



NMPAICON-2019

3rd Annual Conference of
Nuclear Medicine Physicists Association of India

April, 13th & 14th, 2019

April, 2019 Issue



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NMPAICON

3rd Annual Conference of Nuclear Medicine Physicists Association of India



13th & 14th April 2019
DELHI NCR (GURGAON)

2019



Meditorium, Fortis Memorial Research Institute, Gurgaon

WELCOME

Warm welcome to all for the Annual
Conference of Nuclear Medicine Physicist
Association of India (NMPAICON 2019)
in Delhi on 13th & 14th April 2019.

Theranostics-The Future is here

VENUE

Meditorium, Fortis Memorial Research Institute
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email : nmpaicon2019@gmail.com

Dr. Parul Thakral - Mob No: +91 9810654115
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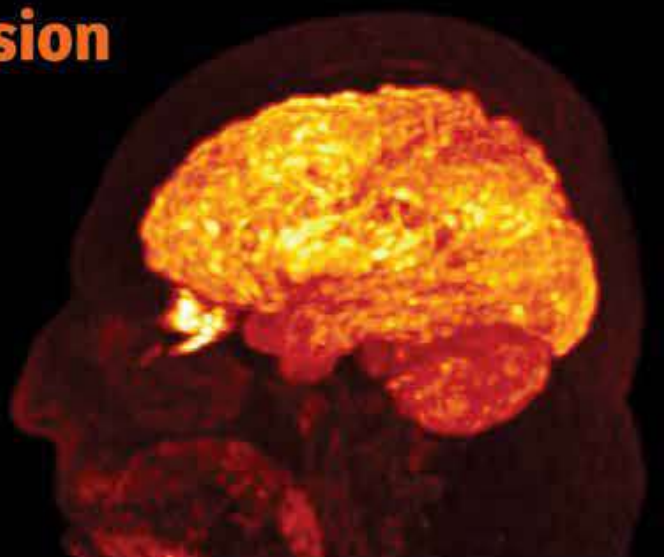
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डा० जी० के० राथ /Dr. G. K. Rath, M.D, FAMS
आचार्य विकिरण अणुवैज्ञान विभाग /Professor of Radiation Oncology
एवं अध्यक्ष, डॉ.बी.आर.अ.स.रो.कैं.अ., /& Chief, DR.B.R.A.I.R.C.H.
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MESSAGE

I give me immense pleasure to write a message for the Third Annual National Conference of the Society of Nuclear Medicine Physicists of India, being held in Delhi-NCR on 13th and 14th April, 2019. It is also bringing out a Souvenir to mark the occasion with more than 200 National delegates likely to be in attendance. As the Head of National Cancer Institute and Chief of Dr. B R A Institute Rotary Cancer Hospital of All India Institute of Medical Science, I can fully understand the importance of physicists and the aptly coined conference theme "**Theranostic- The Future is Here**" reflects its importance. I have gone through the scientific program and could see its rich qualitative and quantitative academic content. I am also able to envisage its great potential to discuss and learn the art and science of nuclear medicine. I hope the gathering of physicists and scientists at the Conference will provide a useful opportunity to the participants to deliberate upon various issues of nuclear medicine. On this occasion, I extend my best wishes to organizers and participants, and wish the Nuclear Medicine Physicist Conference success in its endeavours. I am sure the conference be a grand scientific extravaganza.

(Prof. G K Rath)

Subhash Chand Kheruka

President, Nuclear Medicine Physicists Association of India
Senior Scientist (Medical Physics)
Department of Nuclear Medicine
Snajay Gandhi Post Graduate Institute of Medical Sciences
Rae Bareli Road, Lucknow (UP), India

**Message**

On behalf of the Nuclear Medicine Physicists Association of India, It gives me an immense pleasure to welcome you to the 3rd Annual Conference of association (NMPAICON2019) in Delhi-NCR on 13th and 14th April 2019.

The theme of the conference is "Theranostics-The future is here". The scientific programme under this theme is designed in such a way that it will stimulate both scientific intellect and clinical knowledge in the field of diagnostic as well as therapeutic aspects of nuclear medicine starting from basic radiation physics , radiation protection to imaging and alpha therapy & beta therapy. I hope that this conference would provide a platform for fruitful interaction among delegates, exchanges of ideas, sharing information and experience among eminent faculties in the field of Medical Physics (Nuclear Medicine), Nuclear Medicine Clinics, Nuclear Medicine Radiopharmacy and Radiation Protection.

Nuclear Medicine Physics profession in India has long history and NMPAI was founded in 2007 with objective of encouraging the application of applied physics in Nuclear Medicine.

NMPAI always been in forefront in keeping the scientific sprit alive and organizing the professional and educational activities in various part of India.

I take this opportunity to sincerely thank all the delegates and faculties who have find valuable time to attend this conference in enhancing scientific acumen for each other.

I extend my best wishes to the organizer of this conference for great success.

With Warm Regards

A handwritten signature in blue ink, appearing to read 'Subhash'.

Subhash Chand Kheruka

Message



It gives me immense pleasure to send this message for the Souvenir being brought out on the occasion of 3rd Annual Conference of NMPAI being hosted by organizing committee of Delhi. The theme chosen of "Theranostics-The future is here" is indeed very appropriate, considering the important role & application of Nuclear Medicine Therapy in modern era.

I personally witness, the growth of NMPAI as one of the eminent association for Nuclear Medicine professionals since it is started in 2007. The annual meet is a unique part of development where professionals avail the opportunity of renewing friendships, building up new relationships, to discuss matters of common interest and furtherance of knowledge through various scientific sessions, orations as well as mutual interaction.

NMPAI had always been in the forefront in uplifting the field of Nuclear Medicine professionals by various activities and understand the need of members across the country.

I congratulate the members of organizing committee for bringing out this Souvenir and also express my thanks to those who have enriched this publication by various contributions.

I would like to thank all the participants, sponsors, invited speakers, who have contributed in the successful organization of great events. I wish the conference a grand success and send my congratulations to the organizing committee.

A handwritten signature in blue ink that reads "Amit Nautiyal". The signature is fluid and cursive, with a small flourish at the end.

Amit Nautiyal

Secretary

Nuclear Medicine Physicists Association of India

Dr Parul Thakral, PhD

Clinical Research Officer
Dept of Nuclear Medicine
Fortis Memorial Research Institute, Gurugram



Message

Dear NMPAICON 2019 Participants,

This gives me immense pleasure to write as the Organising Secretary of 3rd Annual conference of Nuclear Medicine Physicists Association of India (NMPAICON 2019) which is being organized under the aegis of Fortis Memorial Research Institute, Gurgaon, Delhi-NCR. The venue is more than just the capital and political epicentre of the country, also known as "City of dilwallas". This city blends modern with contemporary with surprising finesse. Art, culture, architecture, entertainment, fashion and, of course, politics—Delhi-NCR brings together all this and more.

The 3rd Annual Conference NMPAICON-2019 will try to provide a healthy platform to bring all together and share new ideas and recent advances in the field of diagnostic and therapeutic nuclear medicine. Since the theme of the conference is "Theranostics: The future is here", the scientific program is aimed to cover all the diagnostic as well as therapeutic aspects of nuclear medicine starting from basic radiation physics, radiation protection to imaging and alpha & beta therapy. I am sure that all the participants will have great learning experience from this academic meeting. I welcome you all at NMPAICON 2019 with great respect and gratitude.

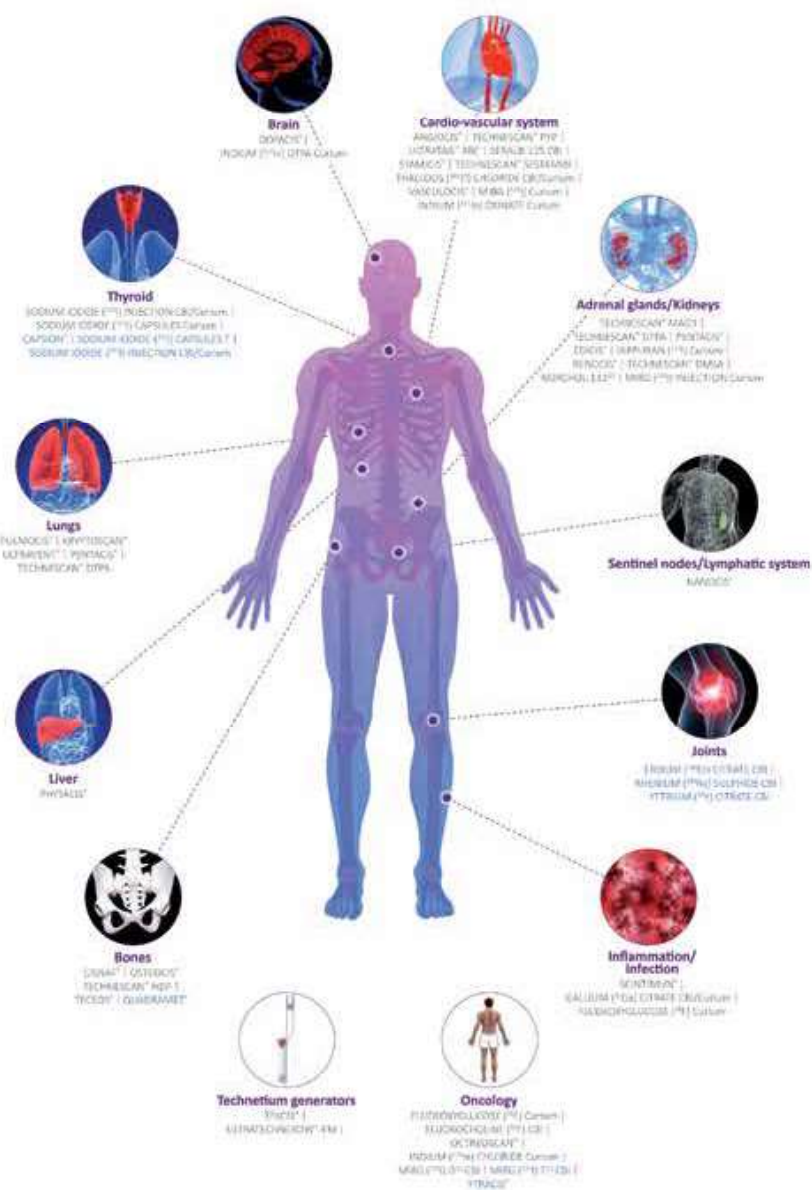
With kind regards



Dr. Parul Thakral

Organising Secretary
NMPAICON 2019

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NMPAICON - 2019

3rd Annual Conference of
Nuclear Medicine Physicists Association of India



Day - 1: Saturday, April 13th, 2019

PROGRAMME SCHEDULE

8:30 - 9:00 am	Registration	
9:00 - 9:30 am	Breakfast	
Session 1 :	Molecular Imaging and Therapy	Chairpersons: Dr Jaya Shukla, Dr Ishita Sen, Dr Anil Mishra
9:30 - 9:45 am	Dr Manish Dixit Asst. Prof. Nuclear Medicine, SGPGI, Lucknow	Cu-64"- Theranostic Radionuclide: Challenges and Opportunities
9:45 -10:00 am	Dr Puja Panwar Senior Scientist, INMAS, Delhi	Preclinical PET & MR imaging to visualize neurodeficits in brain: A step towards therapeutic intervention of neurocognitive disorders
10:00 - 10:15 am	Dr Sharmila Banerjee HEAD, RMC, BARC, Mumbai	Development in theranostic radiopharmaceuticals : options and availability in India
10:15 - 10:30 am	Dr Rakhee Vatsa Scientist, PGI, Chandigarh	188Re – Current scenario
10:30 - 10:45 am	Dr Parul Thakral Clinical Research Officer FMRI, Gurgaon	Preliminary experience with Ac-225 PSMA therapy
10:45 - 11:00am	Dr. Mohammad Mazidi PARS Isotope	New Therapeutic Radiopharmaceuticals of PARS Isotope Company
Session 2:	Radiopharmacy & Dosimetry	Chairpersons: Prof. GP Bandopadhyaya, Prof. Baljinder Singh, Dr Snehlata
11:00 - 11:20 am	Mrs Bhakti Shetye Scientific Officer, TMH, Mumbai	Evolution: New era of PET Rps
11:20 - 11:40 pm	Dr Aruna Kaushik Scientist, INMAS, Delhi	Radiation dosimetry in Pre-Clinical experimental Models
11:40-12:00 pm	Dr Vijayata D Chadha Assoc. Prof. Punjab University	Cellular response to ionising radiations: Role of epigenetic modulation
12:00 - 12:20pm	Dr Ankit Watts Medical Physicist, PGI, Chandigarh	Precision receptor imaging with 68 Ga-labelled peptides to combat various malignancies
12:20 - 12:40 pm	Dr Amit Nautiyal Scientific Officer , TMC, Varanasi	Physical & Biological aspects of Radiation Dosimetry in Nuclear Medicine
12:40 - 12:50pm	Mr Vikas Chaudhary Business Manager, Perkin Elmer	Perkin Elmer Solutions In Radiotherapeutics
1:00- 2:00pm	Lunch	
2:00pm - 2:45pm	Ernest Lawrence Oration	Chairpersons: Mr Subash Kheruka, Dr Amit Nautiyal
	Dr Natesan Ramamoorthy Senior Technical Advisor to Chairman, AEC, DAC	Indelible and continual impact on nuclear medicine by the cyclic accelerator cyclotron

Day - 1: Saturday, April 13th, 2019

Session 3:	Clinical Nuclear Medicine	Chairpersons: Prof. Arun Malhotra, Dr Uma Ravishankar, Prof. C.S.Bal
2:45- 3:00 pm	Dr Madhavi Tripathi Associate Prof, AIIMS, N.Delhi	Software-aided analysis of F-18 FDG brain PET images
3:00 - 3:15 pm	Dr Punit Sharma Consultant, Apollo Gleneagles Hospital, Kolkata	Contrast in PET/CT: Protocols and management of reactions
3:15 - 3:30 pm	Dr Deepanjan Mitra Head, AMRI Hospitals, Kolkata	Knowledge vs skills in a job in Nuclear Medicine Industry
3:30 - 3:45 pm	Dr Vidur Mahajan Associate Director, Mahajan Imaging, N.Delhi	Artificial intelligence & deep machine learning
3:45 - 4:00 pm	Seimens Healthineers	aM I Reddy ? for the Quiz ?
4:00 - 4:20 pm	Tea	(Parallel Poster Presentation in Meditorium)
Session 4 :	Free paper session	Chairpersons: Prof. Rakesh Kumar, Dr P.S Chaudhary, Dr Pankaj Dougall
4:20 - 4:30 pm	Mr Abhinav Baranwal	Comparison between effect of two Acquisition Time on Image Quality in whole body 18F-FDG PET/CT TOF studies in cancer patient
4:30 - 4:40pm	Mr Bhola Kumar	Comparison of Left Ventricular Ejection Fraction (LVEF) derived on Ordered Subset Expectation Maximization (OSEM) & Filtered Back projection (FBP) reconstructed images in 99mTc-MIBI myocardial perfusion SPECT
4:40 - 4:50pm	Mr Biju K Menon	Comparison of Radioiodine uptake by Gamma Camera and Thyroid uptake probe-based methodologies and Diagnostic Radioiodine Scan in Differentiated thyroid carcinoma
4:50 - 5:00pm	Mr Neeraj Sharma	Transport of F-18 FDG by road from distant supplier: Guidelines & Practical aspects
5:00-5:10pm	Mr Raman Kr Joshi	Improvising labelling method for commercially available BRIT [99m Tc]Tc-TRODAT-1 kits
5:10 - 5:20 pm	Mr Shamura CH	4D PETCT: Acquisition Protocol and Advantages
5:20 - 5:30 pm	Mr Satish Nigam	Potential Use of Radionuclide in Nuclear Medicine: New Frontier of Molecular theranostics
Session 5 : 5:30 - 6:00 pm	Brain Teasing Quiz	Chairpersons: Dr Chetan Patel, Dr Vineet Pant Moderator : Mr Sachin Tayal
6:15- onwards	Inauguration, Meditorium, FMRI	Chief Guest : Dr Eswara Reddy, DCGI Chief Guest of Honour : Prof. G.K Rath, Chief B.R.A. IRCH
7:30 pm onwards	Dinner & Cultural Evening	The Palms Town & Country Club B-block, Sushant Lok, Phase 1, Gurgaon

Day - 2: Sunday, April 14th, 2019

8:00 - 9:30am	GBM	
9:30 - 10:00 am	Breakfast	(Parallel Poster Presentation in Meditorium)
Session 6:	Image processing & reconstruction	Chairpersons: Dr Basant Malpani, Mr Sekhar Basu
10:00- 10:15am	Dr Anil Pandey Assoc. Prof. AIIMS, N.Delhi	Texture analysis & its application in NM
10:15 - 10:30 am	Dr Debabrata Dutta HEAD, RP& AD, BARC, Mumbai	Estimation of Uncertainty in Nuclear Medicine Based Radiation Dosimetric Measurements
10:30- 10:45am	Dr Dhananjay Kumar Asst. Prof RMLIMS, Lucknow	Digital Era: Needs to understand DICOM
10:45 - 11:00 am	Mrs Sneha Mithun Scientific Officer, TMH, Mumbai	Applications of natural language processing in onco -imaging
11:00- 11:15 am	Ashish Jha Scientific Officer, TMH, Mumbai	Role of Radiomics in NM leading to personalized treatment in cancer
11:15-11:30pm	Subash Kheruka Senior Scientist, SGPGI, Lucknow	Quantification in Nuclear Medicine
11:30 -11:40pm	Mr Patrik Pollare Director Sales, HERMES	OLINDA + Hybrid Dosimetry
Session 7:	Radiation Safety & Radiobiology	Chairpersons: Dr Debabrata Dutta, Dr Sarika, Mr Rajnath Jaiswar
11:45 - 12:00pm	Dr Pankaj Tandon Head IATS, BARC, Mumbai	Radiation safety aspects during handling unusual incidences and reporting Mechanism in Nuclear Medicine
12:00-12:15pm	Manju Saini Technical Officer, BARC, Mumbai	Regulation during safe transport of Radioactive material
12:15 - 12:30 pm	Dr Basant Malpani Sr. Scientist, BARC, Mumbai	Molecular mechanisms of radiation damage
12:30 - 12:45 pm	Dr Lalit Mohan Aggarwal Prof Radiotherapy, BHU, Varanasi	Experience in managing radiation emergency
12:45pm - 1:00pm	Dr Sudhir Chandana Scientist G, Head, Division of natural Radiation Response Mechanisms, INMAS	Revisiting radiation responses and risk assessment at low doses of ionizing radiation
1:00pm - 1:10pm	Mr Piyush Mathur Business Manager, Wipro GE Pvt Ltd	Latest advancements in Molecular Imaging

Day - 2: Sunday, April 14th, 2019

1:10- 2:00pm Lunch		
2:00 - 2:45 pm	Hal Anger Oration Prof. Sanjay Gambhir Head Dept of Nuclear Medicine, SGPGIMS, Lucknow	Chairpersons: Mr Subash Kheruka, Dr Amit Nautiyal
Session 8:	Quality Assurance & Instrumentation	Chairpersons: Dr Pankaj Tandon, Mr Surya Mishra, Mr Anindya Roy
2:45 - 3:00 pm	Dr Nikunj Jain Head, Molecular Diagnostics, GZB	Planning of a nuclear medicine facility: Clinicians expectation
3:00 - 3:15 pm	Dr Dibya Prakash Technical Officer, Molecular Diagnostics, GZB	Nuclear medicine Solutions
3:15 - 3:30 pm	Dr Rajeev Kumar Medical Physicist, AIIMS, N.Delhi	Challenges in cyclotron facility
3:30 - 3:45 pm	Dr Priyanka Gupta Med Physicist, AIIMS, N.Delhi	QC of SPECT in gamma camera
4:00 pm onwards	Valedictory Function	

Cu-64"- TheronosticRadionuclide : Challenges and Opportunities

Manish Dixit, NileshShanker, SubhashKheruka, Sanjay Gambhir*

Department of Nuclear Medicine, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow-226014

Objective:- ^{64}Cu is a useful radiotracer for positron emission tomography (PET) and a promising radiotherapy agent for the treatment of cancer. It has an intermediate half-life ($T_{1/2}$ 12.7 hrs) and a multiple decay mode that involves electron capture, and positron decay. These characteristic of ^{64}Cu useful for radiotherapy and for PET monitoring of tumors. Many production routes and processes have been reported to obtain no-carrier-added ^{64}Cu from targets of Ni and Zn. Among them, the $^{64}\text{Ni}(p,n)^{64}\text{Cu}$ reaction is a promising route, because this reaction can be performed by low energy protons from a compact cyclotron at a high production yield.

We produced the ^{64}Cu via $^{64}\text{Ni}(p,n)^{64}\text{Cu}$ using M/s Sumitomo Heavy Industries, Japan's HM-18 cyclotron and further target material was purified through automatic synthesizer to produced ^{64}Cu as $^{64}\text{CuCl}_2$.

Method:- Highly enriched ^{64}Ni was plated on a gold disk (24mm in diameter and 2mm thick) by electro deposition. Copper-64 was produced by bombardment of the ^{64}Ni target in a 18 MeV cyclotron with a $20\text{-}\mu\text{A}$ proton current. After bombardment, ^{64}Cu was separated from the ^{64}Ni target and purified from other contaminants by chromatography using an ion-exchange column. Final activity was eluted with concentrated 1.0M HCl yielding high-specific activity ^{64}Cu as anionic copper chloride.

Result:- We obtained ^{64}Cu in dried format a yield of 4-5 GBq at the end of bombardment, or 40 ± 5 MBq/ $\mu\text{A h}$ as the final product and further purification took 3.5 h of processing time. The metallic impurities were a satisfactory low level was obtained by a widely accepted separation using an anion-exchange resin.

Preclinical PET & MR imaging to visualize neurodeficits in brain: A step towards therapeutic intervention of neurocognitive disorders

Dr Puja Panwar

Division of Cyclotron and Radiopharmaceutical Sciences, Institute of Nuclear Medicine and Allied Sciences, Brig S.K. Mujumdar Road, Delhi, India

The functional brain imaging method using PET application with innovative radiotracers in the area of neurotransmitters, peptides and neoligands, have made it possible to track neurocognitive disorders at an early stage. But Multimodal Methodological approach is required to integrate information obtained with number of activity related to surrogate signal from single units to investigate fluctuations in neural activity. Thus advanced MRI and PET preclinical imaging could provide a key to personalized medicine for the treatment of neurocognitive disorders. The advent of attaching metal complexes to larger biologically active molecules has essentially created a new horizon in the field of biomedical applications. Recently there has been a significant growth of this branch with the availability of a number of radionuclides with excellent radiophysical properties and radiopharmaceuticals with high specificity. The functional brain imaging method using PET application with newer radiopharmaceuticals in the area of neurotransmitters, peptides and neoligands etc, have made it possible to study cognitive functions of the human brain across a wide range of behaviours. Recent methods and novel trends for the introduction of fluorine-18 into molecules are intended to serve as imaging agents for the in vivo imaging modality positron emission tomography (PET). The labeling methods for the introduction of radioisotope into complex organic molecules such as peptides or proteins are most often characterized by multistep synthetic pathways. One major concern is the inescapable alteration of an original

biomolecule by using ^{18}F -labeling techniques. Novel labeling methods in ^{18}F -radiochemistry are highly desired to reduce the complicated procedures to produce ^{18}F -labeled compounds for their application as imaging agents in nuclear medicine and life sciences. Great endeavours are currently being made to find novel routes to introduce the radioisotope into molecules to track neurocognitive disorders using PET and MR.

Developments in Theranostic Radiopharmaceuticals: Options and Availability in India

Dr Sharmila Banerjee

Radiation Medicine Centre, TMH Annexe, Parel, Mumbai, India

Abstract The term ‘Theranostics’ was first used by John Funkhouser in 2002 while describing his company’s business model in developing diagnostic tests directly linked to the application of specific therapies. ‘Theranostic’ refers to a combination of two interdependent applications namely therapy and diagnosis, using the same agent. Since both diagnosis and therapy can be effected using this concept of theranosis, the treatment regime can be individualized for planning a specific dose for a specific patient. This possibility forms the basis of ‘personalized medicine’ wherein the appropriate dose of a drug can be administered with respect to safety and efficacy. Since both diagnostic and therapeutic radionuclides are used in radiopharmaceutical preparation, the concept of, ‘theranosis’ is particularly relevant in nuclear medicine practices. In actual practice, theranosis can be effected by replacing a diagnostic radioisotope in a radiopharmaceutical with a therapeutic radioisotope usually with same chemical properties (i.e. ^{188}Re for $^{99\text{m}}\text{Tc}$), while using the same molecular vector, thereby not compromising the biological avidity of the radiopharmaceuticals. Theranosis helps in augmenting a diagnostic dose to a therapeutic one in order to tailor the therapy in a specific patient. In this modality, necessary pre-therapy information of biopharmacokinetics and dosimetry can be utilized to personalize the therapeutic regime. The talk will focus on the current developments based on the options and availabilities, in the field of theranostic Nuclear Medicine practice in India, with particular reference to the use of Gallium-68- and Lutetium-177- labelled theranostic radiopharmaceuticals.

Re-188: Current Scenario

Rakhee Vatsa

PGIMER, Chandigarh

Theranostic describes the combination of therapy and diagnostic imaging. Rhenium-188 (Re-188) is one of the various β^- -emitting theranostic radionuclide having favourable nuclear properties for radionuclide therapy with diagnostic imaging. The Re-188 show chemical similarities with the most commonly used diagnostic radionuclide technetium-99m (Tc-99m). Re-188 has a half-life of 16.98 h and decays via 100% β^- -emission to Osmium-188 (Os-188). In addition to emission of high-energy β^- particle ($E_{\beta\text{max}} = 2.1 \text{ MeV}$), γ ray emission of 155 keV is also present which is advantageously employed to monitor the course of therapy using a conventional gamma camera. Another important advantage of this radio-metal is easy availability through a transportable W-188/Re-188 generator system which offers cost-effective in-house radiopharmaceuticals preparation. Of the various Re-188 radiopharmaceuticals present, the Re-188 bisphosphonate complexes were the first to emerge in clinical application for palliative treatment of painful bone metastases in prostate cancer. The pentavalent Re-188 DMSA (V) complex was used in radionuclide therapy of medullary thyroid carcinoma and for metastatic bone pain palliation, along with the use of Re-188 MAG3 complex as a soluble β^- emitting agent to fill balloons for coronary angioplasty. The advent of other β^- emitting radioisotopes like Lu-177 and Y-90 led to decreased demand of Re-188 based radiopharmaceuticals in

2000s. However, resurgence in the development of Re-188 based therapeutic radiopharmaceuticals has been seen again, reversing the previous trend. Re-188 is now being used routinely for the treatment of non-resectable liver cancer, metastatic bone cancers, non-melanoma skin cancer, keloids, and synovitis. Re-188 has also been explored for radiolabeling of monoclonal antibodies for radioimmunotherapy. Several Re-188 based monoclonal antibodies have reached the stage of clinical trials. These include 'anti-CD66 monoclonal antibody' for patients with high-risk acute myeloid leukemia and an 'IgG based anti-carcinoembryonic antigen monoclonal antibody MN-14' for advanced gastrointestinal cancer. Newer cores like nitrido and tricarbonyl, have been investigated for achieving better radiolabeling yields. Utilisation of these approaches are also adding to higher specific activity products with favourable pharmacokinetics. Overall, the generator produced Re-188 possesses ample scope in cost effective theranostics.

Preliminary experience with ^{225}Ac -PSMA therapy in patients of metastatic castration resistant prostate carcinoma

Dr Parul Thakral, Dr Ishita Sen, Dr Vineet Pant

Department of Nuclear Medicine, Fortis Memorial Research Institute, Gurgaon

Prostate-specific membrane antigen (PSMA) is a promising target in prostate cancer. Recently, we started the first-in-human treatment with an α -radionuclide-labeled PSMA ligand. We report our experience with ^{225}Ac -PSMA-617 therapy in 20 patients who underwent ^{225}Ac -PSMA therapy between July 2017 and Jan 2018 at Department of Nuclear Medicine, Fortis Memorial Research Institute, Gurgaon. Targeted alpha therapy with ^{225}Ac -PSMA-617 was administered in a salvage setting in patients who had exhausted all conventional modes of therapy, had progressive castration-resistant prostate cancer with increased PSMA expression of most lesions as determined by PSMA-targeted imaging. PSMA-11 PET/CT validated the presence of the PSMA-positive tumor phenotype. A 100-kBq activity of ^{225}Ac -PSMA-617 per kilogram of body weight was administered at 2-3 months. Prostate-specific antigen response and hematologic toxicity were measured at least every 4 wk. Serial full blood count, renal function test, and liver function were obtained to determine treatment-related side effects. Restaging was performed with ^{68}Ga -PSMA-11 PET/CT. Post therapy ^{225}Ac -PSMA-617 whole body emission scans were acquired at 2 hrs and 24 hrs using the 440-keV g-coemission of ^{213}Bi (26% emission probability) 218-keV g-coemission of ^{221}Fr (12%) at a speed of 6cm/min, matrix 256 x 1024 pixels equipped with a high-energy collimator. PSA decline was seen after treatment in 16/20 patients, including 4/16 patients with >90% PSA decline and 10 /16 with >50% PSA response following two or three cycles of ^{225}Ac -PSMA-617. Good antitumor activity on ^{68}Ga -PSMA-PET/CT was seen. 15/30 showed partial response, 4/30 patients showed stable disease and 11/30 patients showed disease progression. 7/11 patients died of progressive disease after achieving initial radiological and biochemical response. One patient died of a cause unrelated to cancer while in continuing radiological and biochemical response. Grade 1/2 xerostomia was seen in all patients, and none was severe enough to lead to discontinuation of treatment. The group presented with significant palliation of bone pain and reduced toxicity to salivary glands. Targeted α -therapy with ^{225}Ac -PSMA-617, although still experimental, obviously has strong potential to significantly benefit advanced-stage prostate cancer patients.

Evolution: New Era of Pet radiopharmaceuticals

Bhakti Shetye

Department of Nuclear Medicine and Molecular Imaging, Tata Memorial Hospital, Mumbai

In 1950, neurosurgeon Dr. William Sweet and physicist Gordon Brownell developed a predecessor to PET image using NaI as scintillation detector. But its low density, high scatter led to introduction of bismuth germanate (BGO) as new pet scintillation detector. In 1976, Sokoloff, Wolf et al synthesized

2-fluoro-2-deoxy-D-glucose and labelled by 18-F. Introduction of 18F-FDG as a radiotracer for PET imaging opened up plethora of development of new radiopharmaceuticals for evaluation of biochemical and physiological process.

Currently labelling of biologically active peptides with positron-emitting nuclides has emerged as a useful and interesting field in nuclear medicine. Small synthetic receptor-binding peptides are currently the preferred agents over proteins and antibodies for diagnostic imaging of various tumours. Due to the smaller size of peptides, both higher target-to-background ratios and rapid blood clearance can often be achieved with radiolabelled peptides. Among a number of positron-emitting nuclides, like O-15, C-11 and N-13, F-18 appears to be the best candidate for labelling bioactive peptides by virtue of its favourable physical and nuclear characteristics.

F-18 has characteristics for peptide-based imaging since the half-life (110 min) matches the pharmacokinetics of most peptides. In addition, the low positron energy of 635 keV results in short ranges in tissue, which results in excellent preclinical imaging resolution. The major disadvantage of labelling peptides with 18F is the laborious and time-consuming preparation of the 18F labelling agents. In recent years, various techniques have been developed which allow efficient labelling of peptides with 18F without affecting their receptor-binding properties. Moreover, the development of a variety of prosthetic groups has facilitated the efficient and site-specific labelling of peptides with 18F. NOTA conjugated 18F- Octreotide, 18F-RGD showed promising results.

An alternative production of positron-emitting radionuclides is via a generator. 68Ga produced by 68Ge/68Ga generator is of great interest. It has a physical half-life of 67.71 min, which is compatible with the pharmacokinetics of most radiopharmaceuticals of low molecular weight such as antibody fragments, peptides, aptamers and oligonucleotides. The average positron energy per disintegration is 740 keV ($E_{\beta} \text{ max } \frac{1}{4} 1899 \text{ keV}$), which is higher than that of 18F and potentially leads to a somewhat lower resolution. Ga 3+ exhibits well-established coordination chemistry with different open chain ligand like DTPA and cyclic ligand like DOTA, NOTA. Imaging of neuroendocrine tumour based on somatostatin receptor with DOTATATE, DOTANOC, DOTATOC has gained immense popularity. Targeting of GLP-1 receptor by 68Ga-Exendin-4 helped in localization and imaging of insulinoma where complete tumour resection is choice of treatment.

Gastrin releasing peptide analogue Bombesin is labelled with 68Ga. GRP receptors have been demonstrated in major human tumors such as breast cancer, prostate cancer, in high density prostatic intraepithelial lesions, peritumoral vessels of ovarian cancer, renal cell cancer, small cell lung cancer, and gastrointestinal stromal tumors. $\alpha v \beta 3$ integrin receptors are overexpressed in angiogenesis. 68Ga labelled RGD compounds may be used for the diagnostic imaging, pretherapeutic dosimetry and therapy planning and monitoring. CD163 receptor expressed in monocytes and activated macrophages are targeted with an anti-CD163 antibody labelled with 68Ga in rats with acute collagen-induced arthritis. The agent demonstrated specific binding and its potential for studies of inflammatory diseases. 68Ga labelled biotin, siderophores, ubiquitin, benzofuran have shown promising results.

89Zr has emerged as a promising radionuclide having favourable physical characteristics. It emits positron with mean energy of 0.250 MeV which produces high resolution PET images. It has long physical half-life of 3.71 days which is suitable for imaging of antibodies, nanoparticles, liposomes, targeted nanotubes and other large bioactive molecules. 89Zr can also be used for Cerenkov luminescence imaging. It exhibits application in image guided surgery using 89Zr labelled antibodies. New radionuclides are ushering in various developmental projects to fulfill the requisites of studying numerous biological processes.

Radiation Dosimetry in Pre-clinical Experimental Models

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With the advancement in molecular imaging, the demand for developing specific and sensitive novel molecular imaging agents has also increased. However, the prerequisite to translate the study of these radiopharmaceuticals in animal models to human clinical trials is pre-clinical radiation dosimetry. This enables to estimate radiation dose in humans and compare with the recommended dose limits. The objective of radiation dosimetry is to obtain satisfactory diagnostic images while limiting the harmful effects of radiation.

Prediction or estimation of radiation dose in humans from small animal models can be done either by ex-vivo biodistribution studies or in-vivo imaging studies.

Ex-vivo biodistribution studies:-

For ex-vivo studies, the organs are harvested post injection at several time points to establish the biodistribution of the novel radiopharmaceutical in small animals (Balb-c mice, n=5 per group). The organs/tissues commonly harvested are heart, lungs, liver, spleen, kidney, stomach, brain, muscle, intestines and bone. These organs are weighed and counted in a gamma counter. The uptake of the radiotracer in each organ is expressed as percentage uptake of injected dose per gram of tissue.

In-vivo imaging studies:-

An alternative to ex-vivo biodistribution studies is in-vivo imaging. Small animal imaging facilities like microPET or microSPECT are used to obtain dynamic images post injection of radiopharmaceutical. Uptake and time-activity curves can be obtained in a single scan.

Radiation Dosimetry:

The residence time in various source organs is calculated from the uptake studies. Relative organ-mass scaling method is used to obtain the corresponding values of residence time in humans. This is used as input in the radiation dosimetry software (OLINDA, Version 1.0, Vanderbilt University, USA). The predicted value of radiation dose to various target organs are obtained in terms of mGy/MBq. The estimated effective dose is expressed as mSv/Mbq.

Conclusion:

Pre-clinical radiation dosimetry is required to meet the regulatory standards regarding radiation dose for use of novel radiopharmaceuticals in human clinical trials. Conventional ex-vivo biodistribution studies or in-vivo imaging studies can be used to obtain radiation dose estimates. Maximum injectable dose according to radiation guidelines needs to be determined prior to human clinical trials.

Cellular response to ionising radiations: Role of epigenetic modulation

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Radionuclide therapy is one of the most intensively developing directions of nuclear medicine which is utilized in the case of metastatic cancers or disseminated diseases when conventional radiotherapy is impossible due to tumor localization near to sensitive organ, or when chemotherapy is too toxic. Investigating accurate radiobiology with respect to radionuclide therapy can contribute to the improvement of the therapeutic efficacy as the radiosensitivity of the cells is governed by radiobiological phenomena viz: radiation induced genomic instability and bystander effect. Although there are extensive reports on indirect (non-targeted) effect of external beam radiotherapy that contributes to the result of radiation treatment, however, there is lack of information and studies in context to these effects with radionuclide therapy. The initial events of interaction of ionising radiation with biological substrate involves generation of reactive oxygen species (ROS) via

radiolysis of water molecules resulting in oxidative DNA damage. There is emerging evidence that oxidative stress causes epigenetic modifications to the genomic structure while the underlying DNA nucleotide sequence remains unchanged. Epigenetic alterations are meiotically heritable and mitotically stable alterations in gene expression with no change in DNA sequence, which include DNA methylation, histone modifications, and RNA-associated silencing. Recently published studies indicate that low dose ionising radiation (LDIR) exposure affects DNA methylation patterns and also causes histone modification, thus providing compelling evidence that epigenetic changes generated caused by IR induced oxidative stress provides a mechanistic link between IR induced genomic instability. Further studies are warranted to evaluate IR-induced epigenetic gene regulation for better understanding of IR induced non targeted effects. Also the relative contribution of targeted and non targeted effects in organ and tissue response to radionuclide therapy needs to be explored to better elucidate its role on health outcomes.

Precision receptor imaging with 68 Ga-labelled peptides to combat various malignancies

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Insight into tumor biology has shown that tumor cells are equipped with an array of biologically active surface molecules, and several of this function as receptors for various ligands. The molecular mechanism of malignant transformation is changing the way cancer is being treated. Precision strategies have now been developed that specifically disrupt oncogenically active cell surface receptors and endogenous signaling molecules. Most widely studied cell receptors in oncology are cytokines /chemokine's receptors, growth factor receptors, FAS-ligand, HLA antigens etc. The alteration in their expression usually leads to tumor growth and metastasis. In-depth knowledge about the expression of tumor-cell receptors may provide information essential for the creation of tools paving way to various targeted therapies.

Traditionally the unique or over expression of these receptors has been obtained by in-vitro assay of biopsy material, but in last decade Tumor receptor imaging has emerged a power tool to image these receptors. This non-invasive technique edges over the in vitro assay as it provides in depth information on receptors expression and hence disease burden even of challenging sites which are difficult to sample or assay.

Most challenging part in Tumor receptor imaging is the design of radiopharmaceuticals (RP) and imaging approaches. As the receptors have high affinity for their ligands and are active at nano-molar concentrations of the ligands. Hence ideal radiopharmaceuticals have to be very specific to accurately visualize the receptors and their expression.

The radioisotope of a RP should possess characteristics both of favorable imaging agent as well as versatile chemistry in-order to be easily tagged with peptides.

One potential positron emitting radionuclide that has blossomed in recent times is ⁶⁸Ga (Gallium) because of several reasons. One is superior image quality compared to SPECT radionuclides; another is the potential for an on-demand production via generator (⁶⁸Ge-⁶⁸Ga) technologies that provide reliable & high-purity ⁶⁸Ga in sufficient quantities for routine radiopharmaceutical production without the need for expensive cyclotron operations. Versatile chemistry of ⁶⁸Ga allows it to be labeled with numerous DOTA- peptides as well as variety of mono-functional and bifunctional chelators forming stable complex with various biomolecules.

Though numerous researches have been carried out & are ongoing worldwide trying to tag various biomolecules (peptides/antibodies) with ⁶⁸Ga but there are few ⁶⁸Ga- radiopharmaceuticals that have really transformed from bench to bedside. Few such potential radiopharmaceuticals are: ⁶⁸Ga-DOTA- SSTR's analogues (TATE, NOC, TOC)

⁶⁸Ga- PSMA (Prostate cancer Imaging), ⁶⁸Ga-RGD (Angiogenesis marker), ⁶⁸Ga-Pentixafor (Chemokine CXCR4 imaging)

Physical & Biological aspects of Radiation Dosimetry in Nuclear Medicine

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Increasing the use of ionising radiation in Nuclear Medicine application has raised the concern among society. This is because of associated risk of low dose ionising radiation in Nuclear medicine procedures. Radiation risk mainly associated with biological effects such as indirect effects which may take place due to formation of free radicals in water and sometime direct effects to DNA. Nuclear medicine uses small amount of radioactivity for the functional imaging and treatment of various diseases. It is still unclear the dose response relationship for different short lived tracers being used in Nuclear Medicine.

There are several methods available for the estimation of radiation dose in certain organs. In an Imaging ie. planar imaging, 3D imaging based method, estimation of absorbed dose in internal organs can be done using time activity data. Here activity concentration in source organ is used to estimate the dose in target organ. The Monte Carlo simulations & MIRD method is considered as most accurate and reliable way for the estimation of absorbed dose in internal organs. The dose estimation using Monte carlo simulation is time consuming in comparison to other methods. TLDs (thermoluminescent dosimeters) can also be used externally to estimate the radiation dose in different organ after administration of radiopharmaceuticals. Practically, the dose estimated by MIRD was always accurate than that of TLD method, because the dose measured by MIRD in internal organ always attenuated corrected.

The another method of estimation of absorbed dose of ionising radiation is biological dosimetry, which is an established method to assess the radiation dose following radiation exposure. If physical dosimetry is not feasible, biological dosimetry can also be used as an alternative and reliable method. Biological dosimetry consists of different methods ie. Comet assay, Gamma H2AX assay, sister chromatid exchange, chromosomal breaks, fluorescence in situ hybridization (FISH) or micronucleus (MN) which are used to define the frequency of micronucleated cells in lymphocytes. Recent studies have clearly shown strong correlation between frequency of radiation-induced MN and radiation dose. Apart from this, the dicentric chromosome (DC) is known as one of the most sensitive and reliable biomarker in acute radiation exposure. DC in the FISH images can be estimated using fluorescence imaging software. In order to use the biological dosimetry for dose assessment, the first step is to determine the frequency of DNA damage, MN, aberrations in the peripheral blood lymphocytes of exposed human being. Thereafter, the radiation dose may be estimated using dose response curve.

Software-aided analysis of F-18 FDG brain PET images

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F-18 Fluorodeoxyglucose as a radiotracer reflects glucose metabolism in the resting brain. Patterns of abnormal glucose metabolism characterize various neurological disorders and FDG PET has an important role to play in neurodegenerative disorders like Alzheimers disease dementia and Parkinsons disease.

F-18 Fluorodeoxyglucose brain PET images can be analysed visually, by simple eyeballing. This approach can be prone to interpretation errors and strongly depends on the experience and training of the reading physician. FDG-PET with a quantitative component using software-aided analysis may increase diagnostic performance of FDG PET for detection of disease related patterns. Various robust data-driven voxel-based approaches are presently available with age-adjusted t-statistics. These can be broadly divided into FDA approved vendor-provided softwares, like Scenium (Siemens), Cortex ID (GE), and Neurogam (SegamiCorp.) or softwares developed by neuroimaging groups that are available for free download like statistical parametric mapping (SPM) (Wellcome Trust Centre for

Neuroimaging – UCL), Neurostat-3D Stereotactic surface projection (SSP)(Neuroimaging and Biotechnology Laboratory-University of Utah) and Scaled subprofile models-principle component analysis (SSM-PCA) (ScAnVP-Feinstein Institute for Medical Research) to define disease-related patterns. Another way to classify them would be approach based like SISCOS and SISCOM for brain perfusion images and various automated approaches to evaluate dopaminergic imaging.

The addition of a software aided approach alongside qualitative visual interpretation could significantly improve the diagnostic performance of brain PET images and a dual read approach can greatly improve the confidence of reader interpretation. Fully automated quantitative software approaches without reader input have shown improvements in terms of diagnostic accuracy compared to beginner readers. One benefit of a software-aided approach is its ability to improve reader specificity, especially for readers who may overemphasize physiological minimal changes that are part of inter-subject variability. This could be useful in early stages of the disease process wherein early changes can be unmasked and a negative scan could be useful to rule out the disease process.

Contrast in PET/CT: Protocols and management of reactions

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With the advent of hybrid imaging in the form of PET-CT and SPECT-CT, use of iodinated CT contrast material has gained widespread use in routine clinical nuclear medicine practice. Addition of CT contrast not only improves characterisation of various lesions seen on PET-CT or SPECT-CT, it also improves and simplifies anatomical detailing. Detailed knowledge of various contrast CT protocols is vital for performing an optimised hybrid imaging test. Also, use of CT contrast is associated with its own set of risks and complications, ranging from an innocuous urticaria to life threatening anaphylaxis. Familiarity with these complications and knowledge about how to manage them is very important for patient safety. It's time for the Nuclear Medicine professionals, both physicians and technicians to educate themselves about CT contrast protocols, reactions and their management. Only then we will be able to provide "one stop shop" imaging for our patients.

Knowledge and skill in a job: How does Nuclear Medicine industry look at it?

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The growth of Nuclear Medicine in India has been phenomenal in recent past. We have seen setting up of many new departments across the country including tier 2/3 cities. This has happened largely because of immense impact of PET CT in clinical decision-making. This growth has created a huge demand of Nuclear Medicine professionals, both clinical and paraclinical.

With increasing demand, there are many new teaching institutes who have started offering courses to build an effective manpower. Courses have been designed and redesigned to suit the need of the market. It is heartening to see many young professionals have been offered high paying jobs in different hospitals and diagnostics centers in last decade. The growth looks lucrative even in coming days with many new cancer hospitals being planned.

However, with passing time, it has been realized that uniformity of teaching curricula across different teaching institutes is perhaps required to maintain a certain baseline standard. Due to varying syllabi and exposure, each candidate who passes out their exit examination does not match with another from a different institute. This creates a real problem in job industry. We need to collectively formulate a technical teaching program which addresses this basic tenet of such an important course.

The Indian education system has traditionally been dependent on academic qualifications and their paraphernalia. It is the degree of an individual that matters most in being selected in a job than his/her skill at times. Similarly, the stringent and old criteria of years spent in particular kind of jobs too at

times compromise on the quality of a manpower. We need to understand that knowledge and skill of a technical person should have a balance. This is possible when we inculcate this philosophy in designing the course and teaching modules.

Employability of a candidate should never be based on certain mark sheets. It has to be evaluated against the merit and skill too. The Nuclear Medicine fraternity as a whole hence needs to focus on a real time check on the kind of a teaching module that is required for future need of the specialty.

Texture Analysis & its application in Nuclear Medicine

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Texture refers to a property that refers to the surface and structure of an image. In broader terms, it has been defined as a regular repetition of an element or a pattern on a surface. However, in purview of Medical Imaging, textures can be defined as complex visual patterns that are composed of entities or regions of sub-patterns with algorithms for characterization of various entities such as the brightness, color, shape, size etc. Rosenfeld, considered as one of the pioneers in the field of texture analysis, defines texture as similarity grouping in an image.

More recently, PET image texture analysis was proposed to characterize the heterogeneity of tumor F18-FDG uptake. F18-FDG uptake is not homogeneous across the tumor because of necrosis, cell proliferation, microvessel density, and hypoxia. It has been shown that tumor heterogeneity can be associated with disease progression, response to therapy, and malignant behavior of the tumor.

Texture provides essential information for the classification of many types of images. Texture can be defined as the set of local neighbourhood properties of the gray levels of an image region. Texture analysis is considered a challenging task. The ability to effectively classify and segment images based on textural features is of key importance in medical image analysis.

A wide variety of texture analysis methods has been proposed. Statistical method (for example, the gray-level co-occurrence matrix method) exploit the local correlations of image pixels on a fixed scale. Structural methods make a description using texture primitives and syntactic rules. Recently, there is an increased interest in model based approaches where several studies report highly successful experiments using Markov random fields. Spectral methods look at the properties of Fourier spectra, hereby capturing global information about the energy distribution across scales. All these methods have in common that they extract the characteristics that are believed to be most important in particular texture characterisation problems. They highlight different aspects of texture, which is a too general and vague concept to encompass in a single description.

One of the most important aspects is of texture is scale. Psycho-visual studies indicate that the human visual system processes images in a multiscale way. The "early processing" in the brain performs a kind of spatial frequency analysis, and consequently, the visual cortex has separate cells that respond to different frequencies and orientations. This multiscale processing, which humans obviously apply successfully to texture perception, is a strong motivation for wavelet based texture analysis methods.

This lecture will give an introduction to the application of wavelet based multiscale image analysis methods to texture analysis. The application of texture analysis in classification of responder and non-responder PET/CT fused images of NSCLC patients will be discussed.

Digital Era: Need to understand DICOM

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DICOM (Digital Imaging and Communications in Medicine) standard is now an essential part and backbone of modern image display, equivalent only to film in the pre-digital era. Since the inception of DICOM standard some 25 years ago, it has become the driving force behind the entire imaging workflow and standard protocol for the management and transmission of medical images and related data and is used in many healthcare facilities. DICOM was originally developed by the National Electrical Manufacturers Association (NEMA) and the American College of Radiology (ACR). It is a registered trademark of NEMA and is governed by the DICOM Standards Committee, a collaboration of users across all medical imaging specialties with interest in the standardization of medical imaging information.

This was very important with the introduction of advanced imaging technologies, such as PET-CT, SPECT, Computed Tomography (CT) and day by day growing use of computing in routine clinical work and for that ACR and NEMA saw a need for a standard method to transfer images and other associated patient related information between different vendor devices, according to the International Organization for Standardization. These devices produce a variety of digital image formats. It truly controls all parts of digital image acquisition, transfer, and interpretation and many imaging specialists including Nuclear Medicine Physicist, Medical Physicist, Nuclear Medicine Physician, Radiologist, and other users who may not realize to what extent their work relies on DICOM capabilities. Today's Medical Industries and all of us depend on DICOM extensively, and we cannot think existence without DICOM. DICOM, we use to collect the original medical images with the best possible information. Although this process is much more complex compared to X-ray film but is also much more accurate and complete. We use DICOM to store, distribute, and send, images, irrespective of modal of a machine, machine, and manufacturer. DICOM controls appropriate image display, and without DICOM post-processing of image would be impossible, whether it is simple multiplanar reconstruction, or more advanced perfusion analysis, various types Quantifications, virtual endoscopy, volume segmentation, or computer-aided diagnosis (CAD). DICOM has given us much of the ease and flexibility that we enjoy in our work. As digital Imaging becomes increasingly complex and imaging projects globalize, knowledge of DICOM basics for any healthcare professional becomes crucial. Whether we are thinking about next PACS upgrade, or a new teleradiology/ tele nuclear medicine project, or about merely commissioning a new digital modality, DICOM would be the essential reference now. Hence now we can say that DICOM-based workflow is the only way to build a robust and efficient Imaging practice and it is also the only way to integrate our medical imaging modalities into a complete enterprise-wide EMR (electronic patient record solution).

Application of Natural Language processing in Onco-imaging

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Abstract: A human understanding human language is difficult enough. Imagine getting a machine to do it. Free text discourse is generally used for describing a lot of medical reports or records. This serves not only as a means of record but also as a means of communicating to another the scenario. This method although an excellent way to communicate the disease status and patient condition, however, is still time consuming and fails when specific objective oriented bulk searches are performed. In this era of personalized medicine, the increasing cases of cancer globally, increasing research in the field, it is becoming increasingly important to capture maximum information related to disease processes, treatments, outcomes etc. Most of these are present in free text format in electronic or non-electronic format. All imaging reports are in free text format. This valuable information is in such huge quantity that having a human analyze and interpret them is extremely tedious and time

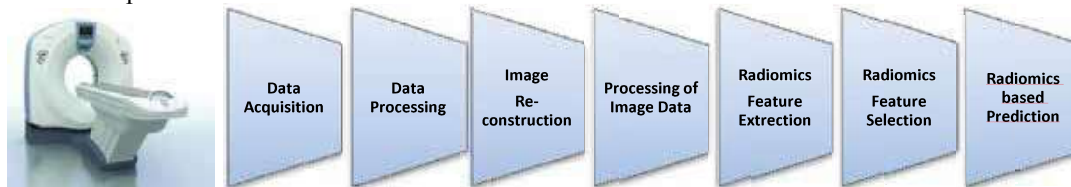
consuming. Hence, machine learning techniques and artificial intelligence is being used to aid humans with this exercise. Natural language processing helps machine learning tools in interpreting and extracting useful information from unstructured free text. The free text is analysed using NLP algorithms in several steps involving pre-processing, syntactic analysis, semantic analysis, negation detection and knowledge extraction Fig(1). Several NLP tools are available and being developed. These have applications in imaging in for diagnostic surveillance, cohort building, query-based retrieval, quality assessment of radiologic practice, clinical support services. Diagnostic surveillance helps in auto-generation of alerts. NLP helps in automating case identification for cohort building. Query-based case retrieval with NLP using lexicons helps in quickly retrieving cases with a broad range of purposes. Quality assessment of radiologic practice helps in improving reporting quality. Clinical decision support services are used for assisting the radiologist at the time of reporting. Other applications include use of error correction in speech recognized reporting. NLP can also be use for converting the existing unstructured reports into structured clean corpus for future use in research. The use of NLP in such data will be useful in furthering and improving research in the field of cancer and aiding in personalized medicine approaches.

Role of Radiomics in Nuclear Medicine leading to personalized treatment in cancer

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Introduction: Medical images (CT/PET/MRI/SPECT/Ultrasound /X-ray) are not only pictures, they are big data, which opens enormous probability for imaging scientists. Several kinds of image analysis are possible by exploring big data in imaging. Radiomics is one of such image analysis by using big imaging data. The high-throughput extraction of quantitative features from medical image and the subsequent analysis of these features for decision support system in medicine are termed as radiomics. Around 2000 radiomic features can be extracted from the medical images. Radiomics features can be divided into following category First-order statistics: first order features are histogram-based methods that reduces the region of interest to single statistical values. These features shows mean, median, maximum, minimum, and uniformity or randomness (entropy) of the intensities on the medical image. The skewness (asymmetry) and kurtosis (flatness) of the histogram of values are also the first order features. Shape base features: shape based features include the various descriptors of the three-dimensional size and shape of the ROI. These features are entirely independent from the gray level intensity distribution in the ROI and are therefore only calculated on the original image and mask of the tumor. Voxel Volume, Surface Area, Mesh Volume, Surface Area to Volume ratio, Flatness, Sphericity, Compactness are the examples of shape based features. Second or Higher-order statistical descriptors: second order or higher order features are based on the gray level intensity distribution, generally described as “texture” features. These features describe statistical interrelationships between voxels with similar or dissimilar contrast values in the images. Important second and higher order features are GLCM, GLRLM, GLSZM etc.

Radiomics process:



Challenges for the radiomics:

There are various parameters of image acquisition and processing that impact the radiomics feature extraction and need to be optimized. Following are the important factor that effect radiomic feature extraction: Image acquisition parameters (kV, mAs, slice thickness, activity administered, time of imaging, imaging time etc) Image processing (reconstruction algorithm) Tumour segmentation (differences) Feature extraction (No of bins , bin width, image filter applied) Feature selection Following stapes can be taken to overcome the challenges of radiomics

extraction: Harmonization the image acquisition and reconstruction parameters across Development of robust automated tumour contouring technique Selection of most suitable features and machine learning technique Implementation of multi-centric distributed learning Nuclear medicine and Radiomics The current radiomics paradigm consists in adding quantitative information to the visual analysis by radiologists and nuclear medicine physicians, rather than replacing it entirely. Various successful attempts have been made to find the utility of PET radiomics feature for prediction of treatment toxicity, progression free survival (PFS) and overall survival (OS). The aim of radiomics in Nuclear medicine in coming years will be Tumour identification, Tumour characterization, Disease staging, Disease Prognostication, Treatment prediction, Toxicity prediction, OS and PFS prediction and Clinical research. PET Radiomics may become a promising domain to assist physicians in decision-making and implement individualized treatment to the patient. In the era of big data and machine learning, closer collaboration is required among image processing researchers, physicians, physicists, and data scientists.

Conclusion: Radiomics and radiomics in nuclear medicine is new but a promising technology, hence standardization of radiomics process is paramount important to achieve the real benefit of the technology. Standardization of radiomics process can be achieved to encourage multi-centric study by distributed learning.

Quantification in Nuclear Medicine Imaging

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Over the past 15 years, there has been a great deal of progress in the development of methods for accurately quantifying nuclear medicine images. However, propagation of these methods into clinics has been slow. Nuclear medicine images can be used for either detection tasks, such as identifying perfusion defects, or quantitative tasks, such as estimating ejection fraction, standardized uptake values (SUVs) or organ absorbed dose. Obtaining images that are suitable for quantitative tasks often requires additional processing compared with those used for visual interpretation. This additional processing often results in improved resolution and contrast and reduced artefacts. These improvements in the image will often, but not always, translate directly to improved performance on detection tasks. For example, the development of attenuation correction methods for cardiac single photon emission computed tomography (SPECT) has improved detection of myocardial perfusion defects, while at the same time providing images which are quantitatively more accurate. Many current applications that involve quantification of nuclear medicine images use relative quantification only. These applications often involve ratios of image intensity values. The underlying assumption is that the effects of physical factors such as attenuation and scatter cancel out. In reality, this assumption often does not hold. This is because the magnitudes of these physical factors are both spatially varying and patient dependent. Computing relative values from images that have been processed to provide improved quantification will result in reduced spatial variance and patient dependence, even for applications where relative quantification is sufficient. Another advantage of using images that are quantitative in an absolute sense is to provide improved consistency. For example, some diagnostic procedures involve the use of diagnostic thresholds derived from normal databases; absolute quantification in creation and use of these databases will ensure that reference values derived from databases are consistent across centres, imaging equipment and time, and are independent of patient variability. In addition to the potential for improving image quality and relative quantification, there are several applications of nuclear medicine that require images that are quantitatively accurate in an absolute sense. Two such increasingly important applications are targeted radiotherapy treatment planning and advanced kinetic analysis. Achieving absolute quantification requires appropriate equipment, software and human resources. The level of these requirements depends on the imaging task. For example, quantifying activity in a tumour in the lungs requires more sophisticated resources than quantifying whole body activity. However, detailed knowledge of the requisite levels of resources is not widely available or appreciated.

Radiation Safety Aspects During Handling of Unusual Incidence in Nuclear Medicine

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Nuclear medicine imaging uses safe, painless, and cost effective techniques to image the body and treat disease. In the public arena, nuclear medicine has struggled with the widely held perception of the risk associated with radiation exposure from the administration of radionuclides for diagnostic imaging. In the media and in public debate, and even among medical professionals, this risk has been highly exaggerated compared to the risks associated with other diagnostic and therapeutic interventions, obviously due to confusion with the risks associated with nuclear power plants and nuclear weapons. On the contrary, nuclear medicine has been characterized by the rare occurrence of acute and chronic adverse events. In one of the study, Hesslewood, in a survey of adverse reactions to radiopharmaceuticals in Europe, found a frequency of 11 events per 105 administrations with no serious, life-threatening events. Data from the US and Japan shows even lower figures: 2.3 and 1.3 events per 105 administrations, respectively. These figures, including all adverse events and no single serious adverse event in the data associated with radiopharmaceutical drugs, should be compared with the overall incidence of serious adverse drug reactions of 6.7% and fatal adverse drug reactions of 0.32% in hospitalized patients. It should be borne in mind, however, that under-reporting of adverse reactions is a significant problem, in part due to the mild and transient nature of most reactions. Guidelines for the general treatment of adverse events in nuclear medicine do not exist. The treatment is supposed to follow general recommendations for the treatment of adverse events, such as, for example, administration of a corticosteroid and an antihistamine in cases of supposed allergy. However, the specific cause of an adverse event is not always obvious. With important recent developments in nuclear medicine including hybrid imaging modalities and several new drugs for radionuclide therapy, different adverse events are being encountered. A dramatic increase in the use of PET/CT has occurred, frequently involving administration of intravenous or oral contrast media. The availability of PET/MRI is still limited, but growing, and this modality is associated with the use of other contrast agents and newly developed radiopharmaceuticals for PET. Expansion in the use of therapeutic radiopharmaceuticals has been modest, but is definitely on its way, and will be accompanied by the occurrence of other, completely different adverse events. The many new PET ligands have not been reported to cause a significant number of adverse events.

Adverse events have been rare in nuclear medicine, but in the future they will be seen more frequently in the departments both because of administration of contrast agents in hybrid imaging and because of increasing use of therapeutic radionuclides with significant risks of causing sub-acute and chronic toxic effects. The potential exists for unexpected adverse events following the administration of new and future PET tracers, many of them likely to be non-commercial compounds that are produced locally. The new combined PET/CT, SPECT/CT and PET/MRI scanners require that nuclear physicians are familiar with the indications for the use of intravenous contrast media and also be aware about the radiation safety during use of radiopharmaceuticals. The staff must be able to manage acute adverse events that may vary from minor to serious allergic reactions and also the incidents due to misadministration. It is therefore mandatory that protocols for the use of intravenous contrast media and administration of radiopharmaceuticals are available in the department.

All of this will lead to new demands for the departments. The clinical staff – physicians, technologists and nurses – must be educated to be aware of the risks of new kinds of adverse events and they must be increasingly alert in their daily work. Diligence in reporting events is more important than ever.

The handling of adverse events due to misadministration must follow up-to-date local instructions for the treatment of allergic, cytotoxic and other kinds of adverse events in accordance with national and international guidelines. Regarding the responsibility for less acute adverse events in relation to radionuclide therapy, instructions about minimization of toxic effects to the kidneys and bone marrow etc. must follow the international recommendations, and clear agreements between the clinical and nuclear medicine departments must be in place, including careful communication about such adverse events between the departments/management. The radiation safety aspects during handling of unusual

incidence in the department of NM needs special training and developed SOPs so as to prevent occurring of such incidences.

There is no single system for reporting of adverse events associated with radiopharmaceuticals. Different countries have different systems of reporting the events to the authorized agencies. In the international scenario, the International Nuclear and Radiological Event Scale (INES) developed in 1990 is the only way to communicate in a consistent way the safety significance of events at nuclear installations to the public. Since then, INES has been expanded to meet the growing need for communication on the safety significance of events giving rise to radiation risks. INES applies to events associated with the transport, storage and use of radioactive material and radiation sources, whether or not the event occurs at a facility. It covers a wide spectrum of practices, including industrial use such as radiography, use of radiation sources in medical and research facilities, activity at nuclear facilities, and transport of radioactive material. When radiation source is used in medical facilities, the current guidance on INES methodology is used to rate events resulting in actual exposures to workers and public, or involving degradation of the device or deficiencies in the safety provisions but does not cover the actual or likely consequences for patients. There are only few countries who are actually following the mechanism of reporting the incidences related to the patient exposure to their regulatory authorities. In 2015, IAEA has made a draft document on Additional Guidance for Rating Medical Events on INES.

In India, AERB, the national regulatory authority have developed the mechanism of reporting the unusual incidence by the radiation facilities through e-Licensing of Radiation Applications (e-LORA). The purpose of reporting the incidence is not to take any stern action against the utilities but to initiate necessary steps to mitigate the incident in a safe manner through the nodal agencies. Moreover, the experience and lesson learnt from such incidence can be shared with other utilities involved in similar activities to avoid/prevent such incidences in the near future and in turn create deterrence. It has been observed that there is some kind of psychological fear in the minds of utility that reporting of such kind of events may lead to regulatory actions against them.

The unique growth and expansion of our specialty will also undoubtedly lead to an increase in the frequency of adverse events, for which we must be well prepared and report the unusual event to AERB in time.

Molecular mechanisms of radiation damage

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When ionizing radiation interacts with human cell, the energy deposited in the cell causes a series of ionizations and excitations which can affect the cell. The deposited energy may be directly imparted to a cell's macromolecule (like proteins or DNA) called as Direct interaction. The direct effect on the cellular proteins or DNA may be inconsequential for a cell as the cells are known to have a high degree of alternate mechanisms to survive in absence of a macromolecule and also can repair the damage to DNA by mechanisms that have been developed and refined because of evolutionary processes. Many different types of direct hits can occur, and the type of damage that occurs determines whether or not the cell can repair itself. Generally, if a direct hit causes a complete break in the DNA or some other permanent damage, the cell dies immediately or will die eventually. However, humans have an abundance of cells and somatic cellular reproduction (mitosis) is always occurring to replace cells that die. Therefore, it is only when this system of replacing cells falters that radiation effects are seen. This occurs at higher doses of radiation.

The other type of interaction is indirect cellular interaction. Indirect interaction occurs when radiation energy is deposited in the cell, and the radiation interacts with cellular water rather than with macromolecules within the cell. The reaction that occurs is hydrolysis of the water molecule, resulting in a hydrogen molecule and hydroxyl (free radical) molecule. If the 2 hydroxyl molecules recombine, they form hydrogen peroxide, which is highly unstable in the cell. This will form a peroxide hydroxyl, which readily combines with some organic compound, which then combines in the cell to form an organic hydrogen peroxide molecule, which is stable. This may result in the loss of an essential

enzyme in the cell, which could lead to cell death or a future mutation of the cell. However in recent years understanding of cell to cell interaction, messaging and communication systems have highlighted the indirect effects caused even by bystander cells or distantly placed cells that release effector molecules.

The molecular events following radiation absorption are still being understood and evaluated.

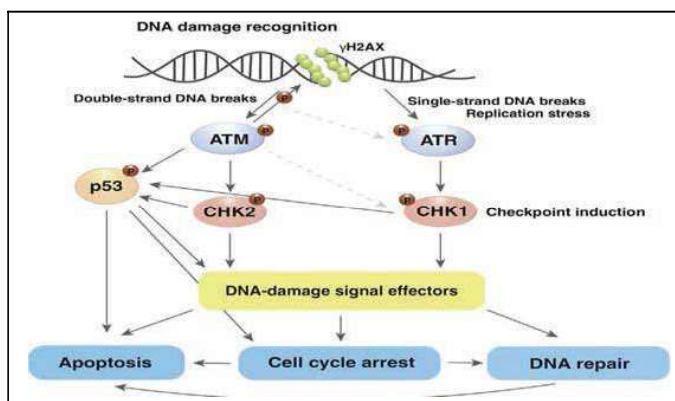
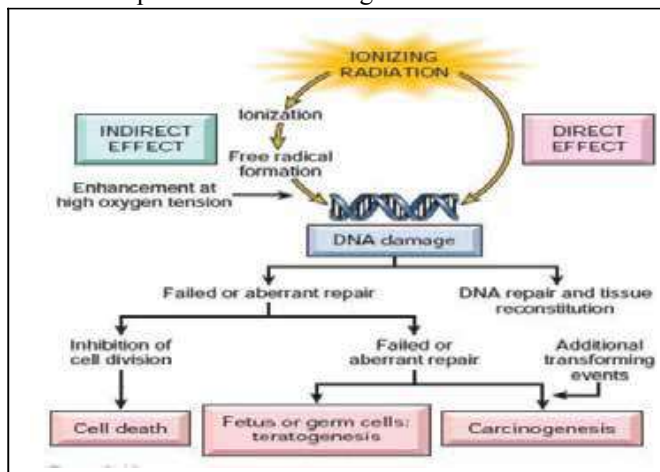
Recovery or Senescence, Programmed Cell death and Carcinogenic Mutations are the known outcomes of a radiation injury to the cell. In spite of not understanding the exact molecular events that lead to cell survival / death, the lag in the dose survival curves at low doses amply demonstrate that repair mechanisms exist. In his book, "What Mad Pursuit (1988)", Sir Francis Crick said 'DNA is, in fact, so precious and so fragile that we now know that the cell has evolved a whole variety of repair mechanisms to protect its

DNA from assaults by radiation, chemicals and other hazards. This is exactly the sort of thing that the process of evolution by natural selection would lead us to expect'. And as Sir Crick expected, we now know that cells have evolved elaborate defense mechanisms to protect against DNA damage.

IR (ionizing radiation) induces a large variety of DNA lesions, including single- and double-strand breaks (DSBs), and base and sugar damage among them, DSB is the most dangerous. The DNA damage response (DDR) is a collective term for the plethora of different intra- and inter-cellular signaling events and enzyme activities that result from the induction and detection of DNA damage. These include events that lead to cell-cycle arrest, regulation of DNA replication, and the repair or bypass of DNA damage. Should DNA repair not be possible or suboptimal repair lead to an unsupportable level of genomic instability, DDR can also impact on downstream cell fate decisions, such as cell death or senescence that can either be dependent or independent of the immune system. Recent analyses suggest that there are at least 450 proteins integral to DDR.

In human cells there are five major repair pathways. Modified bases, abasic sites, and the DNA single-strand breaks (SSBs) these are repaired by the base excision repair (BER) pathway. There are two major forms of repair when dealing with DNA double-strand breaks (DSBs), the most genotoxic form of DNA lesion due to the issues associated with accurate chromosome segregation during cell division. Homologous recombination repair (HRR) is a relatively accurate and efficient repair pathway but depends upon the presence of undamaged sister chromatid DNA, while the non-homologous end-joining (NHEJ) pathways (C-NHEJ and alt-NHEJ) are not dependent on the presence of replicated DNA and, while still effective, are less accurate, potentially introducing DNA rearrangements. The nucleotide excision repair (NER) pathway deals with modified nucleotides that distort the structure of the double helix. The mismatch repair (MMR) pathway deals with replication errors, including mismatch base-pairing as well as nucleotide insertions and deletions.

The response to DNA damage will be different depending on the cell-cycle status. For example, cells in G1 will not have sister chromatid DNA available as an undamaged template and therefore will be dependent upon NHEJ pathways for the repair of DSBs. In addition, there are important differences in the primary roles of checkpoints at different stages of the cell cycle and in the



DDR factors that are involved. For example, the G1/S checkpoint allows the repair of DNA damage prior to the start of DNA replication in order to remove obstacles to DNA synthesis, and key DDR factors regulating this checkpoint include ATM, CHK2, and p53. The intra-S phase checkpoint proteins ATR, CHK1, DNA-PK, and WEE1 can delay replication origin firing to provide time to deal with any unrepaired DNA damage that has occurred, thus preventing under-replicated DNA regions being taken beyond S-phase. The activities of the G2/M checkpoint proteins including CHK1, MYT1, and WEE1 lead to an increase in phosphorylated CDK1, thereby keeping it in its inactive state and delaying mitotic entry. The G2/M checkpoint really represents the last major opportunity for preventing DNA damage being taken into mitosis where unrepaired DSBs and under-replicated DNA may result in mitotic catastrophe and cell death.

Phosphorylation of Histone H2AX, a minor histone H2A variant, at DSBs has been implicated in the timely recruitment and/or retention of DNA repair and checkpoint proteins such as BRCA1 to sites of DNA damage. H2AX encodes a conserved Ser-Gln-Glu (SQE) motif in the carboxyl-terminal tail. Ionizing radiation exposure induces rapid phosphorylation of the Ser residue (Ser139) by ATM/ATR family kinases to form foci of H2AX at DNA double strand break sites. The histone globular domains comprise the nucleosome core, whereas the histone tails protrude, providing potential sites for protein modification such as acetylation, methylation, and phosphorylation. These histone tail modifications alter DNA accessibility and nucleosome dynamics, thereby affecting regulation of gene expression and DNA repair.

Cells have evolved elaborate mechanisms (checkpoints) to monitor genomic integrity in order to ensure the high-fidelity transmission of genetic information. Tumor suppressor, TP53, also known as p53, has been recognized as an important checkpoint protein, functioning mainly through transcriptional control of target genes that influence multiple response pathways and leading to the diversity of responses to IR in mammalian cells. P53, coordinates DNA repair with cell cycle progression and apoptosis. P53 has been considered as the guardian of genome which maintains genomic stability. Cells harboring defects in checkpoint pathways respond to DNA damage improperly, which in turn may enhance the rate of cancer development. More than 50% of tumors have a P53 gene mutation. P53 is a nuclear phosphoprotein containing at least three domains: an N-terminal acidic transactivating domain; a central evolutionary conserved DNA-binding domain; and a complex C-terminal domain that houses nuclear localization sequences, a homotetramerization domain and a putative DNA damage recognition domain. Abundance and activity of the tumor suppressor P53 are regulated by many different post-translational modifications. These include phosphorylation, acetylation, ribosylation, O-glycosylation, ubiquitination and SUMOylation. The turning on and off of genes and the starting and stopping of processes such as cell growth, DNA damage repair and apoptosis are the overt consequences of many events in the dynamic state of the checkpoint control system.

Poly (ADP-ribose) polymerase is a family of proteins involved in a number of cellular processes such as DNA repair, genomic stability, and programmed cell death. The main role of PARP (found in the cell nucleus) is to detect and initiate an immediate cellular response to metabolic, chemical, or radiation-induced single-strand DNA breaks (SSB) by signaling the enzymatic machinery involved in the SSB repair. Once PARP detects a SSB, it binds to the DNA, undergoes a structural change, and begins the synthesis of a polymeric adenosine diphosphate ribose (poly (ADP-ribose) or PAR) chain, which acts as a signal for the other DNA-repairing enzymes. Target enzymes include DNA ligase III (LigIII), DNA polymerase beta (pol β), and scaffolding proteins such as X-ray cross-complementing gene 1 (XRCC1). After repairing, the PAR chains are degraded via Poly(ADP-ribose) glycohydrolase (PARG).

The lecture will aim to elaborate the finer aspects of the eukaryotic cell cycle using a mitotic cell division and identify the importance of the Histones and various other proteins that play a major role in modulating cellular response to radiation.

Experience in Managing Radiation Emergencies

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Discoveries of x-rays & radioactivity brought in great benefits to humanity. It found its application in industry, defence, the medical and research. However, apart from benefits some unforeseen hazards were also associated with this new modality. Because, radiation cannot be detected by our sensory organs; it cannot be seen, smelled, felt, or tasted by humans. Therefore, radiation emergencies are different than the emergencies caused by fire, electricity, chemicals or natural calamities. Radiation poses a potential threat to human health if not handled properly. Early radiation professionals have paid heavy price for using it. Since then radiation safety is of paramount concern. Stringent rules & recommendations have been framed by international and national agencies to make radiation facility safe. But in spite of that some of the radiation emergencies do happen. However, in general radiation emergencies are few in comparison to emergencies created by other hazardous materials, but it generates high levels of public concern and political engagement. The scale and types of radiation emergency may range from small incident to a major catastrophic emergency with global impact. Regardless the scale or a cause of an accident it can affect human health and environment. It may give unnecessary exposure to general public and radiation worker. Any radiation incident demands a well-structured response system. Government or regulatory bodies must have protocols to respond to radiation related emergencies in tandem with the local response teams. Therefore, it is essential that a sufficient level of emergency preparedness be ensured and SOPs should be in place to handle any radiation emergency. Multidisciplinary approach between local administration, radiation safety experts, clinical specialists, nursing staff and psychological experts is required. Because, management of victim of radiation injury poses many challenges which include the evaluation of the damage, need of hospitalization, type of treatment along with the regular monitoring of the exposed persons. We also need to increase our capabilities of responding by identifying the trained radiation workers who have expertise in radiation detection, use of radiation monitoring equipment, radiobiology, decontamination and radioactive waste disposal. Along with trained manpower, availability of proper instruments, facilities, periodical drills and simulation of emergencies are the key to combat any radiation emergency. In our country, we have large number of trained radiation professionals with proper instruments in industry and healthcare facilities. If this manpower is used properly then our country would be able to face any challenge posed any radiation incident. We have managed few radiation emergencies in our institution which proved that above mentioned steps and policies are important in managing any radiation incident.

Planning of a Nuclear medicine department- clinician's expectations.

Nikunj Jain,

Molecular diagnostics, GZB

Planning a good department is the most important requirement for it to be a success. Planning is not just the construction part but everything that adds to the care and comfort for the patients, comfort of the team and good revenue generation from the management's point of view. Often core team is employed at a later stage / licensing stage of the department just before it is about to be functional be it a hospital set up or a diagnostic centre. However few of us get a chance to be involved in planning of a department from the scratch. Especially RSOs are involved in the planning of the department. All the steps to start a nuclear medicine department are laid upon on ELORA and one needs to follow them be it ELORA registration/ getting the design approved/ intimation of equipment arrival etc.

What does a clinician want

- ☐ Good and full time RSO taking care of regulatory issues and paper work.
- ☐ Good HR and team

- ☐ Stationary / forms
- ☐ Clear protocols / policies about TAT
- ☐ Separate reporting room and cabin if the space permits.
- ☐ Points from NABH accreditation point of view.
- ☐ CCTV cameras in reporting room.

To summarize a good department is one which takes care of patient flow, comfort of team and is scalable in future as and when need arises.

Nuclear Medicine Solutions: A website for all. Complete Solutions to all NM needs

Dibya Prakash,

Molecular Diagnostics, GZB

In my career as Nuclear Medicine Professional, have spent lot of time in making departmental standing orders, Standard Operating Procedures (SOPs), Quality Manuals, various consent forms and many such documents and believe others would also be doing the same. Preparing of these documents requires lot of google searches, customization and thus losing lot of productive time, which could have been used towards patient care. We realise this is the problem of all, why not to create a common platform, where once a document is prepared by one of us, can be uploaded and shared with everyone. This would save lot of time nationwide and tremendous amount of manhours can be saved. Similarly, when we were students, spent lot of time on searching study material and then prepare notes. We also thought to share our prepared notes, which may be useful to forthcoming NM Students. A web platform called www.nuclearmedicinesolutions.in is created, where we have NM Professionals support pages on which documents are uploaded as per specialization of all of us.

When we started this, we come across many such possibilities which were unexplored so far and found this platform has lot of potentials for many more such things. In an era of internet, Nuclear Medicine tests and Therapies were not yet mapped for online bookings. The people who were booking other Radiology & Laboratory tests and have no idea about Nuclear Medicine were booking some of profit-making tests from where they can make huge money. Since they do not know NM, their patients also come with no preparation and have no idea about how the procedure would be carried out. An online booking module is added to this website with common preparatory instructions and procedural details for Nuclear Medicine Tests and Therapies. Other relevant details such as centre location, accreditation, empanelments, parking details are also added for patient comfort and knowledge. The rates of tests/ therapies were kept at minimum possible by bargaining service providers and keeping facilitation fee minimum.

As professionals, we are committed to provide quality care to patients and this quality has several certifications such as JCI, NABH, ISO etc. Apart from routine quality practice, these certifications demand lot of documentation. People are there in market to provide consultation on NABH, but they have understanding of Radiology and laboratories and no idea about Nuclear Medicine. The experience of Quality Manager at Nuclear Healthcare Ltd New Delhi, working in tandem with Quality Department of Indraprastha Apollo Hospital New Delhi as Senior Technologist and experience of Manager – Quality & Training at Molecular Imaging and Therapy Ghaziabad, taught a lot on how to prepare Quality Manual specifically for Nuclear Medicine set ups. We successfully achieved NABH accreditations in lowest possible time for Molecular Imaging and Therapy. Through this website, we offer complete assistance on NABH & ISO accreditations consultation as well as consultation for Nuclear Medicine Startups.

There is a page called “Nuclear Medicine Products and Services”. As professionals, we need various consumable items for use and need vendors to supply such items. We keep on asking various people to let know who the vendor of which item. This page connects buyers with sellers and vice-versa of Nuclear Medicine Community. The buyer will be shown products & services, catalogue, contact details with variety of vendors offering the same products. This will empower us to bargain the rates.

At the same time, this page would be advantageous to sellers where they can promote their business, showcase their products & services as they do it in conferences. The drawback of showing in conferences is that it is only for few days, to only few visitors who attend it and the cost involves is also very high. On this website, their products will be displayed 24 x 7 throughout the year in front of prospective buyers who wanted to see the list of products they offer and can contact directly for quotes. The requirement of physical door to door marketing of products would no longer be required and buyers would reach to directly to sellers and that too with very minimal amount of spending.

A Nuclear Medicine Blog page is created, which will give us opportunity to write freely, share our ideas, work, case discussions, unpublished research works etc and get responses from varied specialties of Nuclear Medicine. We can also ask our doubts, clarifications, share opinion, updates about procedures, trends, news, ongoing conversation etc.

Future plans

Nuclear Medicine is a specialty, where qualified professionals are small in numbers. Finding a job or hiring a qualified person is difficult and it is done so far in an unorganised manner. We have planned to create a page, where job seeker and hirers both can meet each other at one stop very conveniently.

Very soon we are going to add "Nuclear Medicine online Journal Club" page where comments, results, discussions of recently published papers will be presented in video tutorials and uploaded on this website as well as youtube.

Online classes for common difficult topics where we as RSO, Physicist, Technologist struggle will also be uploaded on this website. These videos will be on each category pages of NM professionals. Classes may be on eLORA handling, Calculation of Efficiency of equipment, Drawing Renal ROIs etc. Video classes for general NM topics, which can be useful to NM students will also be uploaded on students page.

It will also have a page called "Nuclear Medicine Store", where consumables of Nuclear Medicine will be sold, as other products are sold on online shopping websites. The items such as Cold kits, Decontamination Kit, Signages of Nuclear Medicine like radioactive symbols, Absorbent sheets, Glucometers, Glucostrips etc. will be available for online purchase.

This website has tremendous potential of monetized work for all of our Nuclear Medicine Professionals. We invite entire Nuclear Medicine fraternity to join and associate with us.

Challenges in Cyclotron Facility

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In a conventional cyclotron the charged particles move in two semicircular metal containers called dees (because of the D shaped electrodes). In most of the modern medical cyclotrons there are four gaps with four pie shaped dees instead of two. The particles pass through the same acceleration gap many times with increasing radius before they acquire the desired energy. The entire accelerating system is maintained at high vacuum (10^{-6} to 10^{-8} Torr) and the dees are housed in a vacuum chamber. Hydrogen gas is passed through an arc current to produce the ion source for acceleration in the cyclotron. The ion source is pulled towards the centre of dee structure by applying a positive bias voltage. A high voltage (>36 kV) is applied to the dee structure with the help of an oscillator. The ion located at the center is thus attracted towards a dee that happens to be at opposite potential at that particular moment. As the magnetic and electric fields (in dees) in the cyclotron are at right angles to each other the ion beam moves in a circular path inside the hollow dees. In present scenario negative ion cyclotron accepted everywhere in the medical field.

Components of Cyclotron

Ion source system

Ion source is axially mounted and produces a negative ion. The ion source contains two tantalum cathodes located equidistant from an anode. A potential gradient between the cathodes and anode ionizes the hydrogen gas supplied to this region of the ion source. The ionized gas forms the plasma from which negative ions are extracted, it is pulled with a positive bias voltage for acceleration.

Radio frequency (RF) System

The RF system is the most important and sensitive components of the cyclotron, which supplies an alternating high potential difference to the dee structure, which in turn imparts energy to the H⁺ ions. The structure is composed of four pie-shaped electrodes, which are mounted in the magnet valleys and supported by dee-stems extending down from mounting plates at the top of the magnet yoke.

Vacuum system

The vacuum system consists of a vacuum chamber contained within the magnet yokes. There are mechanical and diffusion pumps, which help both in creating and maintaining, desired vacuum in the tank by constantly removing gas from the ion source and other particles from surfaces inside the vacuum chamber. The vacuum is necessary in the main acceleration region of the cyclotron to maintain the desired acceleration to the ion beam without any loss of ions and their energy.

Magnet system

The magnet system provides the bending force that confines the beam to the circular orbit centered between the upper and lower magnet poles. The magnet system includes the upper and lower magnet yokes with integral pole pieces, the magnet coil, and the magnet power supply. Applying current to the coil mounted between the upper and lower magnet yokes energizes the magnet. The field generated by the magnet coil is concentrated in the small gap between the upper and lower poles where the beam is accelerated. Each magnet pole consists of four pie shaped wedges extending from the yoke toward the opposing pole. These pie-shaped wedges are called hills. Each of the recessed regions between adjacent hills is termed a valley region.

Target system

The target system consists of target body, target changer, collimator assembly and target material. The target body holds the target material during irradiation and is usually made of silver for ¹⁸F production. Titanium and Niobium are treated as good target body for better yield. During target irradiation the beam passes through a vacuum isolation window, helium cooling space, the target window and finally the target material. The target changer assembly controls the movement of the selected target into bombardment position and accommodates as many as 8, 4 or 2 targets in RDS system. The collimator, and a carbon disk of less than 1 cm central hole, is mounted at the exit before the vacuum window inside the cyclotron.

Extraction system

The extraction system consists of one, or two beam extractors that intercept the accelerated beam with a carbon foil, which strips the loosely bound electrons from the hydrogen nuclei. Once stripped of electrons, the positively charged beam arcs outward toward the exit port and target. The dual beam option allows two extractor foils to be moved into the beam path, thus splitting the beam between two targets.

Challenges

Medical cyclotron is a particle accelerator used in producing short lived radioisotopes (¹⁸F, ¹¹C, ¹⁵O, ¹³N, and ¹⁸F₂ Gas) in the medical field. We are here synthesizing ¹⁸F labeled radiopharmaceuticals (¹⁸F-FDG, ¹⁸F₂-DOPA, ¹⁸F-DOPA, ¹⁸F-FET, ¹⁸F-FLT, ¹⁸F-MISO, ¹⁸F-Choline, ¹⁸F-TAU, ¹⁸F-FES etc.) ¹³N-Ammonia and ¹¹C labeled radiopharmaceuticals (¹¹C-Choline, ¹¹C-Methionine, ¹¹C-Flumazenil, ¹¹C-DASB and ¹¹C-Raclopride, ¹¹C-MHED etc). The produced radioisotopes are used in production of PET radiopharmaceuticals for diagnostic purposes in Oncology, Neurology and Cardiology. The daily running of the medical cyclotron involves a number of problems and challenges faced by the operator. Foremost among these would be target window rupture which is considered as a major emergency needing immediate attention. The second cause for concern during cyclotron operation is chiller temperature followed by air compressor. The optimum environmental conditions, gas cylinder pressure, parameters ideal and its feedback values, rinsing and most important trained and qualified working personnel plays very important role in uptime of the cyclotron facility. Trained and qualified working personnel can take immediate action for the remedy of the problems.

The experience helps us gain working knowledge of cyclotron operations, which may help in improving ¹⁸F yield, minimizing the breakdown, and help in the prevention of the occurrence of unusual events. The preventive maintenance should be on time without fail. The experienced engineers are also very crucial in cyclotron facility and uptime is also depends upon them.

For PET radiopharmaceuticals chemicals refrigeration, preparations of chemicals, availability of chemicals, charging of cartridge, malfunction of MVP valve, leak from delivery tube and purification column are crucial.

Medical physicist plays very important role in operations of medical cyclotron. As they are qualified by competent authority, fulfill all the criteria and take any immediate decision during any mis-happening and avoid mishandling of the equipments. Optimal handling of the emergencies also enables reducing personal radiation exposure and breakdown time of the equipment by medical physicist

QC of SPECT & Gamma Camera

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Nuclear medicine is critically dependent on the accurate and reproducible performance of imaging system. So, it is to be ensured that the performance of imaging systems should be within a predefined acceptable range. Quality control is defined as an established set of ongoing measurements and analyses designed to ensure that the performance of instrument within a predefined acceptable range. This includes various periodic QC tests. For quality control of the gamma camera, these tests need to be performed on daily, weekly, monthly, quarterly or annual basis and include tests for uniformity (extrinsic and intrinsic), spatial resolution, spatial linearity, energy resolution and sensitivity. Since imaging on gamma camera also involves SPECT acquisition, regular QC of SPECT is also a mandate. The periodic quality control tests of SPECT include center-of-rotation (COR) alignment, rotational & tomographic uniformity and overall system performance. Data acquisition and analysis protocols for this purpose have been promulgated by various authoritative associations. These tests need to be done on a regular basis to ensure that the patient images obtained are of high quality for accurate clinical interpretation.

ABSTRACTS (Oral)

O01

Comparison between effect of two Acquisition Time on Image Quality in whole body 18F-FDG PET/CT TOF studies in cancer patient

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Aim:- The major aim of this investigation is to assess the image quality of TOF PET image data, acquired with 30sec and 1min frame time, by quantitative and qualitative analysis using 100 patient data. We evaluated its effect on several parameters: lesion volume, lesion detection rate, and standardized uptake value (SUV), total lesion glycolysis (TLG), and image quality for 18F-FDG PET-CT scan in cancer patients.

Methodology:- We have randomly selected 30 patient in 3 months of different age group which referred to our department for Whole body 18F-FDG PET-CT. Study setting - Patients should be overnight fasting or at least 6 hours before 18F-FDG is injected intravenously (with 0.1mCi/kg of Patients) will be imaged on the PHILIPS INGENUITY TF PET-CT. Diagnostic CT scan is acquired during shallow breathing for attenuation correction (using iDose4 (Philips), which automatically adopts radiation dose based on the size and shape of the patient. Immediately thereafter, two consecutive whole-body 18F-FDG PET/CT scans using a 30-sec and 1-min acquisition time per bed position will be obtained for each patient. In all patients, only 1 attenuation-corrected CT scan is obtained and used for both PET acquisitions. Images will be interpreted at a workstation equipped

with NM Viewer software that can display CT, PET, and PET/CT images. Lesions will be visually identified, and their locations to be compared.

Result: - We analyse that the overall image quality of 1min acquisition time per bed is better than 30sec, but there is no effect of lesion visualization, standardized uptake values (SUV max) and lesion volumes at both acquisition times.

Conclusion: - In this above study, we perform and concluded that to minimise the acquisition time with acceptable image quality, and to interpret by nm physicians and convenient for reporting.

O02

Comparison of Left Ventricular Ejection Fraction (LVEF) derived on Ordered Subset Expectation Maximization (OSEM) & Filtered Back projection (FBP) reconstructed images in 99mTc-MIBI myocardial perfusion SPECT: validation with LVEF derived on Equilibrium Radionuclide Angiography

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Background and Objectives: To compare the resting LVEF derived on OSEM (4 iteration 6 subsets with post reconstruction Butterworth filter) with LVEF derived on standard FBP reconstructed images in 99mTc-MIBI myocardial perfusion SPECT (MPS) and validate both with LVEF derived on ERNA at rest.

Materials and Methods: Sixty-three patient studies were included retrospectively who underwent 99mTc-MIBI MPS and ERNA within a period of two weeks. MPS of each patient was processed by FBP technique using standard vendor provided parameters (Butterworth filter with critical frequency of 0.4 and order 10 for stress images and a critical frequency of 0.52 and order 5 for rest images) and optimised OSEM parameters, and LVEF was determined on each. ERNA of the same patient was also processed and LVEF determined. The rest LVEF obtained from FBP and OSEM was compared and validated with LVEF obtained from ERNA. Agreement was determined using Kappa values.

Results: The mean resting LVEF obtained using FBP was $58.74 \pm 15.05\%$ (median 63%, range 16-83%) and on OSEM was $55.77 \pm 16.72\%$ (median 61%, range 10-81%). Though, values for resting LVEF were found to be higher using FBP reconstruction method than OSEM reconstruction method, a strong agreement of 98.41% ($\text{kappa} = 0.967$) was found between them. The mean LVEF obtained on ERNA was $50.98 \pm 14.02\%$ (median 58%, range 16-68%). On comparison of ERNA with OSEM, a very strong agreement of 98.41 % ($\text{kappa} = 0.967$) was found while a lesser agreement of 96.83% ($\text{kappa} = 0.935$) was found when ERNA was compared with FBP.

Conclusion: LVEF derived using the optimized OSEM parameters give comparable result with the LVEF derived from FBP. When compared to ERNA the LVEF derived from OSEM had better agreement than LVEF generated from FBP. Thus, LVEF derived on OSEM reconstruction with optimised parameters can be used for routine clinical practice in Indian population.

O03

Comparison of Radioiodine uptake by Gamma Camera and Thyroid uptake probe-based methodologies and Diagnostic Radioiodine Scan in Differentiated thyroid carcinoma

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Advanced Centre for Treatment, Research and Education in Cancer (ACTREC), Tata Memorial Centre

Aims and Objectives: The objective of the study was to make a quantitative comparison of 72-hrs neck uptake calculated by gamma camera-based and thyroid uptake probe-based methods after administration of low-dose (111-148 MBq) of ¹³¹I capsule in thyroid carcinoma follow-up patients who have already been treated with ¹³¹I.

Methods: The study group consists of 46 patients, of whom 14 were male (average 47.5 yrs) and 32 were female (average 38 yrs.). All patients already had undergone thyroidectomy followed by ¹³¹I treatment at least once and came to the institute after 6 months for follow-up. As per the institutional protocol the patients had their ¹³¹I neck uptake and whole-body scan at 72 hours, the uptake value evaluated by both uptake probe and camera-based method using medium-energy parallel-hole collimator.

Result: Amongst a total of 46 patients, (i) neck uptake was negative in 24 patients by both probe-based (0.1% as cut-off as per institutional protocol) and camera-based methodologies and the scan, (ii) while positive in 10 patients by both the methods which was supported by scan finding, (iii) In further 10 cases thyroid uptake by probe-based uptake method showed (with 0.1% as cut-off) positive while camera-based uptake and scan finding were negative. In most of these cases scatter radiation contribution due to high non-target counts were found to be high. (iv) In two patients, thyroid uptake by probe-based method showed $d < 0.1\%$ where camera-based neck uptake and scan finding were positive for neck uptake. Thus, in 34 out of 46 patients (74%), both methods were found concordant, while in 12 out of 46 patients (26%), the uptakes were discordant with 0.1 % as the cut-off for probe based uptake. Based upon the exploratory analysis of the results obtained, we propose camera-based neck uptake of 0.03% to be the cut-off for positive neck uptake. In the subgroup of patients with negative scan and systemic metastases in the vicinity of neck ($n=7$), an uptake cut-off of 0.1% resulted in positive results in 85.7%. All patients had true negative results with camera-based cut-off of 0.03%. Based upon the analysis of these - 2 - discordant results (between probe-based uptake method and scan), we further propose the cut-off for positivity of the ¹³¹I uptake value by thyroid uptake probe-based method to be considered as 0.2% rather than 0.1% in order to reduce false positivity with appropriate correlation with scan findings.

Conclusion: Thus, in patients of thyroid carcinoma, camera-based uptake during ¹³¹I LDS can also be reliable as conventional thyroid uptake probe-based method and can be used as a Substitute in evaluating neck uptake calculation in patients with functioning metastases in the vicinity of neck or non-specific high physiological accumulation.

O04

Transport of F-18 FDG by road from distant supplier: Guidelines & Practical aspects

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Abstract With the increase in the number of PET-CT centres in India, the transport of F-18 FDG has increased manifold which involves the movement of F-18 FDG from the place of manufacture to the place of use. Most of these PET-CT facilities are supplied with FDG from off-site cyclotrons. Procuring F-18 FDG from a commercial manufacturer is a cost-effective alternative to in-house production of F-18 FDG for any hospital with limited number of scan output. Security during transport of radioactive material is of paramount importance. Transport of radioactive material in India is governed by Atomic Energy Regulatory Board (AERB) safety code AERB/SC/TR-1 which is based on the International Atomic Energy Agency (IAEA) regulations for the safe transport of radioactive material. The basic requirement for the transport of radioactive material is that the package containing the material shall be designed and prepared in such a way that during the whole process of transport, the radioactive material remains contained to prevent contamination and remains shielded to avoid unacceptable radiation exposure to transport handlers and public. The prime

responsibility for ensuring safe transport of F-18 FDG lies with the consignor. The consignor needs to ensure that the appropriate packaging is selected for the transport of F-18 FDG and the package is prepared, marked and labelled as per the regulations. A material such as Tungsten or lead of appropriate thickness and design is used in packaging. Once the package is prepared as per the prescribed procedures, it can be transported by any mode of transport i.e. by road, air etc. Type A packages are used for the transport of dispersible radioactive material of moderate activity such as nuclear medicine sources used for diagnostic and therapeutic purposes. Transport of F-18 FDG comes under this category. Transport documents are very important during transport; they include (a) declaration by the consignor, (b) instructions to the carrier, (c) a Transport Emergency Card (TREM CARD) and (d) Instructions in writing to the carrier for emergency measures. In addition to this, one working radiation survey meter, emergency kit, mobile phone should always be carried along in a suitable vehicle in case of distant transport by road. Labelling of the package with radioactive symbol on the opposite faces with United Nations number (UN number for Type 'A' package non special form is 2915) along with the proper address of the consignor and consignee on the top of the package is also essential. Labelling should include the name of the radionuclide, activity and the transport index. The consignor, consignee and the carrier should contact the competent authority immediately in the event of any untoward incident/ accident during transport or non-delivery of the package at the destination within the normal period. Lastly it is a team effort that involves great communication network, scientific knowledge, time & work management for smooth and safe transport of F-18 FDG from a distant supplier.

O05

Improvising labelling method for commercially available BRIT [99m Tc] Tc-TRODAT-1 kits

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Introduction- Parkinson's disease (PD) is a degenerative disorder of the central nervous system which involves loss of dopamine neurons. TRODAT-1 is a propane derivative having a high binding affinity for the dopamine transporter (DAT) receptors. [99m Tc]Tc-TRODAT-1 is a potential CNS dopamine transporter imaging agent in Parkinson patients. We procured kits from BRIT and sometimes face difficulty in obtaining standard images.

Objective –To troubleshoot the radiolabeling method to improvise the labelling of Trodat-1 with [99m Tc]. **Methods –** The single vial TRODAT -1 kits and [99m Tc] was procured from Regional Centre of BRIT, KIDWAI campus, Bengaluru. The radiolabeling was performed as per the manufacturer instruction with few modifications. Briefly, 60 ± 5 mCi of [99m TcO₄ -] (in a volume of 700 ± 100 μ L of saline) was added to the kit, the contents were mixed and kept for incubation at 95°C for 45 min. The vial mixture was shaken at every 5 min during the incubation. The radiochemical purity was checked by using instant thin layer chromatography (ITLC) on silica gel strip (silica gel 60) using saline as a solvent. The stability of the labelled kit was evaluated up to 4 h after reconstitution. The ITLC strip (10 cm x 1 cm) scanned for 7 min on TLC scanner (EZ scan, California, USA). After passing quality control, the labelled [99mTc]Tc-TRODAT 20 $\pm$ 5 mCi was injected into the patients. Following the injection whole body sweep images were acquired 30 min post-injection followed by SPECT-CT imaging of the brain at 4 h post injection.

Results- The pH of the final preparation was 6.6 ± 0.5 . The ITLC method showed retention time of 5.8 ± 0.6 min for [99m Tc] and 2.1 ± 0.6 [99m Tc]Tc-TRODAT -1. The labelling efficiency was found to be 93.5 ± 2.5 % and no degradation was found in the radiolabeling up to 4 h at room temperature. Diffuse tracer uptake was noted in the brain, nasal mucosa, bilateral lungs, liver, and intestines in whole body sweep images at 30 min. No uptake seen in the thyroid, salivary and stomach confirmed the absence of any free pertechnetate.

Conclusion: The modified standard operating protocol helps us to standardize the procedure as per our lab conditions. The standardization in labelling has made improvement in the distribution of the [99m Tc]Tc-TRODAT -1 and help us to obtain standard images.

O06

4D PETCT: Acquisition Protocol and Advantages

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Introduction: Hypo fractionated stereotactic radiosurgery in the range of 8-10 Gy needs precision and accuracy for delivering high dose radiation to the target for ablation. This is important so as to avoid non target surrounding tissue from getting exposed to unnecessary radiation. Cross section anatomic imaging is suitable but not ideal for peripheral lesions for calculating CTV/GTV/PTV. However, for mediastinal lesions cross section anatomic imaging needs to be complemented with metabolic imaging for high target to non-target dose delivery because of significant respiration movement in chest and upper abdomen.

Purpose: Conventional 3D PET CT or CT gives us detail on static volume/dimension of the target lesion. However, it does not account for range of target movement due to respiration which may cause errors in accurately calculating the PTV. The target movement can be estimated using 4D PET CT/CT which includes a fourth dimension-REAL TIME. As our centre does good number of hypo fractionated stereotactic radiosurgery, we evaluated the preliminary data of 4D-PET-CT done in our department.

Methods: Total of 9 4D PET-CT acquisition using RPM Respiratory Gating Device containing a reflective marker, infra-red camera and a rpm software were performed. Patient preparation was same as whole body PET-CT. All patients were trained to do uniform breathing, which is very important to get a good quality image. In 4D PET CT ACQUISITION, CT scan is acquired in cine mode instead of helical mode.

Conclusion: 4D PET-CT with respiratory gating and patient co-operation is a promising technique for radiation therapy planning of chest and upper abdomen lesion for accurately calculating the PTV.

O07

Potential use of Radionuclide in Nuclear Medicine New frontier of Molecular theranostic

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Background: The term 'Theranostics' was first used by John Funkhouser in 2002 while describing his company's business model in developing diagnostic tests directly linked to the application of specific therapies. 'Theranostic' refers to a combination of two interdependent applications namely therapy and diagnosis, using the same agent or different agent. Since both diagnostic and therapeutic radionuclides are used in radiopharmaceutical preparation, the concept of, 'theranosis' is particularly relevant in nuclear medicine practices.

Objective: To analyze the current and future possible development of theranostic approaches based on different SPECT/PET and therapy Radionuclide.

Material and Methods: A comprehensive literature search was made in PubMed, Google Scholar and references from relevant articles. Literature was analyzed according to the objective. Narrative analysis was adopted to write this review.

Result: After review of literature and to anticipate that new radiopharmaceuticals targeting specific biomarkers will be developed for early diagnosis and prognostic prediction, and to adapt therapies for each patient in oncology. **Conclusion:** Therapeutic nuclear medicine is developing rapidly as an alternative choice of treatment in oncology. Other than its traditional uses in endocrinology and rheumatology, therapeutic radionuclides have now gained attention for tumour targeting therapy using multiple routes and mechanisms to target radionuclides in the tumor site. The non-invasiveness of the

procedure and relatively low toxicity in comparison to conventional chemotherapy and external beam radiotherapy make radionuclide therapy an attractive and realistic alternative in the management of benign and malignant diseases. Although there are still many challenges, such as a low target-to-non-target rate, poorer therapeutic efficacy in solid tumours compared to haematological tumours, and a lack of radionuclide generators, we believe that, with advances in administration methods, a combination of multiple treatment modalities and enhanced therapeutic efficacy, the contribution of therapeutic radionuclides to tumour treatment will significantly increase in the future.

ABSTRACTS(Posters)

P01

A case study

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Background/Introduction: A 60 year old female presented with known case of Ca Oesophagus with multiple bone metastases referred for PET/CT to evaluation of diseases status (Restaging). The pattern of the FDG avid is different from normal uptake. 18F-FDG show intense activity uptake in lesions and diminished metabolic activity (FDG avid) organs like liver and brain

Purpose: To explain the characteristics of 18F-FDG PET/CT Metabolic Super Scan.

Methods: 18F-FDG PET/CT was done with standard protocols with using non-ionic i.v and oral contrast. **Results:** 18F-FDG PET/CT demonstrated extensive multiple FDG avid skeleton lesions throughout the skeleton involving the appendicular and axial skeleton and multiple FDG avid lesions in both lobes of liver. In this case 18F-FDG show intense activity uptake in lesions and diminished metabolic activity (FDG avid) organs like liver and brain.

Conclusion(s): As we say the “Super Scan” of bone scintigraphy in which bones looks too good and include intense activity in the bone and diminished renal parenchymal [activity.in](#) this case 18F-FDG show intense activity uptake in lesions and diminished metabolic activity (FDG avid) organs like liver and brain. Because 18F-FDG same characteristics as in Super Scan on skeleton scintigraphy. This case could be considered as 18F-FDG PET/CT Metabolic Super Scan.

P02

Synthesis of Ga 68-Labeled radiopharmaceutical by First Indigenous synthesis module made in india (Single centre experience)

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Introduction: Gallium-68 somatostatin receptor PET/CT (positron emission tomography/Computed tomography) has been used in the diagnosis of neuroendocrine tumors. At our centre we routinely synthesized Ga-68 Labelled PSMA and DOTANOC by First Indigenous synthesis module made in India

Purpose: The aim of the present study is to share our experience regarding the synthesis of generator based 68 Ga-labeled radiopharmaceutical using a PRPL (PET radiopharmacy Pvt Ltd) Indigenous module.

Method: 68Ge/68Ga generator was eluted with 4 ml of 0.05M HCL manually. The eluted Gallium was directly collected in to reaction vessels. The reaction vessel was heated at a certain temperature. The total heating time depended upon the precursor. After heating, it was transferred in to the cartridge. Bounded Compound will stay in the cartridge and unbounded will collected in the waste vial. From the cartridge product was transferred in to product vial with the help of a solution containing mixture of ethanol and metal free water (1:1 ratio).Product was passed through 0.22

micrometre filter. The product was diluted by adding 10 ml normal saline. The entire synthesis steps were carried out in PRPL Indigenous manual module. The total synthesis time depends upon precursor. During the whole procedure, the radiation level was monitored around the module every 3 minutes. Results: The maximum yield of ^{68}Ga was approximately 90 %. The product was shelf life for 4 h. The whole assembly was kept behind the L-Bench surrounded by Lead-bricks in our radiochemistry lab. Hence, outside L Bench, the radiation level was near background level during synthesis.

Conclusion: We got a good yield using indigenous manual module generator based PET radiotracer ^{68}Ga -radiopharmaceuticals. Being made in India with indigenous technology the cost of running the module is very economical compared with other existing modules

P03

Development and evaluation of Thyroid Uptake in Siemens Symbia Gamma Camera

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Introduction: ^{131}I Thyroid Uptake tests are best carried out with a Uptake Probe. Uptake probe has the advantage of having a Flat field collimator that gives a uniform response with large field of view at 30 cm, sufficient for Thyroid Uptake Evaluation. Because of Open bore, it provides very good sensitivity of counting, and therefore good counting statistics even with low amount of Radioiodine- ^{131}I (~25microCi) that is used. The Gamma Camera fitted with a MEGP Collimator suffers from low sensitivity because of poor geometric function forced by thick septa. Hence conventionally it is recognized that Uptake Probe based calculations are more reliable than Gamma Camera Based Uptake. We decided to investigate this assumption in the patients reporting to us for ^{131}I Thyroid Uptakes.

Methods & Patient: A program was developed in Siemens Symbia Gamma Camera to calculate Thyroid Uptake from the routine thyroid scan that is acquired as a static image. The program required a calibration factor to be provided for conversion of activity in to counts. For this purpose a calibration factor was computed from a set of nine ^{131}I sources of varying strength. The source strength varied from 0.62, 3.58, 5, 9.06, 10, 15, 24.06, 47 and 75.2mCi. Linearity of gamma camera was examined and a calibration factor was derived. Nineteen consecutive patients were selected for evaluation of uptake in Thyroid Probe and Siemens Gamma Camera. Thyroid Probe was operated with a 100KeV window with 364KeV as centre line, and Gamma Camera was operated with a 15% Window centered at 364KeV, and a 256 x 256 pixel matrix was used to acquire an Anterior Neck image with a MEGP collimator for 10 minutes.

Results & Discussion: The measurements from uptake probe were compared with that from Gamma Camera. The Gamma camera counts were about 7 times lesser than that obtained from Uptake probe. The values however correlated well with a correlation coefficient of 0.994, a slope of 0.909 and a Y-intercept of 2.75

Conclusion: Our results show that Gamma Camera can be employed for Uptake calculations in 25microCi Thyroid scan patients with a accurately quantified calibration factor.

P04

Development and evaluation of Large Dose Uptake in Ca-Thyroid patients on Siemens's Gamma Camera

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Introduction: In Ca Thyroid Patients, post thyroidectomy 'Neck Uptake' is usually measured out to assess residual thyroid and plan the dose for ablation of the remnant tissue. ^{131}I Neck Uptake tests are best carried out with an Uptake Probe. Uptake probe has the advantage of having a Flat field collimator that gives a uniform response with large field of view at 30 cm, sufficient for Neck Uptake

Evaluation. Because of Open bore, it provides very good sensitivity of counting, and therefore good counting statistics even with low amount of Radioiodine-131 that is expected post thyroidectomy. At RMC we have conventionally been using 100microCi of 131-I to carry out such evaluation. Recently we migrated to use of 1-2mCi dose instead of 100microCi for reasons of obtaining better quality scans from a gamma camera image which will allow better decision making. Though Uptake Probe based calculations are considered more reliable than Gamma Camera Based Uptake, we suspected uptake probe calculations when using higher doses may suffer from counting losses and therefore may not give reliable results. We decided to investigate this assumption in the patients reporting to us for such 1-2mCi131-I LDS Uptakes.

Methods & Patient: A program was developed in Siemens Symbia Gamma Camera to calculate Thyroid Uptake from the routine thyroid scan that is acquired as a static image. The program required a calibration factor to be provided for conversion of activity in to counts. For this purpose a calibration factor was computed from a set of nine 131-I sources of varying strength. The source strength varied from 0.62, 3.58, 5, 9.06, 10, 15, 24.06, 47 and 75.2mCi. Linearity of gamma camera was examined and a calibration factor was derived. Sixteen consecutive patients were selected for evaluation of uptake in Thyroid Probe and Siemens Gamma Camera. Thyroid Probe was operated with a 100KeV window with 364KeV as centre line, and Gamma Camera was operated with a 15% Window centered at 364KeV, and a 256 x 256 pixel matrix was used to acquire an Anterior Neck image with a MEGP collimator for 15 minutes.

Results & Discussion: The measurements from uptake probe were compared with that from Gamma Camera. The Gamma camera counts were about 7 times lesser than that obtained from Uptake probe. The values however correlated well with a correlation coefficient of 0.975, a slope of 0.833 and a Y-intercept of ~ 0. The Uptake Values obtained from Gamma Camera were lower than that of Probe method by about 17% on an average and needs investigation or appropriate normalization before being reported.

Conclusion: Our results show that Gamma Camera can be employed for Uptake calculations in 1-2mCi131-I LDS Uptakes but after normalization for 17% reduction as compared to Uptake Probe.

P05

Theranosticnanosystems for targeted cancer therapy

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Nanomaterials have revolutionized cancer imaging, diagnosis, and treatment. Multifunctional nanoparticles in particular have been designed for targeted cancer therapy by modulating their physicochemical properties to be delivered to the target and activated by internal and/or external stimuli. This review will focus on the fundamental “chemical” design considerations of stimuli-responsive nanosystems to achieve favourable tumor targeting beyond biological barriers and, furthermore, enhance targeted cancer therapy. In addition, we will summarize innovative smart nanosystems responsive to external stimuli (e.g., light, magnetic field, ultrasound, and electric field) and internal stimuli in the tumor microenvironment (e.g., pH, enzyme, redox potential and oxidative stress).

P06

Peptide receptor radionuclide therapy

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Background: Peptide receptor radionuclide therapy involves administration of radiopharmaceutical composed of beta emitting radionuclide chelated to a peptide for the purpose of delivering cytotoxic radiation to a tumour. The oligopeptides are designed to target cell surface receptors such as

somatostatin receptor subtype 2 that are over expressed on the cell surface of neuroendocrine tumors. Purpose: To implement proper radiation protection measures while performing PRRT procedure and to ensure renal protection. 1. Renal Protection: along with bone marrow, kidneys are critical organs in PRRT because of reabsorption of radiopeptide and retention in interstitium. Positively charged amino acids such as L-lysine or L-arginine are coinfused to competitively inhibit the proximal tubular reabsorption of radio peptide. This ensures reduction in renal absorbed dose ranging from 9% - 53%. Amino acid protection protocols: ensure proper dilution with saline to hydrate the patient. Measures against nausea, vomiting should be taken. Infusion should start 30-60min prior to radiopharmaceutical administration and maintained over 4 hrs. Recent research studies about Metformin for renal protection: metformin reduces renal uptake of radiotracers and protects kidney from radiation-induced damage. Metformin is a hydrophilic base that functions as an organic cation suggesting that it may have the capacity to inhibit the tubular reabsorption of peptide radiotracers. Radiation Protection Measures during and after PRRT procedure: Radiopharmaceutical should be administered via an intravenous line and administered over 10-30min. The radiopharmaceutical should be coinfused with amino acid solution via three way stopcock. After infusion of radiopharmaceutical flush the IV line with saline. During the first 2 days after PRRT the high levels of activity excretion in the urine is of concern. Advise the patients to double flush the toilet. Wash hands after urination. After discharge the patients should be cautioned to avoid contamination for 1 week. Incontinent patients should be catheterised prior to treatment. Urine bags should be emptied frequently. Women of child bearing age should use effective contraceptive and avoid pregnancy for at least 6 months during treatment. Children below 18yrs of age have been excluded in PRRT trials because of lack of information in safety, toxicity and efficacy in this age group.

References: 1.The joint IAEA,EANM and SNMMI practical guidance on PRRNT in neuroendocrine tumors. 2.Abstract: Metformin reduces renal uptake of radiotracers and protects kidneys from radiation induced damage. Department of Nuclear Medicine, Peking University Cancer Hospital & Institute, Beijing, PR China.

P07

Evolution in MRI and various safety aspects

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Purpose- MRI is likely to become even more important in the near future. Medical researchers are working on combining MRI machines with other equipment e.g. PET-MRI in order to provide diagnose complementary information and assist in treatment of patients. We are focusing about the different safety related aspects in MRI, various precautions during imaging.

Methods- We will discuss about the evolution in MRI machine and its safety related issues, firstly there was a strong magnetic field in MRI, and every modern scientific equipment has a drawback with their advantages. Earlier, MRI machine had with open and permanent magnet with low strength and there was less probability of accident and drawback was poor image quality, increase scan time. Recent developments in MRI the strength and power of the magnet is increased (superconducting magnet), and with good image quality so we take necessary steps and Precautions to avoid accident. Various ferromagnetic metallic objects and body implants are restricted in strong magnetic field area because it can be hazardous to patient and damage machine. There are four different zones in MRI department which is safe or unsafe for others, so general awareness is important for every persons. The movements by public near magnetic field or room should be restricted. MRI safety posters and banners are used with pictures and written in different regional languages which can be read easily by everyone. Safe handling of equipment is required ever can minimize the damage which may occur.

Conclusion- As development of the machine revolution in technology is continuous, so the safety steps necessary for protection of patient, staff and public. Proper and adequate knowledge is necessary for all including staff through training and presentations for safety in MRI under the supervision of MRSO/MRI technologist.

P08

Targeted Alpha Therapy (TAT) : A Theoretical Approach

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Introduction: TAT is a new therapeutic approach in which a cancer targeting vector is labelled with an alpha emitting radioisotope. Alpha particle is an ionised 4He nucleus with +2 electric charge, heavier than other subatomic particles, emitting from decaying radionuclide. α particles are more effective ionisation agents with LET of $100\text{keV}/\mu\text{m}$ and highly efficient in depositing energy range over a short range in tissue ($50\text{-}100\mu\text{m}$). α particles deposits 1500 more energy per unit path length than a beta particle.

RATIONALE: TAT has the advantage of delivering therapeutic doses to individual cancer cells. It permits sensitive discrimination between target and normal tissues, which leads to fewer toxic side effects. Monoclonal antibodies that recognize tumour associated antigens are conjugated to potent alpha emitting radionuclides to form alpha immuno conjugate. This AIC can be administered by intralesional, orthotopic or systemic injection. Targeted cancer cells are killed by direct DNA double strand breaks, which leads to cancer cells apoptosis. **Microdosimetry:** It is essential for TAT to investigate the physical properties of radiation energy deposition in biological cells. The specific energy is most important quantity for microdosimetry as it can calculate cancer survival rate. The dosimetry of TAT is distinguished from external beta radiotherapy is by three different ways- 1) short path length of α particles. 2) small target volume 3) non uniform distribution of radioisotopes. The mostly used alpha particle emitters are ^{221}At , ^{213}Bi , ^{223}Ra , ^{225}Ra .

RADIOLABELLING: Targeting moieties for targeted α therapy includes antibodies, peptides or small molecules. Targeting moieties have a broad spectrum of pharmacokinetics profiles, it's important to match the therapeutic radionuclide physical half-life to vectors biological half-life. Conjugating a radionuclide to its vector is achieved by a chelator or prosthetic group. Due to nuclear recoil effect alpha particles release daughter nuclei which affects labelling and dose targeting. It can be minimised by choosing short radioactive half-life and simple decay scheme or by using diffusing alpha emitter radiation therapy (local administration of radioactive sources in or near tumours) or encapsulation of alpha emitting radionuclide into nanocarriers. These was evaluated to retain recoil daughters at the tumour site. TAT is a very promising and effective therapeutic tool against cancer. Reference: Microdosimetry for TAT(article). Targeted alpha therapy from Alpha to omega(article).

P09

Planning and Preparedness for Nuclear Disaster and Radiological Emergencies

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Our nation's vision is to prevent radiological emergencies which are essentially man-made in nature. However, in rare cases of their occurrence, due to natural or man-made factors beyond human control, such emergencies will be so managed through certain pre-planned and established structural and non-structural measures by the various stakeholders, as to minimize risks to health, life and the environment. Radiological accidents can have a lasting impact on public health. Because of the increasing risk of radiological emergencies, public health agencies and first-response organizations are working to increase their capability of responding. Expertise in certain areas, such as radiation safety, radiobiology, decontamination, and the use of radiation detection and monitoring equipment, that could be useful during the response to events that involve radiological materials. Medical staff and worker personnel in the department and in other department using radioactive materials needs to increase their knowledge about how to deal safely with the equipment, early and late hazards of exposure to radiation, and how to save patients and themselves from radiation exposure or from contamination to a radioactive substance. The purpose of this planning is to assess the willingness and knowledge of medical staff and an emergency medical response team to participate in radiological

emergency preparedness and response operations and to determine what radiation detection, measuring, and imaging equipment they would have access to during an event at their workplace. The study also assessed whether years of work experience or past radiological emergency preparedness training had an effect on the willingness and knowledge. But this knowledge needs more study and exercising. The current study concluded that the initial response to a radiological emergency may include radiation detection, population monitoring, decontamination, and dose assessment. Knowledgeable, willing, and prepared individuals will be needed to assist with a response of this nature. Public health agencies will need to coordinate with local RSO and draw on their expertise and knowledge to strengthen the community's capability of responding to a radiological or nuclear emergency. Public health agencies and first-response organizations are working to build the capacity to respond to emergencies involving radiological materials. Recommendations regarding the Continuous education programs shall be designed to increase the awareness about the emergency preparedness and response to radiation accident. Increase the alertness between medical worker and staff about the radiation hazards and its safety measures that prevent these hazards. However, International organizations can provide support to other countries in the education programs. Communities must try to increase the ability of the public health system to handle radiological events of any nature. Good planning leads to better management and good response. In our study we have planned the medical management need for the Jaipur: pink city. Our emergency preparedness programs enable emergency personnel to rapidly identify, evaluate, and react to a wide spectrum of emergencies, including those arising from Nuclear Disaster, Nuclear Emergencies, Nuclear terrorism or natural events such as hurricanes. Although the range and depth of engineering safeguards and regulatory controls that currently apply to nuclear energy and radioactive materials programmes ensures that the probability of any malfunction capable of presenting a significant risk to the operator or the public is extremely small, it is recognized nevertheless that no human enterprise can be entirely risk free, and in the development of any nuclear energy or radioactive materials programme, it would be most imprudent not to recognize that the remote possibility of a failure leading to an accident condition can never be entirely eliminated. Implicit in this recognition is the need to determine in advance the appropriate emergency actions necessary to prevent or mitigate any adverse effects should such an accident occur and to develop formal emergency plans for ensuring that the relevant remedial procedures can be implemented within the requisite time scale should the need ever arise. Radiological emergency planning, which is concerned with the development and preparation of emergency plans to mitigate the consequences to public health and safety, or to the environment, in the event of a radiological accident. Radiological emergency preparedness, which encompasses the training of all persons who will be involved in implementing the emergency plans, the acquisition of resources and facilities, and the testing of emergency plans and procedures by means of drills and exercises to ensure effective response in the event of a radiological emergency. Keywords: Assessment, nuclear emergency preparedness, nuclear medicine.

P10

Human studies with ^{99m}Tc -Zoledronic acid (^{99m}Tc -ZA) for skeletal scintigraphy dose and time optimisation – a preliminary experience.

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Aim: To study the optimal dose and optimal time of human skeletal imaging using Tc^{99m} -ZA. **Materials:** 30 consecutive patients referred to the Nuclear Medicine department for bone scan were enrolled for the study after a valid consent.

Methods: The patients were divided into subgroups as described. Tc^{99m} -ZA was prepared as per the standardised protocol. Patients were divided into 3 groups of 10 each. Group A1 was injected intravenously 5 mCi of tracer, Group A2 was injected 10 mCi of tracer and Group A3 was injected 15 mCi of tracer. The patients were asked to maintain good hydration. In each group the images were acquired at 1, 2, 2.5 hour(s) after tracer injection in all the patient groups in whole body mode using

LEHR collimator. After completion of the study, the images were interpreted independently by two observers for the presence of adequate tracer uptake in the skeleton and also for optimal bone to background ratio. Their findings were then compared and when differences were there the decision was finalised by consensus.

Findings: The skeletal images obtained using Tc99m-ZA were quite similar to those obtained with Tc99m MDP. The optimal dose for skeletal scintigraphy using Tc99m-ZA was 15 mCi. The optimal timing post tracer injection was 2 hours.

Conclusion: The images obtained with Tc99m-ZA are very encouraging. Their revelation of human skeleton matches with that is achieved with established agent Tc-MDP. However, further studies with a large cohort of patients are warranted for clinical use of Tc99m-ZA and establish its performance vis a vis Tc99m-MDP.

P11

Over expression of prostate specific membrane antigen (PSMA)

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Introduction: Over expression of prostate specific membrane antigen (PSMA) is evident in prostate cancer patients and PSMA shows more avidity in tumour lesions wherever receptors are present. PSMA imaging is very effective modality in detection and response evaluation for prostate cancer and its malignancy. Thus present study was undertaken.

Purpose: This study aims to develop 99mTc labelled PSMA-T4 for imaging prostate cancer.

Materials and Methods: 99mTc was eluted as Na99mTcO₄- from commercially available 99Mo-99mTc generator. Radiolabelling was done by adding 20-30mCi of 99mTcO₄- to a ready to use lyophilized kit of PSMA-T4. The reaction mixture was heated at 100°C for 10 minutes and was cooled for 10 minutes. Radiochemical purity was evaluated via ITLC strips using MEK and ACN:H₂O(1:1) as mobile phases. Whole body imaging was performed in 10 patients. Acquisition was done at various intervals i.e. 10min, 1hr, 2hr, 3hr, 4hr, 5hr, 6hr. SPECT-CT was acquired at 2hr in patients showing active lesions.

Results: RCP was found to be ≥98% in every formulation. Physiological uptake was seen in lacrimal glands, salivary glands, liver, spleen, intestine, kidneys, bladder. Tracer showed renal excretion. Prostate, skeletal, lymph node lesions were showing uptake with less intensity than 68Ga-PSMA. Time evaluation for good lesion to background ratio was found to be at 4hr or 5hr.

Conclusion: 99mTc can be successfully radiolabelled with PSMA-T4 with high labelling efficiency. It can be used as promising SPECT radiopharmaceutical in prostate cancer patients with benefits of cost effectiveness, easily available and giving less radiation burden to patients.

P12

The role of integrated 18F-FDG PET/CT in identification of ectopic neuroendocrine ACTH Syndrome (EAS) : A case study Report

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Background: In 10% to 20% of patients, Cushing's syndrome is caused by ectopic production of the hormone ACTH. Often the ectopic ACTH is produced by a tumor of the lung, thymus, or pancreas. However, in approximately 50% of patients the tumor cannot be found even with the use of extensive imaging studies such as CT, MRI, and nuclear scans. Positron emission tomography (PET scan) using

FDG has the ability to detect pathologic tissue based on physiologic and biochemical processes within the abnormal tissue.

Purpose: To find the exact location of the tumor making extra ACTH is necessary for successful surgical treatment and patient care Management.

Material and Methods: Whole body positron emission tomography imaging and contrast enhanced high resolution CT was performed from vertex to mid-thigh level after IV administration of [18F] fluoro-2-deoxy-D-glucose ([18F] FDG) is a positron emitter-labelled glucose analog. Using a full ring dedicated GE Discovery IQ Positron emission tomography (PET/CT) biomedical imaging with 16 slice CT. Oral contrast was administered for bowel pacification. Non-ionic intravenous contrast was administered using a pressure injector (1 mg/kg).specific dose optimization protocols were used on CT to reduce radiation dose to the patient. Results: A semi-quantative analysis of FDG uptake was performed by calculating SUV (Standardized uptake value).this quantitative parameter may improve the diagnostic accuracy of localization ectopic ACTH secreting pulmonary tumors in patient. Conclusion: The role of 18F-Fluorodeoxyglucose positron emission tomography (18F-FDG PET) scan in diagnosis of ectopic ACTH syndrome is still Challenging. Here, we report on 55 year old female who was having symptoms of hyper secretion of ACTH, metabolic alkalosis and referred to our institution with suspicion of ectopic ACTH secreting tumor for further workup, on the use of integrated 18F-FDG PET and computed tomography (18F-FDG PET/CT) in diagnosis of EAS. It allows real-time measurement technique and PET images were acquired and reconstructed to obtain fused PET-CT images (FDG avid soft tissue mass in lung and bilateral FDG avid in adrenal gland). Metabolic imaging with FDG may also provide useful information in patients with other endocrine disorders and systemic diseases. In this case the FDG PET scan helped in localizing the ectopic source of ACTH in the body and to increase the accuracy of tumor localization and further improve the prognosis of the patients. .

P13

Optimized the production of ^{68}Ga -EDTA using an in-house $^{68}\text{Ge}/^{68}\text{Ga}$ generator for measurement of the Glomerular Filtration Rate (GFR)

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Introduction : Nuclear medicine renal imaging provides important functional data to assist in the diagnosis and management of patients with a variety of renal disorders. Physiological stable metal chelates like ethylenediaminetetraacetic acid (EDTA) and diethylenetriamine penta-acetate (DTPA) are excreted by glomerular filtration and have been radiolabelled with a variety of isotopes for imaging glomerular filtration and quantitative assessment of glomerular filtration rate. The measurement of the glomerular filtration rate (GFR) is a good and reliable method to assess the glomerular function of the kidneys. It is directly related to the number of functional nephrons in the kidneys. It is a suitable method to follow the progression (improvement or deterioration) of kidney function over period of treatment which may be of interest for instance in patients with a low grade of chronic kidney disease. When the individual kidney GFR is obtained, the information may be useful prior to nephrectomy. ^{68}Ga EDTA can be suitable substitute for $^{99\text{m}}\text{Tc}$ DTPA for wide variety of clinical indications. A key advantage of PET for renal imaging over conventional scintigraphy is 3 dimensional dynamic imaging which is particularly helpful in patients with complex anatomy in whom planar imaging may be nondiagnostic or difficult to interpret owing to overlying structures containing radioactive urine that cannot be differentiated , Other advantages include accurate and absolute (rather than relative) camera based quantification, superior spatial and temporal resolution and integrated multislice CT providing anatomical correlation. Furthermore, the ^{68}Ga generator enables on demand production, with generator shelf life of 6-12 months compared with 1-2 weeks for the $^{99\text{m}}\text{Tc}$ generator. ^{68}Ga has ideal properties for imaging with a short half-life of 68 minutes minimizing radiation dose to the patient, and high abundance of positron decay ^{68}Ga binds strongly

with EDTA forming a stable complex making radiopharmaceutical production relatively straight forward. There is however no commercially available method or kit for production of ^{68}Ga EDTA production.

Method and Results : 0.5 mmol of EDTA in 0.1 M acetate buffer pH 6 (5 ml) was added to borosilicate vials containing 10 mCi of $^{68}\text{GaCl}_3$ (4 mL of $^{68}\text{GaCl}_3$) and stirred at room temperature for 10 minutes. The radiolabelling efficiency obtained was > 99% and the radiochemical purity of ^{68}Ga -EDTA was above 99% as determined by TLC (silica gel) (0.25M citrate buffer, pH 4 Rf : ^{68}Ga -EDTA 0.5 and Rf : un-complexed $^{68}\text{GaCl}_3$ 0.0 and 0.9 (two spots due to formation of ^{68}Ga -citrate with the solvent at solvent front and at the point spotting due to colloidal ^{68}Ga). Further confirmed using Whatman No. 1 paper solvent a) ($\text{NH}_4\text{OH}:\text{MeOH}:\text{H}_2\text{O}$ (0.35:200:700 v/v/v) Rf : $^{68}\text{GaCl}_3$ 0.0 while the ^{68}Ga -EDTA migrates to higher Rf (0.95) and with solvent b) Water : Ethanol : Pyridine: (4:2:1 v/v) Rf : $^{68}\text{GaCl}_3$ 0.0 while the ^{68}Ga -EDTA Rf (0.95)

Conclusions: In this study, ^{68}Ga - EDTA was prepared successfully with inhouse $^{68}\text{Ge}/^{68}\text{Ga}$ generator. The radiochemical yield of greater than 99% was achieved at the optimized conditions (0.5 millimole of ligand, at room temperature for 10 minutes). The stability of the radiolabelled complex at room temperature showed almost no decrease in the radiochemical purity even after 120 min.

P14

Optimized the production of ^{68}Ga -BPAMD using an in-house $^{68}\text{Ge}/^{68}\text{Ga}$ generator for bone imaging for clinical use

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Introduction: The aim of this study was to optimize the production of ^{68}Ga -BPAMD as an ideal bone imaging agent using an in-house $^{68}\text{Ge}/^{68}\text{Ga}$ generator for future clinical use. Bone metastases are common in the progression of various tumors such as prostate, breast and lungs carcinoma, often entail an occurrence of progressive pain and occur in many patients with solid malignant tumors. Bone metastases occur in many cases at an early stage of the tumor diseases; however their symptoms are recognized rather late. Hence, early recognition of bone metastases is of great interest for further treatment of patients as it leads to severe pain and decrease in quality of life. $^{99\text{m}}\text{Tc}$ phosphonates are well established tracers for the diagnosis of bone metastases in nuclear medicine using single photon emission tomography (SPECT) however due to the higher spatial resolution of positron emission tomography (PET) adequate pharmaceuticals utilizing positron emitters would be of great potential. For this attempt using $^{68}\text{Ge}/^{68}\text{Ga}$ generator with the positron emitter ^{68}Ga ($T_{1/2} = 67.7$ min), high branching = 89%)_ represents a promising system. Bisphosphonates are widely used for scintigraphy of bone lesions with $^{99\text{m}}\text{Tc}$. While BPAMD as a novel macrocyclic diphosphonate with better characteristics compared with the first-generation phosphonates, some diagnostic and therapeutic radiolabelled complexes of this new agent have been reported. Favourable properties of ^{68}Ga , ^{68}Ga -BPAMD namely high target to soft tissue ratios and fast renal clearance is reported in the first human study Fast, efficient, cost effective and facile protocol for ^{68}Ga -BPAMD production for clinical trials using an in house ^{68}Ge - ^{68}Ga generator was optimized with respect to reaction time and temperature.

Method : 50 nanomole of BPAMD was prepared in 0.5 ml of acetate Buffer as stock solution. 50ul (5 nanomole) of stock solution was added to borosilicate vials containing $^{68}\text{GaCl}_3$ (5 ml of acetate buffer pH 4.0 + 4 mL of $^{68}\text{GaCl}_3$). The pH of the reaction mixture was 3 - 5. The vial was heated for 15 mins at 80°C using solid heating block, The reaction mixture was cooled and loaded on a strong cation exchange resin (pre conditioned with 1ml of 4M HCL and 4ml of water, Dowex 50 X 8, 100-200 mesh). The Column was eluted with water to elute ^{68}Ga BPAMD.

Results: The radiolabeling efficiency obtained was > 95% (on measurement of radiolabeled reaction mixture post purification) and the radiochemical purity of ^{68}Ga -BPAMD was above 99% as determined by TLC (silica gel) after purification ((0.25M citrate buffer, pH 4 Rf : ^{68}Ga -BPAMD 0.5

and Rf : un-complexed $^{68}\text{GaCl}_3$ 0.0 and 0.9 (two spots due to formation of ^{68}Ga -citrate with the solvent at solvent front and at the point spotting due to colloidal ^{68}Ga). Further confirmed using Whatman No. 2 paper solvent a) ($\text{NH}_4\text{OH}:\text{MeOH}:\text{H}_2\text{O}$ (2:20:40 v/v/v) Rf : $^{68}\text{GaCl}_3$ 0.0 while the ^{68}Ga -BPAMD migrates to higher Rf (0.8) and with solvent b) acetone: acetic acid (1:3 v/v) Rf : $^{68}\text{GaCl}_3$ 0.0 while the ^{68}Ga -BPAMD Rf (0.7)

Conclusions: In this study, ^{68}Ga - BPAMD was prepared successfully with inhouse $^{68}\text{Ge}/^{68}\text{Ga}$ generator. The radiochemical yield of greater than 95% was achieved at the optimized conditions (5 nanomole of ligand, 80°C , pH: 3-5, 15 minutes). The stability of the radiolabelled complex at room temperature showed almost no decrease in the radiochemical purity even after 120 min.

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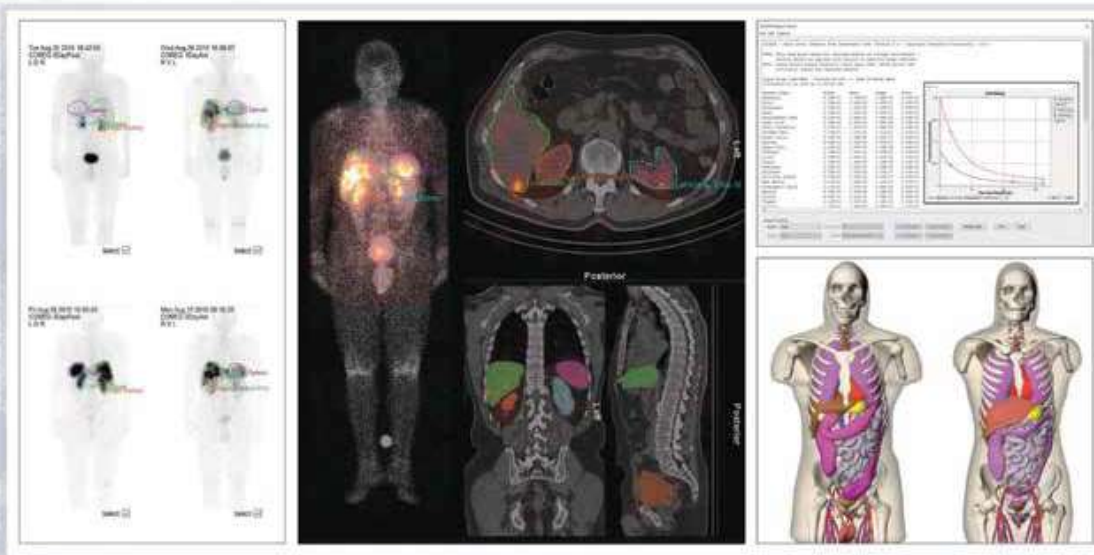


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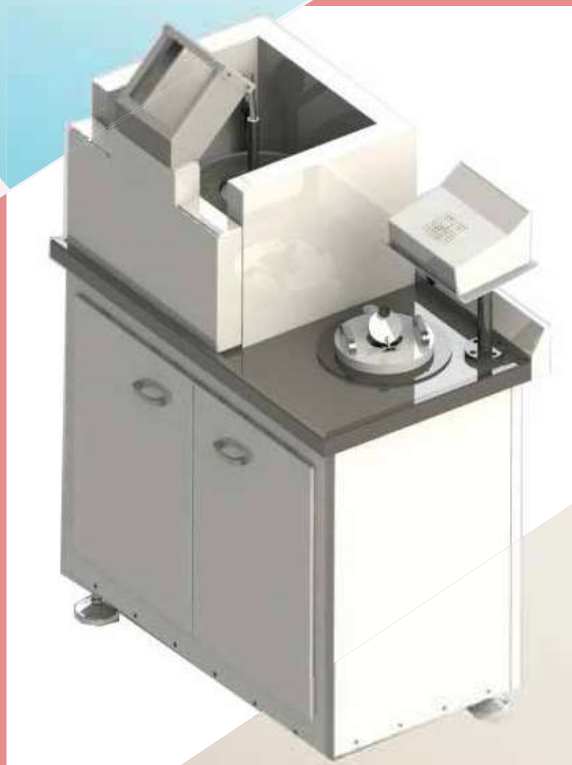
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