phosphorylation was assessed by western blotting and TGF- β1 downstream genes by RT-PCR. **Results**: Exposure to IR increased phosphorylation of Smad2 in all three cell lines. Exposure to doses 1-4 Gy consistently increased phosphorylation of Smad2 ($p<0.01$) whereas in doses 6-10 Gy, this was dependent upon the basal autocrine signalling. SB451342 inhibited the basal autocrine signaling but did not affect radiation induced apoptosis. IR induced Smad2 phosphorylation was also observed in BALB/c mice bearing WEHI-164 fibrosarcoma indicating the relevance of this signalling under in vivo condition. Cytokines TNF-α and IL-10 modulate the basal autocrine Smad signalling and therefore the IR induction. This further had an effect on epithelial mesenchymal transition (EMT) response. **Conclusions**: Exposure to IR increased phosphorylation

of Smad2 in MCF-7, MDAMB-231 (breast cancer cell lines) and WEHI-164 (a mouse fibrosarcoma) which was further modulated in presence of TNF-α and IL-10.

PO 22:Hypoxia appears toovercome inhibition of Rho GTPases

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Introduction:Cancer, a disease defined by uncurbed proliferation of cells. Signaling molecules regulate proliferation and cellular organization in normal cells, and also assist in vesicle transport, membrane protein traffic, phagocytosis, host-pathogen interactions and cell adhesion, motility and migration. One such family of proteins is the Ras superfamily of small GTPases, to which Rho GTPases subfamily belong. Rho family GTPases are molecular switches that oscillate between active (GTP bound) and inactive (GDP bound) state. There are 22 members of Rho GTPase family, of which three are well studied, RhoA, Rac1 and cdc42. We are investigating the effect of inhibition of three well-studied Rho GTPases i.e., RhoA, Rac1 and Cdc42 proteins in hypoxiato elucidate the relevance of these pathways in the tumor microenvironment. **Material & Methods:**We have used the A172 glioma cell-line to investigate the effect of EHT 1864, ML 141 and Rho inhibitor 1 to inhibit Rac1, cdc42 and RhoA respectively. For our read out, we have used MTT assay, wound healing assay, confocal microscopy and qPCR. **Results**: Early observations show that hypoxia appears to overcome the growth inhibition caused by EHT 1864 & ML141. While they showed reduction in migratory potential of cells under normoxia, this reduction was overcome in hypoxia **Conclusion:** Hypoxia overpowers the inhibition of Rac1, cdc42 and Rho A. We are yet to analyze the molecular mechanisms governing our observations.

PO 23: Pro-apoptotic activity of novel 4-anilinoquinazoline derivatives mediated by up-regulation of Bax and activation of PARP in murine carcinoma cells

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Introduction: Quinazolines are very important class of heterocyclic compounds, which shows a broad variety of biological activities, such as analgesic,diuretic, antihypertensive, antimalarial, antibiotic, antitumoral, antiangiogenic and many others. **Objectives**: Evaluation of pro-apoptotic effect of novel quinazoline derivative. **Material and Methods**: The synthesized 4-anilinoquinazolines derivatives were characterized using IR, 1H NMR and mass spectroscopy. These compounds were screened for their cytotoxicity using MTT against Ehrlish ascities carcinoma cell line. The effects of quinazoline compound on the growth of EAC cells were studied in vivo. Further induction of apoptosis in EAC cell lines was monitored by FACS analysis, DNA fragmentation, immunoblotting and caspase-3 inhibition assay. **Results**: Among them, 4G quinazoline compound exhibits more potent activity with an IC50 value of 10.29 ± 1.14 against EAC cell line. An In vivo study showed that, there is reduction in the body weight, ascities volume, cell number and higher survivability of 4G treated mice when compared with control mice. The treated cells also exhibited typical morphological changes of apoptotic damages. Further, 4G induces tumor cell death by activating of proapoptotic protein Bax, release of Cyt c from mitochondria which activates caspase-3 and activated caspase –3 cleaves PARP causes DNA fragmentation. **Conclusions**: The current study showed clearly that compound 4G strongly inhibits cell proliferation and induction of apoptosis by upregulation of caspase-3 and PARP cleavage in EAC cells.

PO 24:Effect of oncogenic K-Ras on the expression of cysteine cathepsin L and B in hepatocellular carcinoma

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Introduction: Cathepsins are lysosomal cysteine proteases that play major roles in proteolysis, protein processing, ECM degradation, and tissue remodeling, cathepsin L and B are overexpressed and secreted extracellulary during carcinogenesis. However, expression of these proteases has shown to be induced by activation of oncogene such as Ha-Ras. **Objectives**: Therefore, we assessed the effect of oncogenic K-Ras on the expression and regulation of cathepsin B and L in hepatocellular carcinoma. **Material and Methods**: The mutant K-Ras cDNA was cloned into eukaryotic expression vector, pcDNA3.1 (+) and was stably transfected in Chang liver cells. Expression of cathepsin B and L were then determined by western blotting, real-time PCR and immunocytochemistry. Transcriptional regulation of cathepsin L by K-Ras was evaluated using promoter reporter assay. **Results**: Both cathepsin B and L transcripts and protein levels were found to be elevated in K-Ras transfected as compared to control Chang liver cells. Similarly, cathepsin L promoter activity was higher in K-Ras expressing cells as compared to untransfected cells. **Conclusions**: Elevated expression of cysteine cathepsins by K-Ras taken together with previously established role of these proteases in tumor invasion and metastasis suggest that cathepsin Band L may be responsible for conferring invasive abilities to mutant K-Ras harboring tumor cells.

PO 25: Role of alternative splicing of FGF-Receptor in regulating EMT and Invasion of ovarian cancer cells

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Introduction: Epithelial ovarian cancer is a lethal gynaecologic malignancy characterized by its detection at an advanced stage. Epithelial-mesenchymal transition (EMT) contributes to the aggressiveness of numerous epithelial cancers.RNA splicing events play a crucial role during EMT. The RNA-binding proteins ESRP1/2 and RBFOX2 have been identified as key regulators of splicing events during EMT. A number of growth factors like FGF, TGF play important role in facilitating EMT. FGFs signal via 4 tyrosine kinase receptors (FGFR1-4). Splice variation in FGFRs leads to expression of mesenchymespecific FGFRs in epithelium-derived cancers broadening the range of FGFs that can bind to these altered receptors and facilitates autocrine signalling in the tumor cells. **Objectives**: To elucidate the regulation of FGFR alternative splicing and their role in ovarian cancer cells. We will investigate the role of the splicing factors and their regulation of function in controlling EMT and invasion in ovarian cancer. **Material and Methods**: Regulation of expression of different genes and factors was assessed by means of Q-PCR, Western blot, ChIP and reporter assay matrigel transwell assay and microscopy. **Results**: The EMT induction by means of growth factor results in a splicing switch of FGFRs in ovarian cancer cells, which is found to be controlled by an epithelial splicing factor that in turn becomes downregulated. The splice isoforms of FGFRs were found to regulate the EMT and invasion of ovarian cancer cells. **Conclusions**: The splice isoforms of FGFRs were found to regulate the EMT and invasion of ovarian cancer cells. The regulation of this differential splicing has been established in this study.

PO 26:Serum miR-182 can act as a promising biomarker for hepatitis B virus associated hepatocellular carcinoma

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Introduction: MicroRNAs (miRNAs) are small evolutionarily conserved non coding RNAs that are present within cell as well as in various extracellular body fluids. It has been shown that levels and profile of circulating miRNAs gets altered in various pathological conditions indicating their potential as diagnostic biomarkers. In the present study, we aimed to study the expression of serum miR-182 as a potential diagnostic biomarker for HBV related HCC. **Objective:** To study the expression of miR-182 in serum during the progression of HBV mediated HCC development and its potential as diagnostic biomarker. **Subjects and methods:** Eighty four participants were recruited which belonged to four groups i.e. 21 healthy controls, 15 chronic hepatitis B (CHB) patients, 14 HBV-associated liver cirrhosis (HBV-LC) patients and 34 HBV-associated hepatocellular carcinoma (HBV-HCC) patients. Quantitative real time polymerase chain reaction (qPCR) was used to evaluate the expression of miR-182 and miR-1228-3p (used as reference gene). The area under the receiver operating characteristic curve (AUC) was used to evaluate the accuracy of miR-182 as diagnostic biomarker for HCC. **Results**: The serum miR-182 levels were found to be upregulated in the HBV-HCC patients compared with the HBV-LC patients (5.4 fold; $P < 0.04$); healthy controls (15 fold; $P < 0.000$) and CHB patients (1.6 fold; non-significant). The investigated miR-182 could also differentiate HBV-HCC patients from healthy (AUC 0.82; $P < 0.0001$) and HBV-LC patients (AUC 0.69; $P < 0.04$) but not from CHB patients (AUC 0.58). Furthermore, elevated levels of serum miR-182 in CHB patients (9.3 fold; $P < 0.008$) wrt healthy controls could discriminate these two groups (AUC 0.74; $P < 0.01$). Although miR-182 were upregulated between HBV-LC patients (2.7 fold; non-significant) and healthy controls, it cannot discriminate these two groups (AUC 0.63). **Conclusions**: Our results suggest that the serum miR-182 level can serve as a potential non-invasive biomarker for HCC patients with chronic HBV infection.

PO 27:Anti – tumor activity of exo and endo polysaccharides isolated from Ganoderma lucidum occurring in South India

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Introduction: Ganoderma lucidum , a medicinal mushroom known as „King of herbs" has been widely used as a single agent or in combination with other herbs in the folklore for years in Asian countries for the treatment of variety of diseases. Among the 400 chemical constituents reported from the mushroom , polysaccharides and triterpenes are the major components. Extracts of this mushroom have been reported to have significant antioxidant, antiinflammatory, antitumor, hepatoprotective and cardioprotective activities. The major active principle that has been reported to possess antitumor activity is the polysaccharides present in the fruiting bodies. **Objectives:** The objective of the present study is to isolate the total exo and endo polysaccharides from the cultured mycelia of Ganoderma lucidum and to determine their antitumor activity. **Material and Methods:** The exo and endo polysaccharides were isolated from the culture filtrate and aqueous extract of the mycelia by ethyl alcohol precipitation and further purification. The antitumor activity was assayed by DLA cell lines induced solid tumor in Swiss albino mice. **Results:** TLC and paper chromatography analyses indicated that glucose is the main monosaccharide component of both exo and endo polysaccharides. Both exo and endo polysaccharides showed significant antitumor activity . However, exo-polysacchride had higher antitumor activity than the endo – polysaccharides. **Conclusions:** The results of present study reveal the therapeutic significance of exo and endo polysaccharides produced by the cultured mycelia of Ganoderma lucidum.

PO 28: Homeopathic preparation of Thuja occidentalis enhances cell-mediated immune responses during tumour progression

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Introduction: Various studies evidenced the immunomodulatory and anti-tumour properties of potentized homeopathic preparations of Thuja occidentalis. It is well known that the cell mediated immune responses are the major effectors during tumour progression which includes various immune cells and mechanisms whose actions are regulated by various cytokines. Hence it is significant to study if a formulation with anticancer property, like Thuja, could influence the anti-tumour immune defence during tumour progression. **Objectives**: The present study aims to analyse the role of 1M potency of Thuja occidentalis on the cell mediated immune responses during tumour progression in mice model. **Material and Methods**: The production of cytotoxic T lymphocytes (CTLs) was studied by Winn"s neutralisation assay using CTL-sensitive EL-4 thymoma cell line, induced in Balb/c mice. The cell mediated immune responses during metastatic progression was studied using 4T1-metastatic model in Balb/c mice. NK cell activity and antibody dependant cell mediated cytotoxicity (ADCC) were analysed by 4 hr Cr-release assay using K-562 cell line and SRBC as targets respectively. Antibody dependant complement mediated cytotoxicity (ACC) was determined using 4T1 cells as target followed by trypan blue exclusion cytotoxicity assay. Serum cytokine levels were analysed by ELISA. **Results**: The production of CTLs, NK cell activity, ADCC and ACC were significantly enhanced by Thuja treatment when compared to the control group. Moreover, the regulatory cytokines such as IL-2 and IFN-γ, were also found to be elevated by Thuja treatment. **Conclusions**: The results signify that Thuja has an effective role in boosting the anti-tumour immune responses during tumour progression.

PO 29:Sarcinol impedes cell proliferation and promotes apoptosis in oral squamous cell carcinoma via NF-κB and COX-2 inhibition

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Introduction: Garcinol, a polyisoprenylated benzophenone is extracted from the rind of the fruit of Garcinia Indica, a plant found extensively in tropical regions. Its ability to inhibit tumour growth has been demonstrated in certain cancers. **Objectives**: In this study we have evaluated the potential anti-tumour effects of garcinol on oral squamous cell carcinoma (OSCC). **Material and Methods**: The oral squamous cell carcinoma cell lines were treated with garcinol for 48h and its effect on growth and proliferation, clonogenic survival, cell cycle and apoptosis was studied by MTT, clonogenic, Propidium iodide (PI) staining and Annexin-V binding assays respectively. The alteration in expression of NF-κB, COX-2 was studied by immuno-blotting and immunofluorescence in treated cells and that of VEGF by ELISA. **Results**: Garcinol treatment significantly inhibited the growth and proliferation and colony formation of OSCC cells with a concomitant induction of apoptosis and cell cycle arrest. It did not show toxic effect on normal cells. It significantly reduced the expression of NK-κB and COX-2 in treated cells as compared to untreated controls besides inhibiting VEGF expression. **Conclusions**: It appears that garcinol exerts anti-proliferative, pro-apoptotic, cell-cycle regulatory and antiangiogenic effects on oral cancer cells through suppression of NF-κB and inhibition of COX-2 and VEGF. Thus, garcinol may be a potential chemopreventive and/or chemotherapeutic agent for treatment of oral squamous cell carcinoma.

PO 30: Homeodomain Transcription factor Pax6 as a potential biomarker for Brain tumour diagnosis

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Introduction: The paired box 6 (PAX6) encodes a transcription factor that is involved in the development of the brain, where it acts as a tumour suppressor gene. Pax6 expression is regulated by Sonic Hedgehog (Shh) signalling pathway which play a vital role in neural development and patterning. The role of Shh signalling in brain tumour development is well known and Low expression of Pax6 homeodomain transcription factor in brain tumour was reported and we are now exploring to make ensure its loss of activity related with brain tumorigenesis. **Objectives**: This study focuses on homeodomain transcription factor Pax6 and its potential role in brain tumoriogenesis. **Material and Methods**: Human primary brain tumour samples were collected from the Department of Neurosurgery, Jawaharlal Nehru Medical College (JNMC) AMU, Aligarh. Thereafter, processed these samples for histochemistry, immune-histochemistry and PCR to check the expression of Shh, Gli1 and Pax6. **Results**: Results awaited **Conclusions**: If there would be possibility of low expression of Pax6 in comparison of high expression of Shh and Gli1 in human brain primary tumour sample. Then this would explain the nature of Pax6 as a tumour suppressor gene. Moreover, Pax6 could be considered as a one of the novel biomarkers for early detection of brain tumour tumours in the suspected patients.

PO 31: A Novel cancer testis antigen: A-Kinase Anchor Protein 4 (AKAP4) is a potential biomarker for early diagnosis of Cervical Cancer

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Introduction: Cervical cancer is a major gynaecological cancer and is one of the leading cause of cancerrelated deaths in developing countries. There is an urgent need to identify novel biomarkers for cervical cancers for better prognosis and cancer management. **Objectives**: we have investigated expression and humoral response of novel CT antigen A-kinase anchor protein 4 (AKAP4) in 74 cervical cancer tissue specimens with different tumor stages, and histologic grades. **Material and Methods**: AKAP4 gene and protein expression was investigated in cervical cancer tissue specimens with different tumor stages (stage I [n = 35], stage II [n = 39]) and histologic grades (grade 1 [n = 17], grade 2 [n = 46], and grade 3[n = 11]) and 62 adjacent noncancerous tissue specimens. In addition, humoral response against purified recombinant AKAP4 protein was determined in 70 patient"s sera of cervical cancer by enzyme-linked immuno assay (ELISA). **Results**: We detected AKAP4 gene and protein expression in 86% of total patients with cervical cancer. Based on the AKAP4 immunoreactivity score, most of stage I (n = 22/29) and stage II (n = 30/35) specimens revealed high AKAP4 expression (>50% AKAP4-positive cells). We observed that A-kinase anchor protein 4 expression was significantly associated with early grades tumor specimens (P = 0.023). In addition, humoral response was detected in 53% of patients irrespective of stages, lymph node positivity, and grades. **Conclusions**: Our data indicate the role of AKAP4 in early detection and diagnosis of cervical cancer and may be implicated as a potential biomarker and immunotherapeutic target for cervical cancer for better cancer management of disease.

PO 32: Expression of cyclin D1 protein and its regulation by glycogen synthase kinase 3 beta signalling in human oral cancer

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Introduction: Oral squamous cell carcinoma (OSCC) is one of the major health problems worldwide including India. Cyclin D1 is one of the most important proto-oncogene and cell cycle regulator but its expression and regulation has not been studied in oral cancer patients of Jharkhand. On the other hand GSK3 beta activation is one of the causes for cyclin D1 rapid turnover and our work demonstrates the inactivation of GSK3beta leads to OSCC. Here, the detail pathways have been analysed to understand the GSK3 beta mediated deregulation of cyclin D1 in chewing tobacco mediated oral cancer population of Jharkhand. **Objectives**: To evaluate the expression and regulation of cyclin D1 by the inactivation of GSK3 beta in various stages of human oral cancer progression. **Material and Methods**: Expression of cyclin D1 and GSK3 beta was analysed in oral cancer tissue samples, premalignat lesions, tumour adjacent normal like tissue and healthy normal tissue samples by using various methods like Western blot analysis, immunohistochemistry and RT-PCR. **Results**: Cyclin D1 expression has been observed more in OSCC samples than PML and normal samples. Consistently more cyclin D1 protein expression and GSK3 beta inactivation was observed with oral cancer progression. A positive correlation was observed with cyclin D1 expression with the inactivation of GSK3 beta. **Conclusions**: Our Results provide evidences of increased over expression and accumulation of cyclin D1 in every step of oral cancer progression. The positive correlation of inactive GSK3 beta and cyclin D1 may be exploited for efficient targeting of OSCC in future.

PO 33: Aberrant lysyl hydroxylase 2 expression leads to ovarian cancer progression through FAK activation

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Introduction: Tumor aggressiveness depends on the multifarious, dynamic interactions of the cancer cells with the surrounding matrix (ECM). A critical balance involving the expression, maturation and degradation of the collagens, the major component of ECM, is essential for the proper function of ECM. Diverse aspects of collagen metabolism are known to be aberrant in epithelial cancer and aggravate tumor progression; however, the regulatory mechanism behind remained uncharacterized. **Objectives**: To elucidate the contribution and the regulatory clues that controls the aberrant collagen maturation contributing to increased ECM stiffness leading to ovarian cancer progression. **Material and Methods**: Lysyl hydroxylase2 (PLOD2) expression in human ovarian tissues was assessed by IHC. Gene expression studies were carried out with Q-PCR (ABI 7500) and western detection after transfection/treatments. Invasion/migration was checked with matrigel invasion chamber (BD Biosciences) and wound healing assay. Binding to promoter was checked using ChIP kit (Upstate) and activation of promoter activity through luciferase assay using Glomax luminometer (Promega). Confocal imaging was done with Andor spinning disk confocal microscope. **Results**: Human ovarian tumors showed enhanced PLOD2 expression, one of the earliest critical factors initiating collagen maturation process. Our study uncovers the enhanced

invasion of ovarian cancer cells through increased collagen deposition in ECM contributing to increased stiffening thereby activating FAKintegrin signaling cascade. Further focussing on the regulatory driver for PLOD2, our study reveals the existence of a homeo-box transcription factor, PITX2, which activates PLOD2 expression ultimately aggravating the ovarian cancer progression. **Conclusions**: The oncogenic potential of PLOD2 and regulatory factor controlling its expression in ovarian cancer was established.

PO 34: Inhibition of tumor derived prostaglandins Results in restoration of dendritic cell immunogenicity and decrease in tumor burden

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Introduction:Tumor microenvironment induced dysfunction of dendritic cells (DC) is one of the important mechanisms to evade immune surveillance which is in turn associated with tumor progression. **Objectives**:To delineate the effect of tumor microenvironment on dendritic cells differentiation and maturation. **Material and Methods**:Flow cytometric analysis of receptors and intracellular proteins, cytokine estimation by ELISA, RT-PCR analysis and in vivo tumor experiments. Supernatant of EL4 murine lymphoma served as tumor conditioned medium (TCM). C57BL/6 mice bearing syngeneic EL4 tumor are designated as tumor bearing mice (TBM). **Results**:Dendritic cells treated with TCM as well as those derived from TBM exhibited defective phenotypic and functional maturation. This was associated with increased erk1/2 mediated activation of cAMP response element binding protein (CREB) and inhibition of NFkB pathway. CREB induced the secretion of IL-10 cytokine. In addition, screening for lineage specific transcription factors revealed downregulation of Zbt46 in TCM treated DC as well as in DC progenitors in bone marrow cells of TBM. This was confirmed atRNA and protein level. siRNA mediated knock down of Zbt46 also showed the same phenotypic and functional defects shown by DC (TCM). Tumor derived prostaglandin E2 (PGE2) seems to mediate observed effects. Treatment with recombinant PGE2 recapitulated all these effects while treatment with COX-2 inhibitor (NS-398) could abrogate the TCM and TBM induced inhibition of DC maturation. Treatment of TBM with NS-398 resulted in increase in DC immunogenicity with a concomitant decrease in tumor volume. **Conclusions**:Tumor derived PGE2 inhibit lineage specific transcription factor Zbt46 as well as activate ERK/CREB/IL10 pathway to result in DC dysfunction. Inhibition of PGE2 restores DC immunogenicity and decrease tumor burden.

PO 35:Identification and investigation of the minimal promoter region of Merkel cell polyomavirus

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Introduction: Merkel cell carcinoma (MCC) is an aggressive, rare and highly malignant skin cancer caused by Merkel cell polyomavirus (MCV). MCV, discovered in 2008, is the newest member of the oncovirus family. It is found to be integrated into the host genome and harbors truncating mutations in one of the important proteins coded by the viral genome, the Large T antigen. The viral genome comprises of 5387bp and its early region encodes the Large T antigen (LT), small T antigen (sT) and 57kT antigen all generated by a major transcript by alternative splicing. Both the LT and sT independently play an important role in viral replication, cellular transformation and tumor cell survival. This makes it is very important to study the promoter region to gain better insights regarding the mechanism of carcinogenesis by MCV. **Objectives**: The objective of this study is (1) to identify and characterize the minimal promoter region of MCV (2) To identify novel interactors of the LT antigen and study the transcription factors (tfs) binding to the MCV promoter. **Material and Methods**: It would involve (1) cloning the suspected promoter region from MS-1 and MKL1 (MCV +ve MCC cell lines) into the pGL3 basic vector and check for its luciferase activity (2) the use of in silico tools like Transfac and PROMO for identification of tfs and its binding site within the LT. **Results**: The expected outcome of this study is to assign a minimal promoter region that drives the transcription of the LT and sT and also to find and validate the tfs binding to it. **Conclusions**: Viral promoters have not been studies this extensively before. Ours studies will help in understanding viral transcription and regulation better. This will hopefully help in designing targeted therapeutics in the future for better management of MCC.

PO 36: A novel drug 3-(3´4´,5´-Trimethoxyphenyl)-5-(Nmethyl-3´-indolyl)-1,2,4-triazole [NMK-T-057] induces cell cycle arrest, apoptosis and reprogramming of epithelial to mesenchymal transition (EMT) and stemness in breast cancer cells via targeting Notch-1 signaling

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Epithelial to Mesenchymal transition (EMT) is an important and coordinated series of events associated with tumor metastasis and invasion. Accumulating experimental evidences had shown the importance of Notch-1 signaling in the regulation of EMT, induction of stemness and acquisition of chemoresistance properties in breast cancer. Hence targeting the Notch-1 signaling in breast cancer can serve as an effective therapeutic approach to combat this disease. Indole ring system is one of the most crucial heterocycles that has found versatile pharmacological implication in medicinal chemistry. Many of the natural and synthetic indole-based heterocycles with various functionalities are reported as potential anticancer molecules. Recently, the diverse biological activities of hydrazide-hydrozones have attracted the researchers to develop their heterocyclic analogues as efficient chemotherapeutic agents. In the present study we have reported the anticancer mechanism of a novel 3-(3´4´,5´-Trimethoxyphenyl)-5-(N-methyl-3´-indolyl)-1,2,4-triazole compoundalso known as NMK-T-057 against the carcinoma of breast. NMK-T-057 was found to be highly cytotoxic against various breast cancer cells such as MDA-MB-231, MDA-MB-468 and MCF-7, while it has negligible cytotoxicity against the non-cancerous MCF-10A. NMK-T-057 significantly induced cell cycle arrest of the BC cells at G2/M phase and initiated mitochondrial-dependent apoptotic signaling. Moreover it was found to alter the mesenchymal morphology of MDA-MB-231 cells and inhibited the EMT process. Further investigations revealed that treatment of MD-MB-231 cells with NMK-T-057 resulted in the drastic inhibition of Notch-1 signaling. Thus we might conclude that NMK-T-057 could be potential drug candidate against breast cancer, which can target Notch-signaling.

PO 37: Chlamydia and ocular lymphomas

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Introduction: Ocular adnexal lymphomas (OALs) constitute 1-2% of all non-Hodgkins lymphomas. It may be an antigen driven disorder, however

antigen source is poorly understood. Different geographical regions have reported association of Chlamydia with OALs. In India, role of Chlamydia in OALs remains unexplored. **Objectives:** The present study was aimed to detect Chlamydia and to correlate with clinicopathological features of OALs in India. **Materials & Methods:** Prospective analysis of 41 NHL cases & 21 control cases (normal orbital tissues) was done. Patients were followed up for 10-48 months. Chlamydia DNA was detected by genus specific PCR amplifying major outer membrane protein (MOMP) gene followed by DNA sequencing. Chlamydia immunoexpression was evaluated by immunofluorescence and immunohistochemistry. The results were correlated with clinicopathological features including follow-up and survival. **Results:** Chlamydia genome was detected in 3/41 (7.3%) OAL cases by PCR. Direct sequencing revealed C.trachomatis in 3 positive cases. Immunofluorescence and immunohistochemistry showed Chlamydia antigen in 5/41 and 1/41 cases respectively. Immunofluorescence demonstrated higher sensitivity and specificity than immunohistochemistry. A significant association was observed between Chlamydia positivity and orbital location (P= 0.05). All the 3 cases were subjected to 4-6 cycles of chemotherapy along with involved field radiotherapy. Follow-up revealed relapse in 2 Chlamydia positive cases (P=0.056). **Conclusions:** Our results demonstrate the presence of C.trachomatis genome in 7.3% OAL cases in India, for the first time. As no other reports are documented from India, more detailed studies from different regions are needed to explore the status of Chlamydia in OALs.

PO 38: Development of drug-seeds targeting JAK-STAT pathway, TNF-a, BCl2 and BAD in hepatocellular and mammary carcinoma

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Drug discovery" has historically been based on phenotypic readouts on the organism level, such as the effect of synthetic heterocycles or other natural products on humans. In my presentation, I will combine the machine-learning tools, chemical synthesis, and biological studies to develop small-molecule targeting JAK-STAT pathway, TNF-a, BAD, and NF-kB in hepatocellular (HCC) and mammary carcinoma (MC). STAT3 has emerged as a promising target for cancer therapy. We recently, synthesized 2-(1-(4-(2cyanophenyl)1-benzyl-1H-indol-3-yl)-5-(4-methoxy-phenyl)-1-oxa-3-azaspiro(5,5) undecane and their biological evaluation against HCC was made, and identified as a potent inhibitor of the JAK-STAT pathway. TNF is a pleotropic cytokine known to be involved in the progression of several proinflammatory disorders. So, we developed biscoumarins as anti-cancer agents in vitro and in vivo and evaluated the mode-of-action as TNF blocker. We also found the anti-cancer small molecule (7Carbethoxyamino-2-oxo-2H-chromen-4-yl)methylpyrrolidine-1-carbodithioate that targets NF-kB in HCC cells. Finally, I will focuss my talk on BAD, which is an apoptosis regulatory protein linked with relaying survival signals to carcinoma cells upon phosphorylation as Ser-136. Recently, we report the synthesis of novel small molecule NC4 as the high ranked compound that found to exert the anti-cancer effect on AKT mediated BAD phosphorylation in MC mouse model.

PO 39: Combinatorial treatment with Anacardic acid followed by TRAIL augments induction of apoptosis in TRAIL resistant cancer cells by the regulation of p53, MAPK and NFκβ pathways

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Introduction: The selective tumoricidal activity of TNF-related apoptosis-inducing ligand (TRAIL) is modulated by agonistic Death receptors DR4 and DR5. Substantial numbers of tumor cells, specifically highly metastatic tumors, are resistant to TRAIL induced apoptosis. Thus identifying compounds that sensitize resistant tumor cells is imperative in anticancer therapy. The resistance of human cancers to TRAIL in vivo has spurred the exploration of newer combinatorial therapies. **Objectives:** We investigated the ability of subtoxic dose of anacardic acid (A1) to sensitize TRAIL resistant human tumor cells in vitro and Ehrlich ascites tumor cells in vivo to TRAIL-mediated apoptosis. **Material and Methods:** Cytotoxicity of A1 and resistance to TRAIL was assessed in MCF-7, MDA- MB231, MDA-MB-435, A549, HT-29, HeLa, SK-N-AS and Kelly cells by trypan blue dye exclusion and MTT assays. Effect of A1-TRAIL combinatorial treatment was evaluated by 3[H] thymidine incorporation assay, caspase3 activation, and flowcytometry, DR up-regulation by immunoflourescence, immunoblotting and qPCR analysis. EAT mouse model was used for the in vivo studies. Signal transduction cascade for DR up-regulation was ascertained by immunoblotting. **Results:** A549 and HT-29 cells were found to be highly resistant to TRAIL. Subtoxic concentration of A1 treatment showed upregulation of DR4 and DR5. A1 treatment for 16 hours followed by TRAIL treatment effectively induced apoptosis in the resistant cells. A1 treatment induced DR4, DR5, p53, Bax, caspase 3 and CAD up-regulation through p53 via JNK and p38 MAPKs while ERK and NFκβ were down-regulated. **Conclusions:** Combinatorial treatment of A1 followed by TRAIL may be responsible for synergizing apoptosis by upregulating death receptors.

PO 40: FUNCTIONAL INTERACTION OF FAT1 & COX2 IN GLIOMA CELL LINES

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Introduction: Astrocytic tumors are most frequent human gliomas affecting an individual at any stage. FAT1 gene in human is found to have a dual role; both as a tumor suppressor and as an oncogene. FAT1 is known to affect the expression of COX2 (Dikshit et al, 2013). Here, we have analyzed the effect of FAT1 knockdown under different serum concentration (10%, 6%, and 2%) on cell survival as well as expression of FAT1 and COX2 in glioma cell lines (A172, U87MG and GOS3). We have also studied the effect of FAT1 over-expression by transfecting FAT1_trunc constructs in GOS3 cell line which has low endogenous FAT1 expression. **Material and methods:** Glioma cell lines (GOS3/U87MG/A172) were maintained under different serum concentration (2%, 6%, and 10%). FAT1 gene was knocked-down using siRNA system and RNA isolated 72hrs post transfection for expression analysis of FAT1, COX2, IL-1β & IL6 by real time PCR. Cell survival under different experimental conditions was analysed by MTT assay at 24hrs, 48hrs& 72hrs. For FAT1_trunc overexpression, FAT1_trunc (wild type and mutated) constructs were transfected in GOS3 cell lines, which has low FAT1 expression. Cell survival by MTT assay and expression of target genes were analyzed. **Result:** We observed maximum number of viable cells in 10% serum and least number of viable cells in 2% which was significant at 48 & 72 hrs [GOS3 (p= 0.041), A172 (p= 0.0121) & U87MG (p= 0.014)] analyzed. In GOS3 cell line, we observed significant reduction in the expression of FAT1 (p= 0.0377), COX2, IL6 (p=0.0395) and IL1β (p=0.0104) in cells maintained in 2% serum concentrations as compared tocells maintained in 10% serum. We observed significant decrease in the viability of cells in siFAT1 transfected cells maintained in 2% serum at 72hrs (p=0.0173) as compared to siControl cells, whereas no significant difference in the viability in 10% and 6% serum cells, in both cell lines. Significant decrease in the expression of COX2, IL6 and IL1β was observed after FAT1 knockdown in all serum concentration. No significant difference in the expression of target genes was observed among cells in 6% and 2% serum treatment. No significant difference in the viability of cells after FAT1_trunc over expression at all time points post transfection. As compared to control plasmid transfected cells the expression of endogenous

FAT1 was observed to be increased significantly ($p \leq 0.05$) in cells transfected with both FAT1_trunc (wild type) construct and FAT1_truncmutated (pro4309Ala) construct. There was also significant increase ($p \leq 0.05$) in the expression of total (endogenous + transfected FAT_trunc) FAT1 in the FAT1_trunc transfected cells as compared to control plasmid transfected cells. Similarly, COX2 and IL6 expression was found to be significantly increased in FAT1_trunc (wild type and mutated) transfected cells as compared to control cells with no difference in the expression of IL1β. **Conclusion:** Our findings reflected the additive effect of FAT1 knockdown and low serum concentration in Decreasing the viability of A172 and U87MG cell lines and decreasing the expression of COX2, IL6 & IL1β in GOS3 and U87MG cell lines. Overexpression of FAT1_trunc in GOS3 cell line increases the COX2 expression,confirming the positive effect of FAT1 on COX2 expression.

PO 41: Effect of turmeric (Curcuma longa L.) essential oil on hepatocarcinogenesis and possible mechanisms of action

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Introduction: Turmeric (Curcuma longa L) is a well-known spice cultivated in most of the Asian countries. Essential oil isolated from turmeric rhizome also possesses many pharmacological properties. Ar-turmerone is the major constituent of turmeric essential oil (TEO). **Objectives:** Presently, we have evaluated the TEO induced apoptosis in human liver cancer cell line (HepG2), antimutagenicity and anticarcinogenecity of TEO in rats as well as their mechanism of action. **Material and Methods:** TEO was screened for antimutagenicity in the bacterial reverse mutation (Ames) test, using Salmonella typhimurium strain. Cell proliferation was tested by MTT assay and the apoptosis of the HepG2 cells was detected by flow cytometry. The anticarcinogenic potential of TEO was studied using hepatocellular carcinoma model induced by N-nitrosodiethylamine (NDEA) in rats. Effect of TEO on phase I (Cytochrome P450) and phase II enzymes were also evaluated. **Results:** TEO was found to have significant antimutagenic effect (>90%) against mutagen needing metabolic activation such as 2-acetamidoflourene. TEO exerts its anticancer effects by inhibiting cell proliferation and inducing apoptosis in HepG2 cell line. TEO was found to significantly reduce the tumour nodule incidence induced by NDEA. TEO also decreased the level of hepatic parameters and γ-GT in serum and liver which were elevated by NDEA. TEO inhibited various isoforms of cytochrome P450 enzymes and induced phase-II enzymes such as UDP-glucuronyl-transferase and Glutathione-S-transferase. **Conclusions:** TEO exhibited significant apoptotic, antimutagenic and protection against NDEA induced hepatocellular carcinogenesis, which might be related with the enhancement of antioxidant enzymes and inhibition of various isoforms of cytochrome P450 enzymes.

Key words: Turmeric essential oil; HepG2; hepatocellular carcinoma.

PO 42: Analysis of variations in TNF and HSP genes in nasopharyngeal carcinoma in high prevalence region of North East India

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Introduction: Nasopharyngeal carcinoma is an epithelial tumour with a distinctive racial and geographical distribution. High incidence of NPC has been reported from China, Southeast Asia, and northeast region of India. The immune mechanism plays incredible role in pathogenesis of NPC. **Objectives:** The HLA-linked TNF and heat shock protein 70 genes are of particular interest because of their involvement in tumour immunity and cancer biology. Polymorphisms in these genes leads to change in expression, which may have significant consequences for the tumour development were studied. **Material and Methods:** Multi-analytical approaches including logistic regression, classification and regression tree and multifactor dimensionality reduction were applied in 120 NPC cases and 100 controls to explore high order interactions at TNF-α (−308 G>A), TNF β (+252 A>G), HSP 70 (+190G>C) and HSP 70 (+2437 T>C) by allelic discrimination experiments. **Results:** TNF β was identified as the primary etiological factor by all three analytical approaches. Individual analysis of results showed protective effect of TNF β GG genotype (OR =0.27, P=0.001), HSP 70 (+2437) CC genotype (OR =0.17, P=0.013), while AG genotype of TNF β was found significantly associated with risk of NPC (OR =1.97, P=0.04). Analysis of environmental factors demonstrated association of alcohol consumption, living in mud houses and use of firewood for cooking as major risk factors for NPC. Individual haplotype association analysis showed significant risk associated with GTGA haplotype (P=0.013) while a protective effect with CCAA and GCGA haplotypes (P= 0.019; P=0.007). **Conclusions:** The multianalytical approaches helped in identification of distinct gene-gene and geneenvironment interactions significant in risk assessment of NPC.

PO 43: Study of Quality of life in Multiple Myeloma patients with Autologous Stem Cell Transplantation

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Introduction: Multiple myeloma (MM) has a significant impact on a patient's quality of life (QoL) because the patient becomes dependent on others, even for routine activity execution and personal care.The aim of MM treatment is to control the disease, particularly its bone destruction. **Objectives:** To characterize the impact of multiple myeloma on the quality of life of patients treated in a tertiary care centre using a questionnaire specific for oncologic patients (QLQ-C30) upon diagnosis, after the clinical treatment, and at day +100 after autologous stem cell transplantation. To evaluate whether autologous stem cell transplantation can improve the quality of patients aside from providing a clinical benefit and disease control. **Material and Methods:** We evaluated 40 patients with multiple myeloma using the QLQ-C30 questionnaire. The scores upon diagnosis,post-treatment/pre-autologous stem cell transplantation, and at D+100 were compared using ANOVA (acomparison of the three groups), post hoc tests (two-by-two comparisons of the three groups), and paired t-tests (the same case at two different times). **Results:** The QLQ-C30 questionnaire demonstrated that physical function, role-physical, social functionand bodily pain were statistically different across all three groups and favored the D+100 ASCT group (ANOVA).The QLQ-C30 questionnaire **Results:** favored the D+100 ASCT with respect to fatigue, the lack of appetite, insomniaand constipation. The post hoc tests and paired t-tests confirmed a better outcome after autologous stem cell transplantation. **Conclusions:** Autologous stem cell transplantation improves the quality of patients aside from providing a clinical benefit and disease control in Multiple myeloma patients.

PO 44: Tumor suppressor role of miR-107 in esophageal squamous cell carcinoma

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Introduction: MicroRNAs have been demonstrated to be associated with the tumorigenesis and tumor progression of various cancers. Previously, in our study the expression of miR-107 was found to be significantly downregulated in esophageal squamous cell carcinoma (ESCC) patients

as compared to the non malignant tissues. However, the exact role of miR-107 in the regulation of the esophageal cancer and the underlying mechanisms remain unclear. **Objectives:** The aim of the present study was to analyze the role of miR-107 in esophageal squamous cell carcinoma. **Material and Methods:** miR-107 mimic was transfected in ESCC cell line followed by MTT assay, cell cycle analysis by flowcytometry and scratch assay. miR-107 targets were predicted by in-silico approach followed by in-vitro validation by qRT-PCR, western blot and luciferase reporter assay. **Results:** Over-expression of miR-107 significantly suppressed the proliferation of ESCC cells at 72 h post transfection. Moreover, miR-107 treatment significantly inhibited ESCC cell migration in a time dependent manner and increased the number of ESCC cells in the G1 phase of the cell cycle, as compared to the negative control (NC). qRT-PCR analysis showed a significant decrease in expression of one of the potential targets of miR-107 at mRNA level. Further validation by western blot and luciferase reporter assay confirmed a significant reduction of the identified target at protein level in miR-107 treated cells as compared to the NC, indicating it to be a direct target of miR-107. **Conclusions:** miR-107 inhibited proliferation and migration and resulted in cell cycle arrest of ESCC cells. Moreover, the decreased expression of the novel miR-107 target observed herein for the first time shows that miR-107 may regulate its expression at mRNA level as well as protein level.

PO 45: Targeting of nanoparticles to CCR5 expressing cells which are overexpressed in cancer cells like basal breast cancer cells

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Background: The currently used forms of cancer therapy are associated with drug resistance and toxicity to healthy tissues. Therefore developing new therapeutic methods of cancer targeted drug delivery using specific ligands targeting specific receptors that are over expressed on the diseasedcells are necessary to the side effects. Many cancer cells are known to express CCR5. The purpose of this study is to develop a method for ligand/peptide mediated targeting of nanoparticles to CCR5 receptors that are also expressed in treat such diseases. Such active targeting systems enhance the internalization of the particles into the tumor cellsandmay result in higher bioavailability of the therapeutic agent at the tumor site and simultaneously reduce cancer cells e.g. U87MG. **Material & Methods:** TZM-bl cells & control cells U87 cells were maintained in Dulbecco"s modified Eagle"s medium (DMEM). Poly (d, l-lactic co-glycolic acid) & polyethyleneimine nanoparticles (PLGAPEI-NPs) were prepared with FITC tagged bovine serum albumin and visualized under transmission electron microscopy. Formulated PLGA-PEI-NPs were tagged with peptide ligand (dimerized RANTES) after pegylation with hetero-bifunctional group (NHS-PEG-Mal). Furtherpeptide conjugated NPs (PEGpeptide-NPs) & pegylated NPs (PEG-NPs) were targeted to the cells expressing CCR5 (TZM-bl cells) & control cells (U87 cells) and viewed under fluorescent microscope. MTT assay were also done to show the cytotoxic effect of PLGA-PEI-NPs in TZM-bl cells. **Results:** The size of formulated PLGA-PEI-NPs were approximately in the range of 50-300 nm. The study showed significantly (<0.05) increased specific targeting of PEG-peptide-NPs in TZM-bl cells as compared to U87 cells. There was also significant ($p<0.05$) efficiency in targeting of PEG-peptide-NPs than PEGNPs in TZM-bl cells. It showed no significant difference in targeting of PEG-NPs in both TZM-bl & U87 cells and between PEG-NPs & PEG-peptide-NPs in U87 cells. MTT assays showed no significant change in cell viability with PLGA-PEI-NPs exposure in TZM-bl cells for 72 hours. **Conclusions:** There was significant increased specific and efficient targeting of NPs to cells expressing CCR5. This study may also be helpful in developing new therapeutic methods for drug delivery where CCR5 are expressed in diseases like HIV, multiple sclerosis, rheumatoid arthritis, GVHD etc.

PO 46: CYTOTOXIC AND ANTIOXIDANT ACTIVITIES OF METHANOLIC AND HOT WATER EXTRACTS OF SIMAROUBA GLAUCA DC

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Introduction: Several incidents on the cure of various types of cancer by the consumption of decoction of Simarouba glauca leaves have gained wide publicity in Kerala over media recently but, no scientific evidence is available on the anticancer, antitumour and chemoprotective properties of S. glauca. **Objectives:** The present study is focused on methanolic (MESG) and hot water (HESG) extracts of leaves of S. glauca in terms of its cytotoxic and antioxidant properties. **Material and Methods:** MESG and HESG extracts of leaves of S. glauca were prepared and their phytochemical, cytotoxic and antioxidant activities were analysed by using standard procedures. **Results:** Phytochemical analysis of MESG and HESG unveiled the presence of tannins, saponins, coumarins, terpenoids, phenols, alkaloids, flavonoids, resins and carbohydrates. The estimation of total phenolic and flavonoids were high in HESG. Compare with MESG, HESG exhibited low levels of cytotoxicity when treated with malignant and normal cells in short term assay. In MTT assay, cell viability was found to be less for HESG in contrast with MESG on the cell lines tested. Both the extracts were effective in a dose depend manner in different in vitro antioxidant assays. HESG was the most active in inhibiting superoxide radical generation however in all other assays MESG gave better efficacy. In vitro lipoxygenase inhibition assay revealed the antioxidant and anti-inflammatory action of both extracts. **Conclusions:** The HESG shows more promising cytotoxicity and antioxidant efficacy.

PO 47: Mapping of HPV infection in cancers of different organ sites

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Introduction: Accumulating evidences indicate a strong association of HPV in the causation of cervical as well as in some proportion of head & neck and other cancers with varied prevalence. Due to lack of organized screening programs, currently there is no comprehensive data is available on HPV prevalence & genotypes in different cancers. Recently, **Introduction:** of HPV vaccines, it is important to know HPV prevalence and type distribution not only in cervical but also in other cancers in order to better management of HPV vaccination program. **Material and Methods:** Present study included a total of 509 histopathologically confirmed cancer biopsies of cervical (n=30), endometrial (n=31), ovarian (n=30), breast (n=40), oral (85), esophageal (75), gastric (n=50), lung (n=28) and 140 controls for all cancer sites except lung. These samples were employed for analysis of HPV infection, genotypes and physical states using PCR, RLB assay & sequencing. Statistical analysis was performed to estimate HPV prevalence, genotypes & its association with various risk-factors. **Results:** The overall HPV prevalence was 80%, 19.7%, 17.65% and 3.2% in cervical, esophageal, oral and endometrial carcinomas respectively whereas no HPV DNA was detected in breast, ovary, stomach and lung carcinomas. Exclusively HPV type 16 was found in 100% of almost all HPV+ve cancers except cervical cancer in which other HPV genotypes such as HPV, HPV52 and HPV11

were also recorded. Interestingly, in oral carcinomas, HPV16 infection was found significantly higher in well differentiated tumors in female patients whereas in cervical and esophageal carcinomas, infection rate was significantly higher in poorly differentiated tumors. HPV16+ve cases showed integration of virus is more common in cervical than esophageal or oral cancer. **Conclusions:** On mapping of HPV in different cancers, HPV16 was found to be most prevalent type mainly in an integrated form in cervical, oral & esophageal cancer suggesting a critical role of viral integration in tumor progression. Interestingly, in cervical and esophageal cancer, HPV infection was seen mainly in poorly differentiated tumors with worst prognosis whereas in oral cancer, it leads to well differentiation with better prognosis preferably in nonsmokers.

PO 48: PHLPP1 is frequently downregulated and AKT1 is frequently upregulated in Gastric Carcinoma

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Introduction: PHLPP1 is known to negatively regulate AKT by direct dephosphorylation and play an important role in cell survival, proliferation, migration, and cell death. The loss of expression of PHLPP can be caused by alterations at the gene level such as loss of heterozygosity or promoter hypermethylation. Dysregulation of signaling pathways that leads to the development of cancer. **Objectives:** To investigate the clinical correlation of the expression profiles of PHLPP1 and AKT1 in Gastric Carcinoma. **Material and Methods:** RNA extraction: Total RNA was isolated from tissue samples using TRI reagent according to the manufacturer"s protocol. RT-PCR: Good quality RNA was reverse transcribed by standard protocol which was further used as template in RT-PCR to profile the expression level of the gene using gene specific primers. The gene specific expression levels were normalized against the expression levels of β-actin for each sample. Differential expression was calculated as Mean of Normal ±2XSD. **Results:** Our semi-quantitative RT-PCR data showed frequent frequent downregulation of PHLPP1 (27%; p=<0.0001) and upregulation of AKT1 (30%; p= 0.0013) in gastric carcinoma as compared to normal gastric mucosa samples. AKT1 expression was higher in diffuse type than intestinal type (p=0.352) of histology; in stage III+IV than I+II tumor stage (p=0.033); in patients with lymph node metastasis than without lymph node metastasis (p=0.007). In tumor differentiation the expression of AKT1 was significantly higher in undifferentiated than differentiated type of tumors (p=0.056). PHLPP1 expression was significantly lower in diffuse type than intestinal type (p=0.006) of histology; in stage III+IV than I+II tumor stage (p=0.008); in patients with lymph node metastasis than without lymph node metastasis (p=0.0006). In tumor differentiation the expression of PHLPP1 was significantly higher in undifferentiated than differentiated type of tumors (p=0.0006). **Conclusions:** Expression profiles of AKT1 and PHLPP1 have significant clinical correlation gastric carcinoma.

PO 49: Barriers in enrolment in lung cancer study

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Introduction: The success of a clinical trial is the recruitment and retention of a study population of an adequate sample size. In all clinical trials, the process starts with a screening period. The screening period starts with the signing of the informed consent. During the screening period, inclusion/exclusion criteria for the study participation is checked. Subjects who meet all inclusion criteria and exclusion criterion are eligible to be randomized . Significant proportion of patient do not participate in clinical trial in spite of meeting exclusion and inclusion criteria. It is important to find out the reasons for not participating in clinical trials. This will help in developing strategies to overcome it **Objectives:** To find out the barriers in enrolment for clinical trial. **Material and Methods:** We retrospectively analyzed a prospectively maintained database during 2015. We have entered the reason for not participating for a specific study of targeted therapy in lung cancer. We have done descriptive analysis of data. **Results:** Information concerning 92 patients with EGFR mutation positive in non small cell lung cancer who were treatment naive and ECOG 0-2 were included in this analysis. In the year 2015 out of 92 patients, 61 patient were randomized (66%) with met protocol eligibility criteria for a particular study and agreed to participate in clinical trial .So, 31 (33%) patient were screen failure. The reason for screen failure were16 of 31 patients were ECOG 3 (17%); 9 of 31patient were already started treatment (9%) in the OPD because they did not want to wait for the report; 5 of 31patient did not want to participate as they preferred oral targeted therapy(5%).1 of 31 had financially constraint(1%) **Conclusions:** Barriers to cancer clinical trial accrual can be prospectively identified. This will help us in addressing these barriers for futures studies.

PO50: Vanadium in Cancer Management: Use of an organovanadium complex as a promising adjuvant chemotherapy together with cyclophosphamide

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Introduction: Various preclinical, clinical and epidemiological studies have already established the cancer chemopreventive and chemoprotective potential of vanadium compounds. In addition to its preventive efficacy, recent studies have also proved the abilities of vanadium compounds to induce cell death specifically in malignant cells. **Objectives**: The aim of the present investigation is to improve the therapeutic efficacy of an alkylating agent, cyclophosphamide, by the adjuvant use of an organovanadium compound, Vanadium(III)-L-cysteine (VC-III). **Material and Methods**: Cyclophosphamide (25 mg/kg b.w) was administered intraperitoneally and VC-III (1 mg/kg b.w.) was given by oral gavage in concomitant and pretreatment schedule in mice bearing Ehrlich ascites carcinoma cell. **Results**: The Resultsshowed that the combination treatment decreased the tumor burden significantly through reactive oxygen species generation in tumor cells, which ultimately led to significant DNA damage, cell cycle arrest, mitochondrial membrane depolarization and apoptosis in tumor cells. Study of the molecular pathway disclosed that the adjuvant treatment caused induction of p53, Bax and suppressed Bcl-2 followed by the activation of caspase cascade. Administration of VC-III also resulted in significant improvement of tumor vasculature and sprouting of the peritoneal cavity along with the normalization of levels of MMP-9 and VEGF in ascites fluid of tumor bearing mice. Furthermore, VC-III significantly suppressed cyclophosphamide-induced liver, hematopoietic and genetic damages. **Conclusions**: The present study suggested that the combination treatment with VC-III and cyclophosphamide may offer potential therapeutic benefit, and utilization of cyclophosphamide in cancer exempt of its limitations.

PO51: A-Kinase Anchor Protein 4 (AKAP4): A potential immunotherapeutic target in management of cervical cancer.

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Introduction: A-kinase anchor protein 4 (AKAP4) is a cancer testis antigen and we have earlier shown an association of AKAP4 expression in cervical cancer patient specimens, indicating its implications as an immunotherapeutic target. **Objectives**: In present study, we have investigated the role of AKAP4 in cervical carcinogenesis in cervical cancer cell lines. **Material and Methods**: AKAP4 mRNA and protein expression was investigated in cervical cancer cell line models; C-33A, CaSki, HeLa and SiHa. Gene silencing approach was employed to evaluate the potential role of AKAP4 in cellular growth, proliferation, colony-forming ability, migration and invasion in aggressive squamous cell carcinoma cells (SiHa). The effect of knockdown of AKAP4 on tumor growth was studied in the cervical cancer xenograft model in nude mice. **Results**: Our Results clearly indicated that AKAP4 was expressed in all cervical cancer. We also found cytoplasmic and surface localization of AKAP4 protein by indirect immunofluorescence and flow cytometry respectively. Ablation of AKAP4 protein significantly inhibited cellular proliferation, colonyforming ability and migration and invasion ability of SiHa cells. Further, gene silencing of AKAP4 also resulted in reduced tumor growth in nude mice in vivo. Collectively, our data have shown surface localization of AKAP4 and its significant association with tumorogenic properties of cervical cancer cells. **Conclusions**: The Results imply its clinical utility as a potential immunotherapeutic target for cervical cancer management and prognosis of disease.

PO52:Adamantyl-tethered-biphenylic compounds induce apoptosis in cancer cells by targeting Bcl homologs

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Development of new anti-cancer drugs is an important area for control of rapidly rising human malignancies.A lot of research has been focused towards finding a potent inhibitors for various cellular proteins. BCL2 has emerged as a promising drug target for cancer therapy. We recently synthesizedbiphenyl-adamantane derivatives by a ligand free palladium on carbon based Suzuki reaction using diisopropylamine as a base for the coupling of adamantane based aryl chloride with a variety of aryl boronic acids. Among the biphenyl derivatives synthesized, compound 30-(adamantan-1-yl)-40-methoxy[1,10-biphenyl]-3-ol (AMB) displayed cytotoxic activity against hepatocellular carcinoma cell lines without significantly affecting the normal cell lines. Further, AMB caused increased accumulation of the HCC cells in SubG1 phase, decreased the expression of Bcl-2, Bcl-xL, cyclin D1, caspase-3, survivin and increased the cleavage of PARP in a time-dependent manner. In silico molecular interaction studies between Bcl homologs and AMB showed that the biphenyl scaffold is predicted to form p–p interactions with Phe-101 and Tyr-105 and the adamantly fragment is predicted to occupy another hydrophobic region in the kink region of the binding groove.

PO53: Thermally oxidized edible oils rich in polyunsaturated fats disturbs hepatic redox equilibrium and heightens hepatic steatosis in rats

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Background: Non-alcoholic fatty-liver is the hepatic expression of metabolic syndrome which ranges from simple fatty-liver to hepatosteatosis, characterized by insulin resistance, dyslipidemia and inflammation. This may later progress to cirrhosis and hepatocellular carcinoma. Diet rich in fats and sugar is reported to be the important risk factor. Sunflower oil (SO) and lard (LD) are the two edible oils rich in polyunsaturated fats (65 and 41%). **Objectives**: Present study was aimed to analyze the effect of prolonged consumption of the fresh and fried SO and LD on the development of hepatosteatosis. **Material and Methods**: Male Wistar rats fed with a diet containing 60% fructose and 10% of either fresh or thermally oxidized SO or LD for 30 weeks. Analysis of serum and liver tissue biochemical parameters and hepatic histology was done as per standard protocols. **Results**: Physico-chemical analysis revealed enhanced lipid peroxidation in both fried oils ($P<0.01$).Compared to SO and LD, TSO and TLD fed animals had high blood glucose levels and reduced glucose tolerance at the end of 30 week. Dyslipidemia status, as observed by increased triglycerides and LDL was seen in TLD group than TSO ($P<0.05$), whereas hepatic GSH level and SOD activity had diminished in TSO than TLD group ($P<0.05$). Consequent elevation in the hepatic oxidative stress status was observed with TSO group ($P<0.05$). Substantiating these **Results**, liver function markers and polyol pathway activation was evident in TSO ($P<0.05$). **Conclusions**: The study thus concludes that prolonged consumption of fried polyunsaturated fats may increase the hepatosteatosis condition by altering glucose metabolism and redox balance of hepatic tissue.

PO 54: Targeting GSK3β in cervical carcinogenesis

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Introduction: GSK3β is a multifunctional serine/threonine kinase which has been implicated in multiple biological processes including embryonic development, neuronal development, cell differentiation, apoptosis and insulin response. Its chromosomal location is 3q13.33. This molecule has perplexing capacity to either increase or decrease the apoptotic threshold. The involvement of GSK3β to act as tumor promoter or tumor suppressor depends on cell type and signaling environment. The mechanism of GSK3βmediated regulation of cell cycle in cervical cancer is poorly understood. **Objectives**: To understand the functional role of GSK3β in cell cycle regulation in cervical cancer cell lines and a primary tumor. **Material and Methods**: Cervical cancer cell lines – SiHa, ME-180, CaSki, & C-33A and a primary tumor culture were maintained at standard culture conditions. Lithium was used as specific and non competitive inhibitor of GSK3β in vitro and in vivo. Expression profiling of GSK3β was done by western blot analysis. Cell viability was checked by MTT assay. Cell morphology was observed and photographed. Cell Cycle Analysis was performed by using flow cytometric technique. Apoptosis Assay was done using Annexin V PI kit. **Results**: Flow cytometric analysis show arrests of cell cycle after treatment of LiCl to cervical cancer cell lines and primary tumor cells at different cell cycle phases. **Conclusions**: GSK3β may be a potential molecular therapeutic target in cervical cancer.

PO 55: Angio suppressive effect of Clitoria ternatea flower extract is mediated by HIF-1α and down regulation of VEGF in murine carcinoma model.

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Introduction: Vascular Endothelial growth factor (VEGF) plays important role in angiogenesis. Tumour growth and progression cannot occur without angiogenesis, which facilitates cancer cell proliferation, survival, and dissemination. Clitoria ternatea is herbaceousperenniallegume, various parts of the plant were used and various phytochemicals were detected are kaempferol, quercetin, flavonoid glucosides and they used in snake bite, scorpion sting, lung cancer, antioxidant and as anti-inflammatory agent. **Objectives**: Elucidation of Anti-angiogenic activity of Clitoria ternatea plant extract. **Material and Methods**: The cytotoxic effect of C. ternatea extract was determined using MTT cell proliferation assay. Anti-angiogenic assay was done by in- vivo mice peritoneal assay and chick chorioallantoic membrane (CAM) assay. Quantification of VEGF was

done by ELISA and nuclear translocation of HIF-1α by western blotting. **Results**: C. ternatea was able to inhibit cell proliferation and decreased ascites volume in murine mouse model. Decreased in micro vessel density is clear evident for anti-angiogenic effect in treated group when compared to control. In the test group apoptotic cell morphology and DNA damage is a proof that EAC cells undergoing apoptosis. The plant extract inhibited the levels of VEGF in ascetic fluid and indicated that, HIF-1α nuclear sequestration is repressed by C. ternatea through inhibition of nuclear translocation, which is key transcription factor for VEGF gene expression. **Conclusions**: We hypothesize decreased levels HIF-1α translocation from cytosol to nucleus by C. ternatea treated EAC cells could be responsible for decreased VEGF expression and angio suppressive effects and may be a potential anti-angiogenic agent which may exploit to treat cancer disease.

PO 56:VEGF A/VEGFR2 axis regulates cell migration & adhesion and protect cervical cancer cells from anoikis.

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Introduction:Vascular endothelial growth factor A (VEGF A) and its receptor (VEGFR2) have been identified as a key molecule for angiogenesis and migration of endothelial cells. Several reports identified the presence of VEGFR2 on tumor cells of non-endothelial origin, mainly tumor cells of epithelium origin, such as ovarian cancer, lung cancer as well as myelomas and haematological malignancies. We demonstrate that VEGFR2 co-express with its ligand VEGF A in cervical cancer cell lines and primary tumor. VEGF A/VEGFR2 axis regulates the cellular migration and proliferation of cervical cancer cell lines. Inhibition of VEGF A/VEGFR2 axis inhibits the proliferation and migration of cells and induces cellular adhesion to fibronectin matrix. This axis also regulates the tumor microenvironment in both auto- and paracrine manner and induces migration of cervical cancer cells via MMP activation. Inhibition of VEGF A/VEGFR2 axis also inhibits the formation of migration associated cellular changes in F-actin molecule such as lamellipodia and filopodia. Inhibition of VEGF A/VEGFR2 axis induces significant apoptosis in suspension cells compared to adherent cells. **Objectives**:Identification of functional role of VEGF A/VEGFR2 axis in cervical cancer. **Material and Methods**:Cervical cancer cell lines and primary tumor tissue. FACS, immunofluorescence, western blotting, migration assay and adhesion assay. **Results**:We have found the co-expression of VEGFR2 with VEGF A in cervical cancer cell lines & primary tumor. VEGF A induced autocrine VEGFR2 activation which regulates AKT/GSK3β axis and was inhibited by VEGFR inhibitor Pazopanib in dose dependent manner. Pazopanib inhibits cell migration & induces cell adhesion in cancer cells in dose dependent manner. Pazopanib also inhibits the cell migration induced by microenvironment in cervical cancer cells. It induces significant apoptosis in suspension cells than adherent cells indicating the role of VEGF A/VEGFR2 in anoikis resistance. **Conclusions**:Our data suggests that VEGF A/VEGFR2 axis regulates the metastatic events in cervical cancer.

PO 57: Role of Notch Signaling Pathway in OSCC in Eastern Indian Population.

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Introduction: Notch signalling pathway (NSP) has been associated with several types of malignancies including T-ALL, breast, lung, stomach cancer etc. However, it remains unclear how the Notch pathway is involved in pathogenesis of Oral squamous cell carcinoma (OSCC). The etiology of oral cancer in Eastern India is different from other regions. It has been reported that NSP can have dual role of both tumor suppression and progression in different solid tumours. According to the Global Adults Tobacco survey India report of 2010, 46.2% men and 27.9% female in Odisha used many different forms of tobacco which is the main reason for the high number of OSCC cases. **Objectives**: To check the expression pattern of Notch signalling pathway in OSCC in eastern Indian population. **Material and Methods**: Sample was collected from different hospitals, with the histological and clinical data. Expressions of the Notch pathway molecule were checked in these samples through Immunohistochemistry and Western blotting analysis.**Results**: Immunohistochemical Results showed elevated expression level of Notch1 and its ligand Jagged1. Strong membranous expression of Notch1 was observed in well differentiated OSCC. However few cytoplasmic and nuclear expressions were also seen. The expression pattern of Jagged1 was both membranous and cytoplasmic. Upregulation of Notch1 and Jagged1 in OSCC were confirmed through western blot analysis. **Conclusions**: These results indicate that altered expression of Notch 1 and its ligand Jagged 1 are associated with increased cancer progression in OSCC and blocking this pathway might be an useful approach for the treatment of patients with OSCC.

PO 58: Drug repositioning on the basis of molecular docking and interactome analysis in Chronic Myeloid Leukemia

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Introduction: Chronic myelogenous leukemia (CML) is a clonal disorder arising in a pluripotent hematopoetic progenitor stem cell having Philadelphia (Ph) chromosome characterized by (9:22) translocation. ABL gene fuses with BCR gene, producing a BCR-ABL fusion gene having constitutively active kinase activity. Imatinib mesylate (Glivec), a small-molecule drug is a potent specific inhibitor of BCR-ABL tyrosine kinase and inhibits by competitively binding at the ATP-binding site. Treatment with Imatinib has been found to be successful in treating patients with chronic-phase CML; however progenitor CML cells show a refractory behavior to it causing disease persistence. Thereby developing Imatinib resistance necessitates designing and development of alternative treatment strategies. Repositioning of other protein kinase inhibitors in place of imatinib may be useful in patients who are either not able to tolerate imatinib or fail to respond to it. **Objectives**: To investigate seventeen chemotherapeutic drugs for their potential to target ABL2 kinase for Chronic Myeloid Leukemia treatment on the basis of molecular docking and Interactome analysis. **Material and Methods**: Seventeen drugs selected by public database mining were used for molecular docking followed by interaction analysis. Interactome map was built on the basis of various drug-disease association parameters. **Results**: All seventeen chemotherapeutic drugs have similar active binding site residues and docked effectively with ABL2, the target protein. It was found that six drugs had more atomic contact energy than Imatinib. Dasatinib has maximum atomic contact energy (ACE), -414.92 kcal/mol, followed by others in a decreasing order. Majority of active site binding residues involved in interaction were found to be similar for all drugs. **Conclusions**: Our study demonstrates that systematically comparing different chemotherapeutic drugs available for targeting tyrosine kinases in various cancers can be used effectively for CML treatment by the phenomena of repositioning. This approach can be highly useful for patients showing resistance to imatinib. This study highlights the importance of drug repositioning, which can be used for the treatment of other malignancies.

PO 59: Quest for novelmolecular targets for the heterogeneous microenvironment

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Background: The hypoxic solid tumor microenvironmentrenderscells to be irresponsive to drugs and radiotherapy. Understanding the process of adaptation in metabolic and cellular signaling in hypoxic cells is extremely relevant to improved and successful cancer therapies. **Materials and Methods**: In order to understand the process of re-adaptation under hypoxia, we performed comparative proteome and phospho-proteome profiling. Cells were exposed to different hypoxic conditions and their proteome profiling was performed to compare it to the proteome of cells grown under normoxia, and versus each other. For the phosphoproteome study, cells were serum starved for 14 hours before hypoxia exposure to synchronize the cell cycle. We have used method of SILAC and analyzed the labeled samples by online coupled liquid chromatography-mass spectrometry. **Results**:Initial analysis of the results reveals, hitherto unappreciatedroles, of many enzymes transporters and proteins. We are in the process of analyzing the proteins for pathways and processes enrichment using GO analysis and DAVID, and for their functional clusters. A few of the molecules and plausible hypothesis associated with their relevance is represented. **Conclusions**:The low rate of conversion of identified molecular targets to those of therapeutic use, demands new approaches for identifying molecules that have relevance among the changing tumor microenvironment. We believe that targeting these molecules while studying their biological relevance will be a more effective strategy.

Key words: Hypoxia, Qunatitative Proteomics, Phosphoproteomics

PO 60: Inhibition of TGFβ signaling by lipoic acid in breast cancer cells

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Introduction: TGF-β signaling pathway plays a major role in the invasion, migration and metastasis of breast cancer cells. TGF-β can induce pro-angiogenic environment and stimulate angiogenesis. Blocking the activity of TGF-β signaling pathway might play a promising role in reducing the metastatic potential of breast cancer cells. **Objectives**: The objective is to study the role of lipoic acid in the regulation of TGF-β signalling as well as the migration and invasion of breast cancer cells. **Material and Methods**: To study the regulation of TGF-β signaling, MDA-MB-231 breast cancer cells were treated with lipoic acid and/or TGF-β1, and the expression of TGF-β downstream signalling molecules were analyzed. Effect of lipoic acid on TGF-β-induced migration and colony formation ability of breast cancer cells were also analyzed. **Results**: Our Results showed that lipoic acid inhibits the proliferation of breast cancer cells in a dose dependent manner. TGF-β induces the expression of ANGPTL4 and MMP-9 which was effectively blocked by lipoic acid pre-treatment. Lipoic acid treatment also reduces the expression of downstream TGF-β signalling genes and inhibits the TGF-β-induced nuclear translocation of β-catenin in breast cancer cells. Lipoic acid significantly inhibits the TGF-β-induced migration and colony formation ability of MDA-MB-231 cells. **Conclusions**: The Results showed that lipoic acid might help in preventing metastasis and angiogenesis in highly aggressive breast cancer and thus can be exploited as a potent therapeutic candidate.

PO 61: Role of c-MYC Expression in Disease Progression of Chronic Myelogenous Leukemia (CML) Patients.

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Introduction: Chronic myeloid leukemia (CML) is characterized by the clonal expansion of hematopoietic stem cells. Without effective treatment, individuals in the indolent, chronic phase (CP) of CML undergo blast crisis (BC), the prognosis for which is poor, with an intermediate `accelerated phase (AP)'. The cytogenetic and molecular mechanism responsible for the disease progression in CML is not conclusive. **Objectives**: To elucidate the role of Chromosomal Aberrations, BCR/ABL gene rearrangements &c-MYC expression pattern in disease progression of CML. **Material and Methods**:Chromosomal analysis,BCR/ABL gene rearrangements and c-MYC expression were carried out in bone marrow samples of 60 CML patients (30 CP, 10 AP & 20 BC) by using GTG banding.,Flourescent Insitu Hybridization (FISH) and Quantitative Real Time PCR respectively. **Results**: The t(9;22) translocation is the sole chromosomal abnormality detected in most cases of CML-CP. Besides t(9;22),Additional Cytogenetic Abnormalities (ACA"s)such as monosomies, deletions, duplications, three way translocations were frequent in AP & BC.FISH analysis revealed that atypical signal patterns were more common in AP & BC than CP.In qRT-PCR analysis ,compared to CP, we found a 2 – 8 fold c-MYC over expression in patients at advanced phases of the disease (AP & BC). **Conclusions**: The genetic instability caused by the hyper activity of c-MYCmay be one of the reasons behind the acquisition of additional chromosomal aberrations in advanced phases of the CML and therefore synergic effect of cytogenetic and molecular parameters subverted the road to the therapeutically challenged advanced phases of the disease.

PO 62: Molecular alteration in Transforming Growth factor β receptors/SMAD in gallbladder diseases.

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Introduction: Gallbladder disease may be looked upon as any abnormality associated with the gall bladder. It involves chronic cholelithiasis, cholecystitis and finally progression towards gall bladder cancer. Cholecysectomy may be the only option for treating initial stages of the disease, but gall bladder cancer is marked with lack of effective treatment and poor survival rates. Possible strategies to understand the molecular mechanisms underlining the initial phases of the disease are necessary to control the progression towards gallbladder carcinoma. Any alteration of TGF-β signalling pathways underlies many human disorders, in particular, tumor promotion by inducing cell invasiveness through a process of Epithelial to mesenchymal trasdifferentiation (EMT). In cancer, overexpression of TGFβR occurs with constitutive SMAD signalling. The SMAD2/3-SMAD 4 can directly regulate gene expression by acting as transcription factors and binding to promoter regions of genes. Our study highlights the role of TGF-βR/SMAD signalling axis in initial stages of gallbladder disease which would help us better understand the mechanism of progression towards gallbladder carcinoma and metastasis. **Objectives**: To study expression and mutations of TGFβ/SMADs in the Gallbladder normal and Disease samples. **Material and Methods**: RNA isolation from normal and diseased samples: RNA was isolated from Tissue using RiboZol. This was followed by cDNA synthesis using RevertAid RT Reverse Transcription Kit. Expression analysis of candidate genes by RT PCR: Primers were designed for candidate genes (TGFβRI/II - SMADS) to study their gene expression across samples. **Results**: TGFβ receptor I, II and smads are upregulated in the disease cases as compare to the normal. **Conclusions**: At epidemiological level, we can determine the role of TGFβ/SMAD as possible prognostic and diagnostic markers.

PO 63:Differential expression of AKT isoforms in patients with Oral Squamous Cell Carcinoma (OSCC)

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Introduction: AKT (PKB), a serine threonine kinase is a downstream effector of Phosphoinositide 3 Kinases (PI3K). Activation of AKT triggers a plethora of intracellular responses ranging from metabolic regulation to cell proliferation, survival, and inhibition of apoptosis. AKT exists as three different isoforms AKT1, AKT2 and AKT3. There are increasing number of literature resources connoting the fact that AKT isoforms are differentially expressed in various human cancers. **Objective:** The present study was planned to evaluate expression of different isoforms AKT in patients with OSCC. **Material and Methods:** m-RNA expression of different AKT isoforms (AKT1, AKT2, AKT3) was tested in tumor and normal tissue specimen of oral cancer patients by RTPCR and qRTPCR analysis. Additionally, the expression of AKT-1 &ser473p-AKT was assessed in 30 paraffin embedded tissue samples of OSCC patients and 10 adjoining normal mucosa. **Results:** Approximately 1.4 fold higher expression of AKT1 m-RNA was observed in tumor tissue sections of oral cancer patients as compared to their normal counterparts whereas expression of AKT2 and AKT3 m-RNA was found to be downregulated in tumor sections of these patients. Furthermore, the m-RNA expression of AKT1 (Expression Ratio=2.604; p=0.007) as obtained from qRTPCR analysis was also found to be significantly increased in tumor sections as compared to those of the normal area whereas the mRNA expression of AKT2 (Expression ratio=0.153; p=0.003) & AKT3 (Expression Ratio=0.074; p=0.027) was observed to be significantly decreased in tumor tissue specimens of these patients. Significantly strong immunostaining of ser473p-AKT in comparison to AKT-1 was documented in all paraffin fixed oral cancer tissues. Additionally, a strong positive co-relation between the immunohistochemical expression of AKT-1 and ser473p-AKT in the paraffin sections of oral cancer tissues was observed with r value of 0.7504 ($p \leq 0.0001$). **Conclusions**:The present study suggests AKT1 is the dominantly expressed isoforms of AKT in OSCC patients of Asian origin and hence can be a suitable target for chemoprevention and prognostication of patients with oral carcinoma.

PO 64: Mitol/MARCH5/RNF153 dependent ubiquitylation negatively regulates the entry of mitochondrial replicative proteins into the mitochondria

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Background: RECQL4 belongs to RecQ family of helicases which participates in mitochondrial DNA replication by acting as an accessory factor to mitochondrial polymerase, PolaA/B2. Loss of both RECQL4 and PolaA/B2 cause decreased mitochondrial DNA replication and incorporation of mutations in mitochondrial DNA. However the molecular mechanism behind the entry of mitochondrial replicative proteins into the mitochondria has not been reported. Mitol, a mitochondrial E3 ligase in the outer mitochondrial membrane is involved in the protein quality control of mitochondria. Hence it was hypothesized that Mitol may play role in the regulation of mitochondrial replicative proteins like RECQL4 and PolaA. **Methods**: To determine the effect of Mitol on RECQL4 and PolaA, overexpression and western analysis were carried out. Enhanced ubiquitylation of RECQL4 and PolaA was observed in presence of Mitol both by in vivo and in vitro ubiquitylation assays. RECQL4 and PolaA import into the mitochondria was elucidated by in vitro import assay using isolated mitochondria. **Results**: Overexpression of Mitol causes decrease in the level of RECQL4 and PolaA, an effect which was rescued by the inhibition of the proteosmal pathway. RECQL4/ PolaA ubiquitylation at specific lysine residues by Mitol hampered its interaction with TOM20 receptor protein and their decreased its entry into the mitochondria. The complete elimination of RECQL4 from mitochondrial matrix was due to Lon peotease dependent proteolysis via PKA phosphorylation. **Conclusions**: RECQL4 and PolaA ubiquitylation by Mitol negatively regulates its entry into the mitochondria. Proteolysis of RECQL4 by mitochondrial LON protease occurs via PKA phosphorylation.

PO 65: LDCA- a „Dual hit" metabolic modulator competitively inhibits LDH-A to selectively subvert apoptosis in the neoplastic population

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Introduction: The cancer cell is characterized by a metabolic shift known as the "Warburg effect" that enhances resistance towards apoptosis and one important enzymes involved in aerobic glycolysis of the neoplastic cells is lactate dehydrogenase A (LDH-A) that interconvert pyruvate to lactate and is seen to be responsible for aggressive cancer outcomes. **Objectives**: The objective of this study is to develop a novel molecule that would potentially target LDH-A and resultantly shutdown the energy supply and associated anabolic reactions to accentuate apoptosis within the malignant population. **Material and Methods**: LDCA was chemically synthesized where a fluorine analogue was tactically coupled with a –NHCOCHCl2 backbone. Spectrophotometric techniques demonstrated a competitive inhibition of LDH-A by LDCA and its effect on cancer cell survival and migration was studied employing flow cytometric and confocal imaging techniques. NMR spectroscopy was used to estimate the levels of lactate production in vitro and in vivo. Mice with breast cancer were treated with LDCA to determine the effect on tumor growth, angiogenesis and ultimately survival. **Results**: LDCA competitively inhibited LDH-A enzyme activity, abrogated lactate formation and compromised mitochondrial bioenergetics. Studies profoundly exhibited selective cytotoxicity of LDCA on cancer cells where it significantly altered mitochondrial membrane potential (MMP), heightened ROS generation to subvert apoptosis via the caspase cascade. In vivo experiments exhibited the robustness of LDCA where it appreciably retarded breast tumor progression via intrinsic mitochondrial death pathway without toxic manifestations. **Conclusions**: These findings highlight the prospective of LDCA as a potential candidate that would highlight the role of metabolic modulators in the arena of cancer therapeutics.

PO66: Nkx2.2 a potential target for Brain tumour treatment.

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Introduction: Sonic hedgehog signalling pathway is a developmental key regulator of nervous system. Binding of sonic hedgehog active ligand (Shh-N) to 12 transmembrane patched1 (PTCH1) triggers the cascade of this signalling pathway. Signalling cascade begins with the retrieval of Smoothened (SMO) a 7 transmembrane protein which is repressed by PTCH1 in the absence of activated Shh signalling ligand. Now, activated Gli1, an immediate downstream activator of Shh pathway enters nucleus and binds to the promoter region of target genes and regulate their expression. Nkx2.2 is a putative downstream target gene of Shh signalling pathway, which is positively regulated by Gli1 and has great role in neuron development and regeneration (Briscoe et al: 1999). **Objectives**: This study is aimed to determine the role of homeobox transcription factor II Nkx2.2 in human brain tumour development. **Material and Methods**: Surgically removed human brain tumour samples were collected from Jawaharlal Nehru Medical College AMU, Aligarh, and performed histochemistry, immuno histochemistry

and PCR **Results**: awaited **Conclusions**: If there would be possibility of high expression of Shh and Nkx2.2 transcript and protein in human brain tumour tissue sample, then Nkx2.2 would be one of the potential targets for the treatment of the brain tumour and novel biomarker for early detection of most common brain tumour Glioma and paediatric medulloblastoma.

PO 67: Emerging biomarkers: Sperm associated antigen 9 (SPAG9) in Head and Neck Cancer

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Introduction: Cancer is the leading cause of death in economically developed countries and it has been reported that 1 in 4 cancers in male occur in head and neck region and accounts for 30% of all cancers. Importantly, salivary gland cancer accounts for 3–5% of total head and neck. **Objectives**: To investigate the association of sperm associated antigen 9 (SPAG9) expression with salivary gland tumor (SGT). **Material and Methods** Clinical specimens of benign (n = 16) and malignant tumors (n = 86) were examined for the SPAG9 gene and protein expression by RT-PCR, in situ RNA hybridization and immunohistochemistry. In addition, humoral response against SPAG9 was determined in the sera of 72 SGT patients. **Results**: In situ RNA hybridization and immunohistochemistry analysis demonstrated significant SPAG9 gene and protein expression in benign (63%) and malignant tumor (84%) specimens. Further, significant association was also observed between SPAG9 expression and malignant tumors. A cut-off value of >10% cells expressing SPAG9 protein predicted the presence of SPAG9 in malignant SGT with 83.72% sensitivity, 100% specificity, 100% PPV and 83.72% NPV. Circulating anti-SPAG9 antibodies were found to be present in the sera of 68% of SGT patients. **Conclusions**: Our data suggested that the majority of SGT show significant difference and association among benign and malignant tumors for SPAG9 gene and protein expression and also exhibit humoral response against SPAG9 protein. Hence, SPAG9 may be developed as a biomarker for detection and diagnosis of salivary gland tumorsfor better prognosis and cancer management.

PO 68: Synthetic Oleanane Triterpenoid as Targets for Neuroblastoma Differentiation Therapy

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Introduction: Neuroblastoma (NB) is an extracranial cancer derived from undifferentiated primitive neural crest cells. The differentiation process is forestalled in NB and therefore differentiation therapy could be used to induce tumour regression and steer the cells to differentiate; eventually completing the maturation process. Peroxisome proliferator-activated receptor-gamma (PPARγ) is a known critical regulator of adipocyte differentiation and several research groups have indicated its regulation in neuronal differentiation using PPARγ agonists (endogenous and synthetic). **Objectives**: In this study, we used synthetic oleanane triterpenoid, 2-cyano-3,12-dioxooleana-1,9-dien-28oic acid (CDDO), a PPARγ agonist and its combination with all trans retinoic acid (ATRA) to investigate its effect on neurite formation and neuronal differentiation. **Material and Methods**: IMR32 cells (NCCS,Pune) were treated with CDDO (Cayman Chemicals) and in combination with ATRA (Sigma Aldrich) for 5 days followed by methylene blue staining and imaged by phase contrast microscope. Quantitative PCR was performed using SYBR Premix E Taq (Takara) on Stepone-plus PCR machine (Applied Biosystems). **Results**: Our results indicate that CDDO and its combination with ATRA promotes neurite outgrowth in IMR32 cells with a simultaneous increase in expression of neuronal differentiation markers like neuron specific enolase, neuronal nuclei, synaptophysin and synapsin. This is accompanied by decrease in N-myc and increase in Tropomyosin receptor kinase A (TrkA), expression. **Conclusions**: Taken together the study reveals the potential role of PPARγ stimulation in IMR32 cell line differentiation in TrkA dependent manner. This research demands further attention to study the underlying mechanisms involved for its use in diseases having glitch in differentiation pathways.

PO 69: Precise distinction of general Akt Inhibitors into Akt Isoformspecific inhibitors

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Introduction: The serine/threonine kinase Akt/PKB act as a critical signaling node in higher eukaryotes that regulates different cellular processes such as cell proliferation and survival, cell size and response to nutrient availability, tissue invasion and angiogenesis. This kinase has three isoforms Akt1, Akt2 and Akt3 which plays diverse and sometimes contrasting functions in different cancers. **Objectives**: To classify the general inhibitors of Akt kinase more precisely into Akt-isoform specific inhibitors through in silico and in vitro analysis. **Material and Methods**: A set of 28 inhibitors have been selected for docking analyisis. 20 of these inhibitors were chosen from Medkoo"s anticancer molecular libraries for Akt inhibitors and 8 other potential anti-cancer natural compounds were chosen for the study. Docking was achieved with the Glide (Grid-based Ligand Docking with Energetics) program, version 10.3. Moreover, the Results were validated on cancer cells by using some of the inhibitors through different methods such as MTT assay, PCR analysis and Western blot assay. **Results**: Based on the GScore obtained, the ranking of Akt inhibitors was made according to their interaction with Akt isoforms. Furthermore it was validated through in vitro assay on cancer cells. **Conclusions**: Through in silico and in vitro analysis, the ranking of Akt inhibitors was achieved into Akt isoform-specific inhibitors; however more studies are required to confirm this investigation.

PO 70: "Regulation of vascularization by co-culture of MTA1-gene silenced human mesenchymal stem cells and endothelial cell 3D spheroid encapsulated in PEG – maleimide hydrogels"

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Introduction: The metastasis-associated (MTA) gene family is a family of cancer progression related genes and their encoded products. We have shown that MTA1 is a potent pro angiogenic protein. Human mesenchymal stem cells (hMSC) are known to secrete VEGF and could therefore enhance the proliferation and differentiation of endothelial cells (EC). The combination of EC and hMSC is expected to not only accelerate the vascularization essential for delivery of nutrients to the developing tumor but also to be beneficial for the growth and differentiation of both cell types. **Objectives**: With an interest to understand the role of MTA1 in hMSC interaction with EC which act as pericytes by encircling ECs in capillaries, we have silenced the MTA1 gene by using MTA1- shRNA and stable tansfection . **Material and Methods**: We have in 3D endothelial cell spheroid culture in PEG- maleimide hydrogel shown that either VEGF or MTA1 induce sprouting of capillaries in a dose and time dependent manner. hMSC"s when co cultured with EC spheroids showed that they bind to the sprouting capillaries and modulate angiogenesis. **Results**: Our data on using MTA-gene silenced hMSC"s indicated that there is a differential binding to ECs when compared to that of control hMSC"s.

Gene expression studies by qPCR upon co culturing, revealed differential expression of angiogenic genes and their receptors. Our studies also revealed that the extracellular matrix plays an important role in cell-cell interaction and cell signaling in promoting angiogenesis.

PO 71: Saliva Based Noninvasive Method for Early Detection of HPV Infection in Oral Tongue Cancer.

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Introduction: Tongue squamous cell carcinoma (TSCC) is emerged as an alarming public health problem with increasing incidence and mortality rates, which is characterized by its aggressive nature, poor prognosis and distant metastasis. Of several risk-factors, the infection of HR-HPV type 16 has been strongly associated with a sizable proportion of TSCC. Since this cancer is preceded by a long duration of precancer stage, early detection of the disease by using a noninvasive method will be served as an immense importance. Therefore, this study aimed to use saliva samples to detect early diagnosis of HPV infection in TSCC patients. **Methods**: Present study included one hundred twenty (n=120) pretreatment specimens comprising forty saliva samples and forty corresponding tissues from the cases along with forty saliva from healthy normal controls. HPV detection was done by consensus L1 and type-specific PCR and followed by line blot assay and correlated with epidemiological risk factors and histopathological grading of the disease. **Results**: The exclusive prevalence of HR-HPV 16 was found in 25% (10/40) of tongue tumor tissues while 20% (8/40) in corresponding saliva samples, and only 2.4% (1/40) in normal healthy controls. No other HPV types could be detected. The majority of the cancer cases (77.1%) were male and tobacco users. **Conclusions**: Exclusive prevalence of HPV type 16 was significantly higher in saliva of nonsmoker female tongue cancer patients. Detection of HPV16 in saliva has serve as an emerging reliable noninvasive biomarker for early detection and diagnosis for HPV-associated oral tongue cancer.

PO 72: Targeting Kinases for neurodegenerative disorders caused by ischemic injury.

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Introduction: Under ischemic condition, Ischemic injury can be mediated by necrosis and apoptosis, which are activated through reactive oxygen species/reactive nitrogen species production and overloading of Ca2+. Cerebral ischemia recruits some kinases into the NMDA (N-methyl D-aspartate) receptor complex which gets phosphorylated and causes injurious Ca2+ influx through NMDA receptor channels, resulting in an irreversible neuronal death. These activated kinases may phosphorylate p53 and mediate apoptotic neuronal death via inducing the expression of proapoptotic genes, such as Bax. Hence, the Death domain (DD) and catalytic domain of these kinases may be targeted for inhibition to restrict the interactions necessary for transducing a death signal. **Objective**: In this approach, we aim to build a library of domain specific kinase inhibitors which will be used to perform pharmacophore modelling and pharmacophore-based virtual screening. The selected hits will be used for docking and molecular dynamic simulation. **Material and Methods**: In-silico Approach: ligand-based drug designing Collection of known inhibitors using pubchem assay database Pharmacophore modelling using Ligandscout or pharmer Docking using autodock 4.2 MD Simulation using GROMACS In-vitro Approach: in-vitro phosphorylation assay/Kinase assay. **Results**: A library of known inhibitors was built which will be used to find out domain specific kinase inhibitor (Lead compound) with higher dock-score than the reference inhibitor. Further through experimental analysis the specificity of the lead compound will be validated. **Conclusions**: Structural information on target−inhibitor complexes would be helpful in the logical development of selective and potent inhibitors in future.

PO 73: Expression of gonadotropin releasing hormone receptor in glioblastoma cell line-derived exosomes andpotential as circulatory biomarker

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Introduction: Glioblastoma Multiforme (GBM) is one of the most malignant and aggressive forms of primary brain tumors. They exhibits local metastasis and are resistant to current modalities of treatment, generally resulting in tumor recurrence. Effective methods for post-treatment surveillance of glioblastoma are still in the waiting and there is strong need for high Confidence identification of blood-based biomarkers. **Objectives**: The present study aimed at investigating the expression of GnRH receptor, belonging to the rhodopsin-like Gproteincoupled receptor (GPCR) family, in glioblastoma cell line, LN229, and cell linederived exosomes to explore itspotential as circulatory marker for post-treatment monitoring of GBM patients. **Material and Methods**: GnRH receptor expression was studied at gene level by RT-PCR analysis and at protein level by dotblot and Western blot analysis in cell lysate. Further, cell line-derived exosomes were isolated from culture media bydifferential centrifugation method and expression of GnRH receptor was studied at protein level by dot blot assay. **Results**: GnRH receptor was observed to be expressed both at the gene and protein level in GBM cell line, LN229, and wasalso found to be expressed at protein level in LN229 cell line-derived exosomes. Interestingly, we observed significantenrichment of GnRH receptor protein in cell line-derived exosomes in comparison to cell lysate.

PO 74: Role of FAM171A1 in Triple Negative Breast Cancer

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Introduction: TNBC is a more aggressive form of breast cancer owing to non-availability of targeted therapy. Its increased metastatic behaviour and non-responsiveness to current therapy is a major concern. We identified FAM171A1 as a potential candidate gene overexpressed in both TNBC cell lines and clinical samples. Understanding the biological significance of this molecule is very important to link its functional significance in TNBC. **Materials and Methodology**: Breast cancer cell lines MCF7, T47D, MDAMB 231, SKBR3, SUM149 and SUM159 were cultured and maintained in their respective media. Colony formation assay, Scratch assay, Invasion assay, mammosphere formation assay, MTT assay and cell cycle analysis were performed as per standard protocol. Knockdown and over expression of ERα and FAM171A1 were performed

using Lipofectamine reagents. CHIP was performed according to Cell Signaling protocol. **Objectives**: To analyze the differential expression of FAM171A1 in breast cancer cells and tissues with different hormone status. To understand the functional role of FAM171A1 and its downstream effectors and targets. **Results**: WB and qRT PCR results showed increased expression of FAM171A1 in TNBC compared to non-TNBC cell lines. Overexpression of ERα leads to decreased FAM171A1 expression indicating the possible regulation of FAM171A1 by ERα. However CHIP Results failed to show direct association of ERα indicating indirect regulation. Even though the overexpressed cells were not invasive as observed by Scratch assay, Invasion assay, MTT assay, the cells showed increased mammosphere formation and EMT transition. **Conclusions**: FAM171A1 is specific to TNBC and may contribute to the stem cell dependent aggressiveness.

PO 75: A-Kinase Anchor Protein 4 (AKAP4): A Potential Target for Immunotherapy of Ovarian Cancer

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Introduction: Ovarian cancer is the leading cause of cancer related deaths amongst all the gynecological cancers because of the lack of early symptoms and effective screening methods. Early-stage ovarian cancers are often asymptomatic and hence, diagnoses are made at an advanced disease stage. Cancer-testis antigens (CTAs) have potential to be a good immunotherapeutic targets. **Objectives**: To study the role of novel CTA, A-Kinase anchor protein 4 (AKAP4) with ovarian cancer. **Material and Methods:** AKAP4 gene and protein expression was evaluated in 38 ovarian cancer and 21 matched adjacent non-cancerous tissue (ANCT) specimens using RT-PCR, in-situ RNA hybridization and humoral response was investigated by ELISA. **Results**: AKAP4 gene and protein expression was observed in 89% (34/38) of ovarian cancer patients as compared to no expression in 21 matched ANCT. Circulating anti-AKAP4 antibodies were found in 58% (22/38) of ovarian cancer patients as analyzed by ELISA. Particularly, 65% (22/34) patients positive for AKAP4 mRNA and protein expression showed humoral response against AKAP4. The majority of the specimens obtained were of ovarian serous adenocarcinoma and serous papillary carcinoma histotype, and 93% (28/30) and 100% (6/6), respectively, expressed AKAP4. 79% (19/24) of ovarian serous adenocarcinoma and 67% (4/6) of serous papillary carcinoma patients exhibited humoral response against AKAP4. **Conclusions**: Expression of AKAP4 only in malignant cells and not in normal cells except testis, and humoral response against AKAP4 in ovarian cancer patients, shows that AKAP4 might be potential immunotherapeutic target for ovarian cancer.

PO 76: PTEN mediated regulation of mTORC2 in grade IV glioma: signalling to therapeutic approach

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Introduction:mTOR complex 1 (mTORC1) and complex 2 (mTORC2) are two functionally distinct complexes play central role in cell proliferation. PTEN mutation is involved with aggressive form of grade IV glioblastoma multiforme (GBM). Therefore, there is an urgent need for understanding cellular crosstalk between PTEN and mTORC mainly mTORC2 in GBM. **Objectives:**Our aim was to decipher the function and regulation of mTORC2 with respect to PTENwt vs. PTENmu. We established a carbazole alkaloid (mahanine) which showed apoptosis in different cancers with various oncogenic mutations including GBM1-7. Therefore, we wanted to verify the sensitivity and the mode of activity of mTORC2 towards inhibitors/mahanine/rapamycins. **Material and Methods:** siRNA/plasmid/inhibitor/rapamaycin/mahanine-treated/untreated GBM cells were used to study the expression/interaction of different proteins through immunoblot/immunoprecipitation experiments and analysed by various techniques. **Results:** We demonstrated that PTENmu cells had higher mTORC2 formation and signalling than PTENwt cell. PTEN Knockdown enhanced mTORC2 signalling in PTENwt cells. This reduced mTORC2 formation in PTENwt cells was related with increased Rictor (Thr1135) phosphorylation. However when Thr1135 was replaced with alanine, mTORC2 formation was enhanced even in PTENwt cells. Furthermore, we confirmed the sensitivity of both mTORC1/2 towards mahanine. However, the activity of mahanine was enhanced in combination with PI3K inhibitors in PTENwt cells and it exhibited better cytotoxicity compared to known GSK3β-inhibitor against PTENmu-GBM cells. **Conclusion:** Taken together we have established that PTEN negatively regulates mTORC2 formation/signaling via Rictor-hyperphosphorylation (Thr1135) and directs the mode of action of mTORC1/2 inhibitor. Mahanine is a potent mTORC1/2 inhibitor and thus open up a new therapeutic strategie8

PO 77: Increased expression of MARCH E3 Ligase in human esophagealsquamous cell carcinoma

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Introduction:In the recent years, E3 ubiquitin ligases haveemerged as important players in cancer. Membrane Associated RING-CH (MARCH) protein family, an E3 ubiquitin ligase family, has also been reported to downregulate various cancer-related proteins such as TRAIL-R1, E-Cadherin, Fas, etc. but their expression pattern in cancer is still not very clear. **Objectives**:To analyse the MARCH transcript variants and protein expression in esophageal squamous cell carcinoma (ESCC) and distant matched non-malignant tissues. **Material and Methods**:mRNA expression of MARCH transcript variants was evaluated in ESCC and distant matched non-malignant tissues usingquantitative real time PCR. Moreover, MARCH protein expression was determined in ESCC and distant matched non-malignant tissues using immunohistochemical analysis. **Results**:Differential expression of MARCH transcript variants was found in ESCC tissues when compared with distant matched non-malignant tissues. In addition to this, significantly upregulated MARCH proteinexpression was observed in the ESCC as compared to distant matched non-malignant tissues. MARCH protein was found to be localized in nucleus as well as cytoplasm of the tumor cells. **Conclusions**:For the first time our findings propose the aberrant expression of MARCH mRNA as well as protein in esophageal squamous cell cancer patients suggesting its role in esophageal carcinogenesis.

PO 78: Molecular crosstalk between the NFκB and STAT3 signaling pathways play key role in regulating cancer progression in oral carcinoma

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Introduction:In India, oral cancer accounts for a high percentage of all malignancies registered annually. Around 90% of oral cancers are squamous cell carcinomas (SCCs). Overexpression and activation of Nuclear factor (NF)-κB and signal transducer and activator of transcription

3 (STAT3) transcription factors are implicated in many human cancers, especially in those of squamous cell origin; however, exact underlying molecular mechanisms in OSCCs have not yet been fully understood. **Objectives**:This study focused on the functional importance of NFκB and STAT3 signalling pathways in development and progression of OSCC. **Material and Methods**: Oral cancer cell line (UPCI:SCC029B) and normal human keratinocyte cell line (HaCaT) were propagated and maintained in DMEM Medium supplemented with 10% FBS. SCC029B cells were transfected with control, NFκB and STAT3 siRNAsby lipofection. Protein expression analysis in knockdowned and control samples were done by immune-blotting using antibodies against NFκB, STAT3, cyclin D1and β-actin and knockdown effect on proliferation and migration potential of control and treated samples were assessed by MTT and wound healing assays respectively. **Results**: Immunoblotting results showed that basal level expression of NFκB and STAT3 transcription factors are significantly higher in SCC029B cells compared to HaCaT. In SCC029B cells, NFκB and STAT3 protein expression were prominently diminished upon respective siRNA transfection. Notably STAT3 expression markedly decreased in NFκBknockdowned cells and vice versa. This result indicates the presence of functional crosstalk between NFκB and STAT3 signaling pathways in OSCCs. Cyclin D1protein level was also decreased in NFκB and STAT3 siRNA transfected samples. NFκB and STAT3 siRNA treated cells showed typical apoptotic and senescent characteristics compared to control siRNA treated cells of the same time period. MTT assay results revealed that, compared to control siRNA transfected cells, percentage of cell viability was significantly decreased in NFκB and STAT3 silenced cells. In wound healing assay, control siRNA treated cells showed complete wound healing whereas NFκB and STAT3 silenced cells showed only ~50% wound closure after 24 hours of transfection. **Conclusions**:The present study thus revealed that a functional crosstalk between NFκB and STAT3 signalling pathways are exists in OSCC and also showed that these pathways have key role in controlling cell proliferation and cell migration. Loss of cyclin D1 expression upon NFκB and STAT3 knockdown indicates that the cell death caused may be due to G1 cell cycle arrest. In conclusion, our study provides evidence for the possible therapeutic potential of targeting NFκB/STAT3 liaison in oral cancer.

PO 79: Metabolic modulator „Bet-CA" alters mitochondrial membrane potential to effectively suppress cancer associated angiogenesis and metastasis

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Introduction: Solid tumors characteristically reflect a metabolic switching from glucose oxidation to glycolysis that plays fundamental role in angiogenesis and metastasis to facilitate aggressive tumor outcomes. Fuelled by conviction we fabricated a co-drug Bet-CA, by esterifying betulinic acid (BA) with dichloroacetic acid (DCA) that with ultimate precision targets cancer metabolism and establishes itself as a potent antitumor agent. **Objectives**: The objective of this study is to scrutinize the merits of Bet-CA as a potent anti-metastatic and anti-angiogenic mediator and establish it as a therapeutic and strategic tool that would simultaneously interferes with cancer development at multiple points. **Material and Methods**: 4T1 murine breast cancer cells were treated with scalar concentrations of Bet-CA. Effects on cell proliferation, signalling, migration, invasion and neo-angiogenic vasculature formation were determined employing flow cytometry and confocal imaging techniques. Mice harbouring breast cancer were treated with Bet-CA to determine the effect of tumor growth, angiogenesis, lung metastasis and ultimately survival. **Results**: In mice syngeneic 4T1 breast cancer model, Bet-CA abrogated angiogenesis and concomitantly obliterated lung metastasis consistent with altered mitochondrial bioenergetics. Furthermore, Bet-CA significantly lowered vascular endothelial growth factor (VEGF) levels and obviated matrix metalloproteases (MMP-2/9) production directly to the criterion where abrogation of autocrine VEGF/VEGFR2 signalling loop was documented. In vitro studies anticipatedly documented the role of Bet-CA in inhibiting actin remodeling, lamellipodia formation and cell membrane ruffling to constitutively suppress malignant invasion. **Conclusions**: The results substantiate that Bet-CA with preeminent pro-apoptotic effects, contain within it services of a potential metastatic and angiogenic suppressor that would future efficacious treatments against metastatic breast cancer.

PO 80: Deciphering the functions of overexpressed miRNAs in BLM helicase-deficient cells exhibiting high levels of DNA damage

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Introduction: Bloom Syndrome (BS) develops as a result of mutations in Bloom Helicase (BLM). BS patients accumulate high levels of DNA damage leading to genomic instability and predisposition to a wide spectrum of cancers. MicroRNAs (miRs) are 19-25 nucleotide long double stranded RNA molecules that are involved in the post-transcriptional regulation of gene expression. Hence, deregulated expression of miRs can lead to cellular abnormalities including hyper-recombination and neoplastic transformation ultimately leading to cancer. **Objectives**: The objective of this study was to determine the miRs whose expression was regulated by DNA damage. Cells lacking BLM cannot efficiently remove DNA lesions. Hence, the aim was to determine the deregulated miRs in cells lacking BLM, decipher their regulatory mechanisms, identify their targets and finally elucidate their roles during neoplastic transformation. **Material and Methods**: Next Generation Sequencing (NGS) of miR was carried out in multiple isogenic lines either expressing or lacking BLM. The overexpressed miRs in BLM-deficient cells were validated by quantitative real-time PCR. A transcription factor, which regulates these miRs in vivo was identified. Functional analysis was carried out to study the biological role(s) of the miRs. **Result**: Twelve miRs, all regulated by the transcription factor CDX2, were significantly upregulated in cells lacking BLM expression. Overexpression and ablation studies indicated that the high levels of these miRs in cells lacking BLM correlated with increased amount of DNA damage and SCE levels, which manifested in enhanced metastatic capability.

PO 81: Proapoptotic and antiangiogenic activity of a novel synthetic compound benzo[d]isothiazole involves repression of VEGF gene expression and phosphorylation of JNK

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Introduction: The aim of the work is to focus on the synergetic and additive effects of the novel synthetic compound with benzo[d]isothiazole as a parent compound. Benzoisothiazoles exhibit their antitumor activity through different mechanisms including inhibition of raf-1, protein tyrosine phosphatase-1β, topoisomerase II and lysophosphatidic acid acyltransferase-β. The compound, benzo[d] isothiazole, has chlorophenyl, dihydroisoxazol and piperazine (NS7) structural moieties. **Objectives**: The objective of this work is to study the Proapoptotic and antiangiogenic activity of a novel synthetic compound benzo[d]isothiazole and its molecular mechanism during the process. **Material and Methods**: The antiproliferative effect of NS7 was assessed in mouse mammary carcinoma and MDA MB 231 cells using [3H]-Thymidine uptake, and MTT assays. NS7 (1μM, 5μM, 10μM, 50μM and 100μM) inhibited proliferation in a dose- dependent manner. The antiangiogenic activity of NS7 was done using shell-less chorioallontoic membrane (CAM) and rat corneal micropocket assays. The mechanism of antiangiogenesis was delineated using an in vivo mouse mammary carcinoma model. VEGF gene expression was

studued by VEGF promoter-luciferase reporter gene analysis. In mouse bearing mammary tumor, 100Mμ of NS7 was injected to study the in vivo assays. Differential expression of bax and bcl2 was also seen. The pro apoptotic activity of NS7 was mediated ny the JNK signalling pathway. NS7 increased phosphorylation of JNK as revealed by the data on western blotting. **Results**: When compared to the control vascularized CAM or to VEGF- induced corneal neovascularization, NS7-treated CAM showed vessel regression and antiangiogenic activity. NS7 not only reduced tumor volume but also showed complete absence of peritoneal angiogenesis. In mouse bearing mammary tumor, NS7 induced apoptosis in vivo, showing fragmentation of DNA, blebbing of plasma membrane, appearance of apoptotic nuclei. Differential expression of bax and bcl2 was also seen. The pro apoptotic activity of NS7 was mediated by the JNK signaling pathway. NS7 increased phosphorylation of JNK as revealed by the data on western blotting. **Conclusions**: anti angiogenic and pro apoptotic property of the compound was observed by performing the above assays.

PO 82: Novel mutations in MUC2 and MUC17 serve as prognostic marker in differential phenotypes of diffuse large Bcell lymphoma.

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Introduction: Gene Expression profiling of Diffuse Large B-cell Lymphoma (DLBCL) into molecular phenotypes and International Prognostic Index (IPI) does not predict survival. Indian DLBCL still remains enigmatic as its molecular profile has not yet been deciphered. We postulate role of microenvironment; which includes stromal secretome profile and stromal mutations which may evolve as promising prognostic markers in DLBCL. **Objectives**:Immunophenotypic classification of DLBCL as per Han"s algorithm. Whole ExomeSequencing (WES) for stromal genes. In vitro study on secretome profile of stromal and neoplastic cells. Correlation of stromal profile with IPI. **Material and Methods**: Two cases each of ABC and GCB-DLBCL were subjected to AmpliSeqExome(WES) [Ion ProtonTM] and aligned to human reference genome (hg19). Ion ReporterTM software and Integrated Genome Viewer for variants and pathway analysis using DAVID, PANTHER, KEGG and STRING was performed. Expression levels of mutated stromal genes were evaluated using customized stromal PCR array (SABiosciences). The secretome analysis of cultured lymphoma cells and serum from DLBCL patients were evaluated and correlated with IPI data. **Results**: Analysis revealed 34 genes coding for extracellular matrix mutated specifically in GCB subtype and 26 in ABC DLBCL. STRING identified LAMC3, LAMA2,MUC17,LAMB2, COL5A2, COL13A1in GCB phenotype whereas LAMB1,LAMA3,COL4A2,COL28A1,COL5A3,MUC2 were mutated in ABC DLBCL. Secreted cytokine profile revealed increased IL-6, IL-10, TNF-α, IFN-γ, IL-4, IL-17 levels Conclusion: This study advocates role of collagen scaffolding and laminin cross-linking in DLBCL progression. Further, MUC2 and MUC17 are promising novel biomarkers for prognostic risk stratification and refinement of treatment in DLBCL.

PO 83: Multiple Non-B DNA conformations at BCL6 Breakpoint Regions can explain its Fragility during Chromosomal Translocations Involved in Diffuse Large B Cell Lymphoma

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Introduction: Diffuse Large B Cell Lymphoma (DLBCL) is an aggressive malignancy of mature B lymphocytes. BCL6 translocation involving chromosome 3 and as many as 26 partner chromosomes is considered as a characteristic feature of this lymphoma. However, the mechanism of BCL6 fragility is largely unknown. **Objectives**: To investigate mechanism of chromosomal fragility at BCL6 breakpoint region both at DNA sequence and structural levels in vitro and ex vivo. To check recombinogenic potential of BCL6 breakpoint regions at intracellular level. **Material and Methods**: Mapping of patient break points, bioinformatic analysis, gel mobility shift assay, mutation analyses, S1 and P1 nuclease Assays, KMnO4 assay, primer extension assay, bisulfite modification assay, circular Dichroism studies, intracellular recombination assays etc. **Results**: Breakpoint analyses showed that breakage at BCL6 gene on chromosome 3 occurs nonrandomly. We observed stretches of guanines and inverted repeat sequences near the breakpoints. Various biochemical and biophysical studies revealed existence of altered DNA structures such as cruciform DNA and G-quadruplexes. Formation of non-B DNA structures affected both replication and transcription. Bisulfite modification assay, mutation analysis and DMS protection assays defined precise base pairing. Finally we also assessed the recombinogenic potential of BCL6 breakpoint region. **Conclusion:** Our study reveals, the occurrence of two independent non-B DNA structures at the patient break point regions, which explains the mechanism by which BCL6 is getting translocated in DLBCL.

PO 84: Deregulation of p70 S6 kinase and their relation with Akt and mTOR in oral squamous cell carcinoma progression

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Introduction: Oral squamous cell carcinoma (OSCC) is the most common cancer of the oral cavity and it is one of the leading causes of cancer-related death in India. The Akt, mammalian target of rapamycin (mTOR) and p70 S6 Kinase are serine/threonine protein kinases and have been implicated in tumour development through Akt-mTOR-p70 S6 Kinase pathway. **Objectives**: The aim of the study was to identify expression and alteration of Akt-mTOR-p70 S6 Kinase pathway in the progression of human OSCC. **Material and Methods**: The expression of phosphorylated p70 S6 Kinase, p70 S6 Kinase, Akt and mTOR were assessed in human OSCC (n=43), PMLs (n=21) and normal tissues (n=24) using immunohistochemistry and western blot analysis. **Results**: The expression of phosphorylated p70 S6 Kinase was significantly higher in tumour samples compared with adjacent normal ($p < 0.01$). Moreover, increased expression of both phosphorylated p70 S6 Kinase and p70 S6 Kinase were correlated with disease progression and also positively correlated with increased expression of Akt ($r=0.521$, $p<0.001$) and mTOR ($r=0.562$, $p<0.001$) in OSCC. Interestingly, increased nuclear localization of phosphorylated p70 S6 Kinase was observed than the cytoplasmic localization as the severity of the disease increased. **Conclusions**: This study provides the evidence that aberrant accumulation of the phosphorylated form of S6 Kinase plays a significant role in progression of OSCC through the activation of Akt-mTOR-p70 S6 Kinase pathway. It can be used as a marker for assessing disease severity and may be exploited for therapeutic intervention.

PO85: UPREGULATION OF Immune check-point molecules PD-1 and PD-L1 IN HPV16 related cervical cancer pathogenesis: significant impact on cases with episomal HPV16

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Introduction: For prolonged persistence and transformation of cervical epithelium, Human Papillomavirus (HPV) employs several immune-evasion strategies. **Objectives**: To determine the role of immunosuppressive factors, such as inhibitory receptor molecules programmed cell death 1 (PDCD1/PD-1) and its ligand (PDCD1LG1/PD-L1) in HPV16 related cervical cancer (CaCx) pathogenesis in association with viral factors (viral physical status and expression of the oncogene, E7). **Material and Methods**: Quantitative real-time PCR was done to estimate mRNA expression levels of PD1/PD-L1 in samples from discrete stages of CaCx progression model: histopathologically confirmed HPVnegative normals (N=35), HPV16-positive normals (N=27) and HPV16-positive CaCx cases (N=78) of various grades/stages. **Results**: A significant linear trend of progressive PD-1 and PD-L1 up-regulation through the discrete stages of CaCx progression (p trend < 0.01) was apparent. Compared to HPV-negative controls, PD-1 and PD-L1 up-regulations were significant among the CaCx cases (p = 0.013 and 0.045 respectively), particularly among those with episomal HPV16 (p = 0.018 and 0.036 respectively) and revealed positive correlation with E7 expression among episomal CaCx cases. Transfection of cloned E7 in HPV-negative C33A CaCx cell-line resulted in a significant increase in PD-L1 expression concomitant with increase in HPV16-E7 expression. But, PD-L1 expression was found to be significantly lower among SiHa cells with higher E7 levels as compared to CaSki cells with lower E7, both harbouring integrated HPV16. **Conclusions**: Thus, up-regulation of the immune check-point molecules appears to be an early event in CaCx pathogenesis, substantially contributing to disease pathogenesis in cases harbouring episomal viral genomes, in an E7-dependent manner.

PO 86 :Neem leaf glycoprotein attenuates carcinoma and melanoma metastasis by editing DC-CD8 + T cell interaction and angiogenesis.

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Introduction: Metastasis attributes 90% mortality in cancer patients, hence, new therapeutic strategies to prevent metastasis is still in search. NLGP therapeutically restrict primary tumor growth but its role in relation to metastasis is unknown. **Objectives**: To ascertain the anti-metastatic role of NLGP with elucidation of the underlying mechanism(s). **Material and Methods**: Spontaneous and experimental metastasis models were established with LLC and B16F10 cells in C57BL/6J mice. Metastasis was macroscopically and histo-pathologically defined. Immunohistochemistry, Immunofluorescence, RT-PCR and Flowcytometry were performed to assess expression of various molecules (VEGF, TGFb, IFNg, CD8, CD4, IL-2, IFNg, GranB, CD69, CD44, MHC-I/II, CD80, CD86, CCR7) and to detect proliferation, viability, cell-cycle etc. Several bio-assays, like, scratch assay, trans-well migration, vascular mimicry, cytotoxicity, adoptive transfer, CD8 depletion were performed. DC: T cell co-culture assay was also done. **Results**: Melanoma and carcinoma induced spontaneous and experimental metastasis were significantly attenuated by NLGP along with prolonged mice survival. NLGP didn't inhibit/alter tumor cell proliferation, viability, cell-cycle and antigenicity though reduced in vitromigration and invasion was noted. However, similar reduction was not evidenced invivo. Hence, we conclude, that metastasis reduction isn't resultant of reduced migration or alteration of tumor cells. Metastasis cascade requires colonization which needsneoangiogenesis and immune-evasion. Here, we evidenced normalized angiogenesis along withreduced angiogenic factors (VEGF, TGFb) in lungsof NLGP treated mice with a high infiltration of activated CD8+ T cells with maximized IFNɣ secretion that inhibits colonization. Isolated NLGP influenced T cells showed greatertumor cell cytotoxicity and systemic CD8+ T celldepletion reduced NLGP's anti-metastatic potential. Further studies showed NLGP aids T cell priming by increasing the expression of MHC I/II, CD80/86, CCR7, IL-12 on DCs thus intervening tumor induced DC suppression. Moreover, NLGP mediated DC alteration was independent of intrinsic antigen processing but dependent on antigen presentation. **Conclusions**: NLGP mediated metastasis attenuation is not due to alteration or reduced migration of tumor cells but dependent on NLGP activated CD8+ T cells and normalized angiogenesis. Therefore anti-metastatic potential of NLGP might be helpful to propose NLGP as an arsenal against cancer in clinical settings.

PO 87: Molecular Profiling of Genetic Alterations in Prostate Cancer Patients from Northern India.

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Introduction: Gene rearrangements involving ETS transcription factors are frequent pathogenetic somatic events observed in prostate cancer (PCa). Incidence of ETS rearrangements in Caucasian PCa patients has been reported, however occurrence in Indian population is largely unknown. **Objectives**: The aim of this study was to determine the prevalence of the ETS and RAF kinase gene rearrangements, SPINK1 over-expression and PTEN deletion in this cohort. **Material and Methods**: In this multi-center study, we procured formalin-fixed paraffin embedded (FFPE) PCa specimens (n=121) from four major medical institutions in India. PCa specimens were analyzed by either immunohistochemistry, or RNA in situ hybridization and/or fluorescence in situ hybridization (FISH) for molecular subtyping. **Results**: ERG over-expression was detected in 48.94% (46/94) PCa specimens by IHC, which was confirmed by FISH. Among other ETS family members, while ETV1 transcript was expressed in one case, no alteration in ETV4 was observed. SPINK1 over-expression was observed in 12.5% (12/96) and PTEN deletion in 21.52% (17/79) of the total PCa cases. Interestingly, PTEN deletion was found in 30% of the ERG-positive cases (p=0.017) but in only one case with SPINK1over-expression (p=0.67). BRAF and RAF1 gene rearrangements were detected in ~1% and ~4.5% of the PCa cases respectively. **Conclusions**: Our findings suggests that ETS gene rearrangement and SPINK1 over-expression patterns in North Indian population largely resembled those observed in Caucasian population but differed from Japanese and Chinese patients. The current study provides molecular sub-type data for Indian PCa patients that could aid clinicians in diagnosis and selection of therapeutic intervention.

PO 88: Transcriptional regulation of wild type and mutated androgen receptor in prostate cancer cell

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Introduction: The androgen stimulated transcriptional regulation of androgen receptor (AR) is critical for prostate differentiation and development, as well as malignant transformation. Mutations in AR changes AR ligand specificity and allow AR to be activated by non-steroids or anti-androgens. The LNCaP cells correspond to a lymph node metastasis, containing a ligand-binding domain-mutated version of the receptor. VCaP (Vertebral-Cancer of the Prostate) cells in turn are derived from a hormone-refractory cancer, possessing amplified AR gene locus encoding otherwise normal AR protein. It has been reported that advanced prostate cancer tumors consist of multiple colonies of cells containing different AR mutations, and therapeutic treatment often results tumor leaving cells with AR mutations conferring a selective advantage to stage a relapse. Therefore, in the present study we set out to investigate mechanisms involved in AR wild type and AR mutated –mediated gene expression in prostate cancer

cells by using RNA sequencing and AR ChIP sequencing. **Objectives**: To study a detailed map of wild type and mutated AR-regulated genes in prostate cancer cell lines in the presence or absence of androgens in order to understand the essential signalling pathways downstream of the wild type and mutated AR in androgen dependent and castration recurrent prostate cancer. **Material and Methods**: For androgen response experiments, LNCaP & VCaP cells will be seeded in 10% charcoal stripped serum with phenol red free RPMI media for 48 h. Cells will be then stimulated for 24 h (for RNA sequencing) and 16hr for AR ChIP sequencing by replacement of growth medium with medium containing 10 nM dihydrotestosterone (DHT) (Sigma). **Results**: 75 genes and 55 genes were differentially expressed in DHT induced LNCaP &VCaP cells respectively. ERRFI, SGK1 and PRKCA genes were differentially expressed unique gene sets in DHT induced LNCaP cells. KLF4, SDK1 and NBL1 genes were differentially expressed unique gene sets in DHT induced VCaP cells. Predominant AR binding sites were observed in Intron and Distal Intergenic Region. In LNCaP Cells, out of 54 DHT induced genes, 26 genes reported in ARGDB & 16 genes reported in Invasive Prostate Adenocarcinoma (Oncomine data base). In VCaP Cells, out of 41 DHT induced genes, 18 genes reported in ARGDB & 20 genes reported in Invasive Prostate Adenocarcinoma (Oncomine data base). 14 genes were commonly differentially expressed in DHT induced condition of AR wild type and mutated prostate cancer cell. **Conclusions**: Differentially expressed unique genes regulated by DHT induced wild and mutated AR receptors may serve as a potential new therapeutic targets and pathways to treat prostate cancer malignancy.

PO89 : Nucleosomal response pathway and cancer

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Introduction: The RAS-mitogen-activated protein kinase (MAPK) pathway has been deregulated in many cancers. Induction of the RAS-MAPK pathway triggers the initiation of transcriptional responses, which drive the cells towards cell proliferation. Mitogen and stress-activated kinases 1/2 (MSK1/2), act downstream of the MAPK signalling pathway and phosphorylate histone H3 at S10 (H3S10ph) or S28 (H3S28ph) (nucleosomal response) at regulatory region of immediate early genes (IEGs), but the extent of effects and mechanisms has not been completely understood. **Objectives**: To investigate the nucleosomal response pathway and transcriptional programming. **Material and Methods**: RNA-sequencing, RT-qPCR, Co-Immunoprecipitation, Sequential-ChIP, Immuno-FISH). **Results**:RNAseq results validated by RTq-PCR on primary human fibroblast cells (CCD1070SK70) and colon cancer (HCT-116) show that MAPK mediated nucleosomal response pathway triggers IEGs transcription. MSK inhibitor H89 reduced the expression of IEGs. Immuno-FISH results of JUN and COX2 genes in primary human and mouse fibroblast cells show that MSK-catalyzed H3S10 and H3S28 phosphorylation are located at distinct nuclear sites which suggested that these do not coexist on the same histone tail. Sequential ChIP and Immuno-FISH analyses show that epi-alleles of IEGs are transcriptionally active regardless of phosphorylation site (H3S10ph/H3S28ph). Our co-IP experiments show that H3 modified at S28ph is associated with K27ac and K14ac but not at K9ac, while H3 modified at S10ph is associated with K9ac but not in K14ac and K27ac. Both H3S28ph and H3S10ph are modified at K4me1. **Conclusions**: MSK-catalyzed phosphorylation of H3S10 and H3S28 are located at different distinct nuclear sites and phosphorylation events are independent of each other.

PO 90:Association of prognostic parameters with cytogenetic and molecular markers at presentation in Indian children with highrisk acute lymphoblastic leukemia

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Introduction: Acute Lymphoblastic Leukemia(ALL) is the commonest leukemia in pediatric age group with relapse rate of up to 20-25%. Despite improved treatment regimens and targeted treatment, the mortality and relapse rate are still high in India. **Objectives**: To determine the association of clinical and hematological prognostic parameters as assessed with treatment responsewith cytogenetic and molecular markers **Material and Methods**: The association of 18 Indian children with acute lymphoblastic leukemiawith hyper-leukocytosis(total leucocyte cont >1,00,000 cells/cmm) was studied with cytogenetic and molecular markers in this observational case series. Chromosomal analysis, Fluorescence in situ hybridization and RT-PCR was done on these patients for known recurrent translocation associated with ALL. IKZF-1 deletions were detected by multiplex ligand probe amplification assay (MLPA) method (IKZF1 P335, MRC-Holland, Amsterdam, NL) was used to detect IKZF1 deletion and validated withIKZF1 P-202, MRC-Holland, Amsterdam, NL according to the manufacturer"s instructions. Fragment analysis was performed using GeneScan v.3.5 ABI3130, Applied Biosystems, Foster City, CA) or coffalyser analysis software. CRLF-2 gene expression was performed by quantitative real time polymerase chain reaction (qRT-PCR) using comparative Ct method to quantify relative mRNA levels using endogenous control gene, GAPDH with Taqman gene expression assay **Results and Conclusions**: 5/18 ALL cases with hyper-leukocytosis were associated with high risk cytogenetics, while 4/18 cases were associated with adverse treatment outcome. Newer molecular markers like IKZF-1 and CRLF-2 expression were studied in children with acute lymphoblastic leukemia and association of these markers with other prognostic parameters was evaluated (results will be discussed).

PO 91: Immunohistochemical expression of cyclo-oxygenase 2 and peroxisome proliferator activated receptor γ: Role in aggressive behaviour of eyelid sebaceous gland carcinoma

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Introduction: Sebaceous Gland Carcinoma (SGC) is a malignancy associated with pilosebaceous unit and occurs at ocular and non ocular sites. Cyclooxyegenases (COX) are enzymes crucial for lipid metabolism. COX-2 is over expressed in carcinomas. Inhibition of COX-2 through nonsteroidal anti-inflammatory drugs is known to reduce the risk of many cancers. PPARγ (Peroxisome Proliferator Activated Receptor γ) is a transcription factor involved in adipogenesis. PPARγ is a key potential therapeutic target for treatment of malignant tumors including colon carcinoma. The status of COX-2 and PPARγ in human eyelid SGC was evaluated to explore their utility as diagnostic and prognostic marker. **Objectives**: Given the potential clinical use of an immunohistochemical marker applicable to formalinfixed paraffin-embedded sections and to provide insight into the role of COX-2 signalling pathway and PPARs in eyelid normal skin and sebaceous carcinoma, the present study was designed to study the role of PPAR- γ and COX-2 in eyelid sebaceous carcinoma. **Material and Methods**: The immunohistochemical expression of COX-2 and PPARγ

was evaluated in 31 SGC cases. **Results**: Cytoplasmic expression of COX-2 was detected in 80% of the SGC cases and nuclear staining of PPARγ in 87%. PPARγ expression significantly associated with well differentiated SGC 19/21(90%). COX-2 over expression showed significant association with reduced disease-free survival. (P=0.0441, log rank analysis). **Conclusions**: COX-2 is highly expressed in eyelid SGC, suggesting that over expression of COX-2 could contribute to the aggressive behaviour of SGC. PPAR-γ was identified as a novel marker for terminal sebaceous differentiation in eyelid SGC. COX-2 signalling pathway in SGC could offer potential new therapeutic targets

PO 92: Cross-reactive antibodies against nontargeted HPV subtypes upon quadrivalent HPV vaccine administration

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Introduction: The quadrivalent-HPV vaccine is reported to elicit limited cross-protection against genotypically related HPV-subtypes. We utilize the IARC-initiated, ongoing, multi-centre vaccination study in India to assess cross-protective responses against non-targeted HPV types upon single, two and three doses of HPV vaccination. **Objectives**: Evaluation of the immune-responses of quadrivalent HPV vaccine against non-targeted HPVtypes. **Material and Methods**: We compared four cohorts of girls(9-18 years) from 9 sites receiving 3 doses on days 1, 60 and 180 or later (3-dose); 2 doses on days 1 and 180 or later (2-dose); 2 doses on days 1 and 60 by default (2doses/D); and 1 dose by default (1dose/D) for their levels and avidity of L1-binding antibodies through HPV-luminex assay and neutralizing antibodies by Pseudovirion-based neutralization assay for non-vaccine-targeted types related to HPV-16 and HPV-18. **Results**: The 2-dose protocol induced high peak geometric-mean immune-responses non-inferior to the 3dose protocol at month7 after first dose for the non-vaccine-targeted HPV-31/33/35/52/58/45. The geometric-mean immune-responses in 2doses/D groups at month 18 after first dose were non-inferior, whereas responses of 1dose/D group were inferior to 3-dose group for all 7 non-vaccine targeted HPVtypes analyzed. Avidity indices above 50% were observed at month18 after first dose in different dose groups for these 7 HPV-types except in 1dose/D for HPV-33, and 2-dose, 2doses/D and 1dose/D for HPV35. The proportion of samples with detectable concentrations of neutralizing antibodies for the 3-dose, 2dose, 2dose/D and 1dose/D vaccination cohorts at month18 after first dose were 51%, 39%, 29%,5% for HPV-31, 12%, 12%, 3%, 3% for HPV-33, 8%, 5%, 3%, 7% for HPV-45, and 2%, 0%, 0%, 2% for HPV58, respectively. **Conclusions**: These observations need to be correlated with genital HPV-DNA status and disease endpoints as immune correlates of protection are still unknown.

PO 93: Emerging role of Notch-3 in uterine cervical carcinogenesis.

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Introduction: Cervical cancer remains the most common cancer in women worldwide and the most frequent in developing countries like India due to infection with high risk human papilloma virus (HRHPV)-16. Limited reports are available for Notch signaling alterations in cervical carcinoma which play an important role in cell proliferation, differentiation, and apoptosis. **Objectives**: This study was aimed to evaluate the expression of Notch-3 in HPV positive Caski and HPV negative C-33A cervical cancer cell lines and to evaluate its role in context to HPV infection in cervical carcinogenesis. **Material and Methods**: Both cervical cancer cell lines were purchased from NCCS, Pune. Notch-3 protein expression was analysed by Real time PCR and Western blotting. **Results**: Up-regulated expression of Notch-3 was observed in HPV positive Caski ($p<0.001$) as compared to HPV negative C-33A cell lines by means of both Realtime PCR as well as by Western blotting. **Conclusions**: This suggest that the upregulation of Notch-3and its synergism with HPV infection may play an important role and may serve as a new marker for early diagnosis and therapeutic intervention for cervical carcinogenesis. This may lead to the design of novel strategies to improve therapeutic outcome of patients with cervical cancer.

PO 94:To study the association of C-Reactive protein with Prostate-specific antigen in patients with Benign prostatic hypertrophy and prostate cancer

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Introduction: C-Reactive protein (CRP) is a general marker of inflammationcorrelated with cancer risks and is also reported to have usability as a biomarker in urologic cancer. Prostate-specific antigen (PSA) is produced exclusively by epithelial cells of the prostate gland and increased serum PSA levels are an important indicator for prostate cancer. **Objectives**: In this study we aimed to examine serum CRP levels in men with prostate cancer and benign prostatic hypertrophy (BPH) and finds its association with serum Prostate specific antigen (PSA) level. **Material and Methods**: This case control study was conducted in Department of Biochemistry in association with Department of Urology. Twenty cases of newly diagnosed prostate cancer, twenty cases of BPH confirmed by trans rectal needle biopsy and forty age and sex matched healthy controls were included in the study.Patients with acute infections, rheumatoid arthritis, gout, asthma, chronic lung disease, myocardial infarction and those who had taken nonsteroidal anti-inflammatory drugs were excluded from the research. Serum CRP level was measured by ELISA. **Results**: The serum CRP level of the prostate cancer group was higher than that of the BPH group and controls. There was also a significant ($P < 0.05$) correlation of CRP level with prostate specific antigen (PSA) in those with cancer but not in BPH patients. **Conclusions**: The strong association of CRP with PSA in prostate cancer patients suggests a potential correlation between prostate inflammation and prostate cancer and that chronic inflammation may be a potential target for prostate cancer chemotherapeutics.

PO 95: Clinical Relevance of Senescence related genes (Stratifin and p16INK4a) in Ocular Squamous Cell Carcinoma

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Introduction: Ocular surface squamous neoplasia (OSSN) is the most common tumour of ocular surface. Senescence is a potent anticarcinogenic program, and neoplastic transformation involves a series of events that allow cells to bypass senescence. Stratifin and p16INK4a regulate senescence in human keratinocytes. Epigenetic silencing of the Stratifin and p16INK4a

through promoter methylation has been reported in various malignancies and is associated with aggressive behaviour. **Objectives**: To evaluate the status of Stratifin and p16INK4 in OSSN patients. **Material and Methods**:Sixty-four histopathologically confirmed OSSN cases (44 SCC and 20 CIN) were included. AJCC staging was done and patients were followed up for 36-58 months. Immunohistochemical expression and methylation status of Stratifin and p16INK4a was evaluated and correlated with clinicopathological features. Statistical analysis was also done to assess the prognostic significance of Stratifin and p16INK4a. **Results**: Loss of Stratifin and p16INK4a observed in 75% (48/64) and 72% (46/64) cases respectively. Promoter hypermethylation of Stratifin was seen in 63% (40/64) and p16INK4a in 53% (34/64) OSSN cases. Simultaneous methylation of both Stratifin and p16INK4a was present in 34% (22/64) (P=0.02) of OSSN cases. Stratifin loss was significantly associated with tumor size >2cm, AJCC T3 and T4 category, poor histopathological differentiation and reduced disease free survival (P 0.05). Cox analysis showed Stratifin to be an independent prognostic marker (p =0.03). **Conclusions**:Stratifin loss emerged as useful biomarker to identify high risk OSSN patients. Loss of Stratifin and p16INK4a in OSSN cases suggests that bypassing senescence is one of the important molecular mechanisms in the pathogenesis of OSSN.

PO 96: Differential expression profiling identifies pathways deregulated in early onset breast cancer

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Introduction: Breast cancer patients in India are younger in developing countries than their counterparts in developed nations. The proportions of young patients (< 35 years) vary from about 10% in developed to up to 25% in developing Asian countries, which carry a poorer prognosis. Changes in gene expression pattern that reset a cell program from a normal to a diseased state involve creating a characteristic signature of gene expression that defines the cell's unique identity. **Objectives**: To identify discriminating molecular signatures associated with pathogenesis of breast cancer in Indian women. **Material and Methods**: Study includes 40 histologically confirmed breast cancer patients with age ranging in two groups, Early aged <40yrs and Late aged >55yrs. Core biopsy tissue collected from tumor (40) and adjacent normal area (12) in RNA laterwas used for gene expression study using Ilumina Human HT-12vA Expression bead chip array. **Results**: Identification of Gene expression signatures in cancer has significant value in predicting the prognosis and treatment outcome. Here we identified key pathways getting dysregulated including mainly Axon Guidance, Cell Cycle, Viral carcinogenesis, Focal adhesion, Cyotkine Receptor Interaction, Neuroactive ligand receptor interaction. We identified various differential gene sets amongst Early vs Late, having significant role in cancer. Gene regulator network modelling helped in identifying key differentially regulated genes amongst TNBC vs TPBC, different STAGE"s of breast cancer. **Conclusions**: In this study we identified specific genes and biological pathways playing role in early aged onset of breast cancer

PO 97: Microtubule targeting agents Theaflavin and Epigallocatechin-3gallate synergistically induce autophagy as alternate death mechanism in cervical carcinoma HeLa cells.

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Introduction: Theaflavin (TF) and Epigallocatechin-3-gallate (EGCG), the potent polyphenols of tea, are well known to have anticancer activities in various cancer cell lines and in animal models. We have previously reported that their anticancer activity was significantly attributed by perturbation of tubulin- microtubule equilibrium of cancer cells. Both polyphenols depolymerize cellular microtubule, causing G2/M cell cycle arrest and apoptosis in cervical carcinoma HeLa cells. **Objective**: The aim of our study was to determine the effect of TF and EGCG on growth inhibition through induction of autophagy in cervical cancer HeLa cells and observe the underlying mechanism. **Materials and methods**: Autophagy was monitored by confocal microscope and was quantified in flow cytometer after staining cells with either Acridine orange or MDC stain and also studied the expression level of autophagy related proteins by western blot technique. Microtubule was seen under confocal microscope with rhodamine tagged antibody and all protein-ligand binding experiments were performed in fluorescence spectrophotometer. **Result**: Here we found that TF and EGCG could induce autophagy as a second type of programmed cell death in HeLa cells beside cellular apoptosis. Both TF and EGCG increased formation of acidic vacuoles in HeLa cells as revealed by acridine orange (AO) staining and MDC staining methods. Under similar conditions these polyphenols stimulated expression of Beclin-1 and conversion of MAP-LC3-I to LC3-II. Microtubule depolymerization was found to be the potent reason behind this autophagy induction. We also found that TF and EGCG could simultaneously bind to tubulin at two different sites and caused stronger microtubule depolymerization. TF binds at vinblastine binding site on tubulin and EGCG binds near colchicines binding site on tubulin. Thus, when combination of these two polyphenols was applied, a synergistic increase in autophagy as well as cell death was observed. **Conclusion**: We concluded from our observations that simultaneous binding of TF and EGCG at two different sites on tubulin exerted stronger microtubule depolymerization which contributed to synergistic induction of autophagy and subsequent cell death.

PO 98: Intrinsically disordered proteomic environment: A driver force in leukemogenesis

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Introduction: Association of ETV6-RUNX1 pre-leukemic origin with early clonal expansion fetal B-cell lineage cells is an in utero primary event generating numerous preleukemic clones. The accumulation of secondary hits acts as a catalyst in transformation of preleukemic clones into leukemia. ETV6 makes different fusion partners in broad range of myeloproliferative disorders through translocation. Since numerous studies have shown ETV6 involvement in chromosomal translocation, we have checked whether ETV6 is an intrinsically disordered protein. **Objectives**: To analyze proteomic interactome of ETV6 and its functional characterization. **Material and Methods**: STRING server was used for network prediction which builds network of interacting partners on the basis of known protein interactions. Protein-Protein interaction network was generated using ToppGenet which prioritizes neighbouring genes in Protein-Protein Interaction map. **Results**: ETV6 was found to be an unstable protein with instability index (II) computed to be 73.31 and is rich in amino acids promoting disorderliness. Protein-protein interaction network (PPIN) analysis using STRING web server showed multiple interacting partners with high confidence score. Strongest partnership was found with GATA binding protein 1 (globin transcription factor 1), which is a transcriptional activator having a role in erythroid cell development. It binds within regulatory regions of globin genes and to some other genes as well expressed in erythroid lineage cells. Majority of partner genes found were protein kinases, transcription factors or genes playing important role in signalling pathways.