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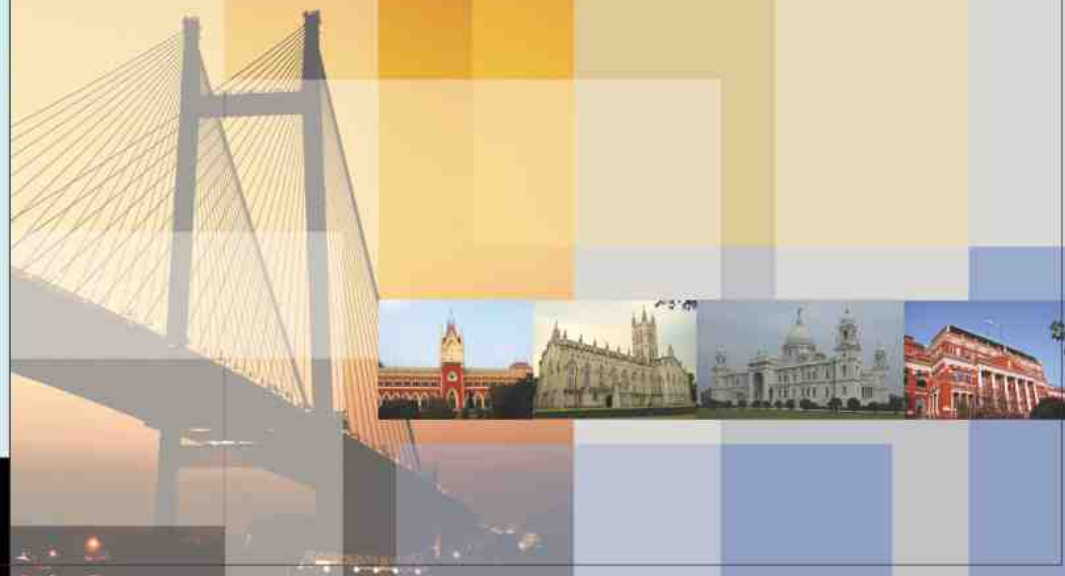
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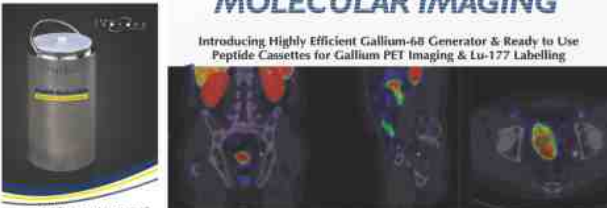
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New Delhi - 110011

MESSAGE

The Prime Minister is happy to learn that Nuclear Medicine Physicists Association of India, Kolkata is conducting National Conference on the theme 'NM SCIENCE: Eruption of Radionuclides in Imaging & Therapy' from 25th- 26th February, 2017 and publishing a souvenir to mark the occasion.

On this occasion, best wishes to the organisers and participants.

**(Chandresh Sona)
Deputy Secretary**

New Delhi
January 20, 2017



जगत प्रकाश नड्डा
Jagat Prakash Nadda



स्वास्थ्य एवं परिवार कल्याण मंत्री
भारत सरकार
Minister of Health & Family Welfare
Government of India



MESSAGE



I am happy to know that the Nuclear Medicine Physicist Association of India (NMPAI) is organizing the First National Conference of the Society of Nuclear Medicine Physicists of India with the theme 'Eruption of Radionuclides in Imaging and Therapy' from 25th to 26th February, 2017 at Kolkata.

This Conference, I am informed, will be conducted by the stalwarts from the field of Nuclear Medicine and will be attended by delegates from across the country. I am hopeful that the Conference will provide a platform to discuss and learn the art and science of nuclear medicine. I hope the gathering of physicists and scientists will provide a great opportunity to the participants to deliberate upon various issues of the field towards the better good of humanity.

I congratulate the organizers and the participants of the Conference and extend my best wishes for its success.

(Jagat Prakash Nadda)

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अध्यक्ष
CHAIRMAN



MESSAGE

I am indeed most delighted to be given an opportunity to occupy a leaf in the Souvenir of the very first conference of the Nuclear Medicine Physicists Association of India (NMPAI). I congratulate the organisers and the founding members for coining this association which fills the gap in the field, a need of the present era.

I am happy to see that the field of Nuclear Medicine in India has flourished to this extent within a span of few decades. It is further evolving with time. In this context this Conference of NMPAI is very important step. Conferences are the medium for the exchange of thoughts and discussion on new trends in the relevant field. I hope this event brings together a good programme that stimulates both our clinical knowledge and scientific intellect. The latter being more relevant; focus on improving radiation safety of patients as well as of occupational workers and the environment is of paramount importance.

In Nuclear Medicine, radiation sources in unsealed form are used in safe manner to perform diagnostic and therapeutic procedures complying with regulatory norms. It is an important event, where "Eruption of radionuclides in imaging and therapy" will be discussed. The role of Nuclear Medicine Physicist is becoming more challenging day by day with the introduction of advanced imaging and therapy techniques and new radiopharmaceuticals.

Let me urge to the participants at this annual conference to not remain confined with the safety concerns at their own workplace, but take it as moral responsibility to observe regulatory compliance across all radiation installations they come across.

I extend my warm greetings and good wishes to all the distinguished delegates participating in the conference and wish all the success in achieving its objectives to disseminate the current knowledge in the field of Nuclear Medicine and Radiation Safety.

(S.A. Bhardwaj)



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Subhash Chand Kheruka

President, Nuclear Physicist's Association of India (NMPAI)



It is my great pleasure to welcome you to the 1st Annual conference of Nuclear Medicine Physicist Association of India-2017 which takes place in beautiful Kolkata the capital city of vibrant West Bengal. This association NMPAI was established in the year 2007 in Kolkata.

The conference would not have been possible without the enthusiastic and hard work of a number of colleagues. I would like to express my appreciation to the organizers committee led by spirited team of Institute of Nuclear Medicine of AMRI Institute Limited (Mr. Anindya Roy, Mr. Aditya Jha and Mr. Amit Nautiyal) for their valuable contribution in assembling the high quality conference program, which will not leave any stone unturned in making your stay comfortable and memorable one. They are great host and will make all of us feel great.

Scientific committee under the leadership of Dr. P.S. Soni had arduous task of preparing an academically rich program. I hope that 2 days academic deliberations will enhance our professional skills.

I am also grateful to all the authors who trusted the conference with their work.

We are focusing on strengthening the organization structures of NMPAI with the help of our members.

We look forward to an exciting two days of insightful presentations, discussions, and sharing of technical ideas with colleagues from around the nation. We thank you for attending the conference and we hope that you enjoy your visit to the City of Joy.

Rajnath Jaiswar

Secretary, Nuclear Medicine Physicist's Association India (NMPAI)



It gives me a great pride to mention that First Conference of Nuclear Medicine Physicist's Association of India (NMPAI) is being organized at Kolkata on 25th-26th February 2017 by Anindya Roy, Aditya Nath Jha and Amit Nautiyal.

The conference of such nature provides great opportunities to share the knowledge and keep abreast with the latest developments in the field of Nuclear Medicine Science. The scientific schedule is designed to discuss, debate and document every possible aspect of latest technology.

I would like to personally thank to the organizers of First NMPAI Conference. I also thank to all participants for their scientific contributions which encourage the younger generation of upcoming Graduates/Post Graduate in NM students, Nuclear Medicine professionals.

Thank you all for their contribution to make the First NMPAI Conference a great success.



PET/MRI fusion imaging System: A technical challenges

Ashish Kumar Jha, Tata Memorial Hospital, Mumbai

PET/MRI is the latest fusion modality introduced in nuclear medicine practice to diagnose the complex disease processes based on improved and reliable anatomical and functional information provided by this combined system. But combining Positron Emission Tomography (PET) and Magnetic Resonance Imaging (MRI) in a single device was a challenging task as both the imaging device faced lots of interference from each other resulting in many new developments and changes in both the system. Hence it is very important to understand the real technical problem faced by two systems in the process of combining with each other.

Ways in which PET can affect MRI:

The introduction of PET detectors inside the gradient coil and magnet can lead to interference.

- PET Scintillation detector like GSO and LGSO may cause small differences in magnetic susceptibility within the magnet bore may result in an inhomogeneity in the main magnetic field (B_0).
- Gradient of MRI may induce eddy current in shielding material and electronics of PET scanner may lead to distortion and non linearity in MRI image.
- PET electronics and power cable interfere with RF detection and can interfere with FR pulse detection.

Ways in which MRI can affect PET:

The high static magnetic field (B_0), quickly changing gradient fields (B_1), and radiofrequency signals (RF) from the MRI scanner prevent the normal operation of photomultiplier tubes and front-end electronics of PET detectors used in current generation PET/CT System.

- **Main magnetic field:** The magnetic field perturbs the paths of electrons moving from the photocathode down the dynode chain to the anode resulting in a loss of gain.
- **Gradient fields:** Rapidly switching magnetic fields can induce eddy current loops in any conductive components introduced into the magnet bore, including PET circuitry. In addition to signal interference, these can lead to heating and mechanical vibration.
- **RF interference:** Any electronics situated within the magnet bore may be susceptible to RF interference generated by the MRI transmit coil. This effect is responsible for the drop in PET count rate that is observed in many MRI-compatible PET systems during MRI acquisition.

MRI compatible PET detectors:

The most widely used PET scintillators LSO, LYSO and BGO, have a magnetic susceptibility similar to that of human tissue and have been demonstrated to have negligible effects on MRI. Scintillators containing gadolinium, such as GSO and LGSO, are not suitable; however these are less commonly used for PET nowadays.

Sequential v/s simultaneous imaging:

PET/MRI system development was based on two major approach, namely, sequential imaging and simultaneous imaging. Based on these two approach two different models, separate gantry model and integrated gantry model were developed.

Sequential imaging:

In sequential imaging approach, gantries for MRI and PET separated by patient table were developed to minimize the interference from each other (fig1). In this kind of system no modification is required either in PET or MRI system.

Philips Ingenuity TF PET/MRI is an example of sequential imaging approach. A 3T multi-transmit MRI and a high resolution Time-of-Flight PET are connected by a patient turntable that conveys the patient from one examination to the next without requiring them to move from the table. All PET and MR applications that are available on standalone systems are available on the hybrid PET/MR.



Fig 1: Sequential PET/MRI with separate gantry

Simultaneous imaging:

In simultaneous imaging approach, PET gantry is integrated in MRI gantry (fig 2.). Several modifications were required to develop such system. Inability of PMT to work in side magnetic field was the major challenge to develop such a system. Hence PMT was replaced with new generation of solid-state photo detectors i.e. avalanche photodiode (APD) which do not get influenced in magnetic field. Other electronics associated with PET were shielded for magnetic and RF interference for proper operation in the MRI gantry.

Siemens Biograph mMR and GE Healthcare SIGNA PET/MRI are the truly integrated PET/MRI system available in the market for clinical use. This PET/MRI system is capable of performing simultaneous imaging. These two PET/MRI systems consist of a dedicated whole-body PET scanner built into a dedicated 3T MRI scanner.

Fig 2: Simultaneous PET/MRI with integrated gantry

MRI based attenuation correction in PET:

Since MRI signals do not have the same properties as gamma photon and unable to produce attenuation value as CT scan, hence MRI based attenuation correction in PET was one of the major challenges in PET/MRI fusion. Two approaches have been extensively tested for MRI based attenuation correction of PET image i.e. Atlas based approach and Segmentation based approach.

Atlas-based attenuation correction: A template MRI image is created from multiple subjects (atlas) and the attenuation values on it are assigned by using transmission or CT scans of the same subject. These template images can then be co-registered with the MRI image of subject, and the attenuation values can then be assigned to the PET image. Atlas creation and co-registration is the main issue with this method.

Segmentation based attenuation correction: Usually T1 weighted images are segmented into areas with different attenuation values for air, lung, soft tissue, fat and then this attenuation map is applied to the PET images. Bone segmentation is not possible in this method and assigned the attenuation valued of soft tissue.

Due to the simplicity of segmentation based approach, this has been utilized in most of the clinical PET/MRI scanners available commercially.

Clinical utility of PET/MRI:

Integrated PET/MRI systems may potentially be used for a number of indications in oncology, neurology and cardiology but clinical utility over the PET/CT scanner yet to be established. Primarily this modality should be used for the functional assessment of cancer, in particular those cancers that are difficult to assess using CT, such as head and neck, brain and prostate cancer.

Evolution of PET and PET/CT systems: From conventional to modern technology

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The Modern PET-CT scanner, the more popular version of a PET scanner as it stands in clinical practice today has evolved due to a large number innovations and advances in physics, mathematics, chemistry, computer science and better understanding of understanding of the fundamental biological processes. The advances in one of these fields prodded further evolution of the other and each complimented by driving the progress and more careful tuning of other to bring the modern day marvel. Historically speaking, the concept of a PET Scanner was placed much before the 1950's and infact of the earliest prototype PET Scanners was demonstrated by Michel M. Ter-Pogossian in the late 1960's. This was preceded by prototypes of emission-computed tomography system by David E. Kuhl in late 50's and invention of cyclotron by Ernest O. Lawrence in mid 1930's.



Over the periods, PET scanner design and performance have improved dramatically. The number of detector elements has increased from ~20 to ~40,000 and the axial field of view from ~2 to ~20 cm, the spatial resolution has improved from ~25 to ~3 mm, and the sensitivity has increased by at least 5000-fold. Detector geometries have undergone significant transformation, from Rotating Flat Detectors to Ring Detectors, from 2D PET systems to 3D PET systems and now the functionally useful Time of Flight systems enabled by the faster integrated electronics. The BGO crystals have already given way to LYSO and other more faster crystals with better stopping power. 4D PET scanners that depict the depth of interaction within the crystal are being tested in clinical situations. The 3D PET reconstruction algorithms now use "adaptive statistically smart iterative reconstruction algorithms" instead of filtered back projection, improving the image quality manifold and also reducing patient doses and imaging times.

The integration of PET scanner with a CT scanner though proposed much earlier was demonstrated in 1998 by David W. Townsend has now come a long way, and multi modality imaging is the showing the path for future applications of PET technology. 16/32 slice CT scanners integrated with TOF-PET Scanners are the order of the day. Application of attenuation correction maps generated by CT scanners are now universally accepted to improve the quality of PET scans, though the issues of motion correction and CT artifacts are still being sorted out. The modern PET-CT scanners have evolved from step and shoot mode to continuous motion systems. The CT scanners today are capable of varying the exposure parameters across the length and breadth of the patients, allowing better dosimetric controls and scan quality. Integrated PET CT scans are being more often used for radiation treatment planning than ever leading to better outcomes. The futuristic vision is more exciting with innovations in detector crystals, integration of semiconductor detectors, ASIC and computing powers permitting smarter image processing and fusion capabilities.

Evolution of SPECT and SPECT/CT system from conventional to modern technology

Dibya Prakash, Nueclear Healthcare Limited, New Delhi

Abstract

At the end of the 1970s single photon emission tomography (SPECT) was introduced. SPECT/CT has emerged over the past almost two decades as a means of correlating anatomical information from CT with functional information from SPECT. The integration of SPECT and CT in a single imaging device facilitates anatomical localization of the radiopharmaceutical to differentiate physiological uptake from that associated with disease and patient-specific attenuation correction to improve the visual quality and quantitative accuracy of the SPECT image. The first clinically available SPECT/CT systems performed emission-transmission imaging using a dual-headed SPECT camera and a low-power x-ray CT sub-system. Newer SPECT/CT systems are available with high-power CT sub-systems suitable for detailed anatomical diagnosis, including CT coronary angiography and coronary calcification that can be correlated with myocardial perfusion measurements. The high-performance CT capabilities also offer the potential to improve compensation of partial volume errors for more accurate quantitation of radionuclide measurement of myocardial blood flow and other physiological processes and for radiation dosimetry for radionuclide therapy. In addition, new SPECT technologies are being developed that significantly improve the detection efficiency and spatial resolution for radionuclide imaging of small organs including the heart, brain, and breast, and therefore may provide new capabilities for SPECT/CT imaging in these important clinical applications. Another important aspect of SPECT/CT is the fact that the technique, like PET, allows quantification of the amount of tracer in terms of Bq/mL or as a SUV. Numerous publications have shown that absolute quantification is feasible. This can be expected to further boost diagnostic confidence, e.g. for judging the efficacy of a treatment through follow-up acquisitions from the same patient or for improving dosimetry for radionuclide therapy.

Key words:

SPECT, SPECT/CT, Quantitation.

Introduction

Single photon emission Computed Tomography (SPECT) were developed during end of 1970s [1]. SPECT-CT systems were introduced commercial in 1999 [2]. The development of these technologies has been rapid over the past several decades and has led to use of sophisticated instruments that are both cost-effective and yield diagnostic information. Along with these technological advances, both the quantity and the complexity of information used in the medical diagnostic process have reached levels that were unimaginable even a decade ago. Software techniques have been developed that can register and fuse images from multiple sources and are best suited for correlating images from rigid structures such as the brain and skeleton. Even when multi-modality image data are available from dual-modality systems, structures within the images can be displaced by respiration, cardiac motion, and other voluntary and involuntary motions. This implies that software-based methods will retain important roles in achieving accurate levels of image registration even when patient studies are performed with SPECT/CT devices.



Early Development of SPECT & SPECT/CT

At the end of the 1970s single photon emission tomography (SPECT) was introduced. By rotating the gamma camera around the body axis and acquiring images at every few degrees of rotation it was possible to reconstruct three dimensional images in a way analogous to the well known X-ray CT systems [2]. In the late 1980s, researchers began devising methods to combine radionuclide emission imaging directly with x-ray transmission imaging in a single system. Possibly the earliest such system was proposed by Mirshanov [3], who received a Soviet patent for a combined transmission-emission tomograph in 1987. This system was designed so that the patient could undergo simultaneous radionuclide and x-ray imaging with separate scintillation and semiconductor detector viewing the same patient volume, with the resulting emission and transmission data then were recorded with a common image buffer. Although apparently not reduced to practice, this system was perhaps the first that envisioned a combined system with which an x-ray rather than a radionuclide source was integrated directly to produce the transmission data as part of a radionuclide imaging study. Another early design for a dual-modality imaging system was disclosed in an international patent application "Transmission/emission and registered imaging (TERI) computed tomography scanners" by Kaplan. This work proposed acquiring the CT transmission and SPECT emission data simultaneously using imaging detectors to maintain spatial registration between the two image data sets and to obtain maps of attenuation coefficients to compensate the SPECT data for attenuation. A critical challenge in implementing a simultaneous SPECT/CT system lies in the still-unresolved difficulty of designing a common detector with sufficient temporal and energy resolution to discriminate the primary radionuclide photons from both the x-ray signal and from scatter of the radionuclide photons. Designing a detector capable of simultaneous x-ray and radionuclide imaging remains a fundamental technical barrier in developing a system for truly simultaneous emission and transmission imaging with performance levels matching those achieved with currently available CT and SPECT systems.

The "modern" SPECT/CT system was originally developed by Hasegawa, et al, at USCF in the mid-1990s. SPECT/CT data simultaneously with a single detector. The modern SPECT/CT system utilizes an alternative approach which has proven to be more robust and incorporates separate state-of-the-art SPECT and CT sub-systems. The SPECT and CT sub-systems can be placed in tandem (i.e. in-line) for imaging and integrated with a common patient (or animal) table and computer system. This group integrated a GE XR/T SPECT and GE 9800 Quick CT systems with an elongated table that could be positioned for either CT or SPECT imaging without removing the patient from the system. The patient table was mechanically supported with an external brace at the far end of the CT system to minimize downward table deflection when it was extended to the SPECT sub-system. This allowed the CT and SPECT data to be acquired sequentially with the CT data reconstructed in the CT scanner with a conventional filtered backprojection algorithm, then transferred to an external host computer via magnetic tape. The CT data were available for anatomical display, or could be converted (as described below) to obtain a CT-derived map of linear attenuation coefficients to correct the radionuclide data for photon attenuation. The radionuclide projection data acquired with the scintillation camera system were transferred via diskette onto the host computer for iterative reconstruction, allowing the SPECT data to be reconstructed with attenuation correction using the CT-derived attenuation map. These reconstruction and post-processing steps produced three different displays: the x-ray CT data reconstructed from the CT scanner; the radionuclide emission data reconstructed with attenuation correction from the x-ray CT data; and a fused image in which the radionuclide data were displayed in color over a co-registered CT image displayed in grayscale.

Current SPECT/CT Technologies

The current SPECT/CT system from General Electric Healthcare now has been upgraded and are named as the GE Infinia Hawke. This system incorporates an x-ray source with significantly lower power than a conventional diagnostic CT scanners (which operate at 120-140 kV, 500 mA, and 0.4-s (or faster) rotation speed). Although these first-generation SPECT/CT systems are relatively limited in their spatial resolution, scan speed, and signal-to-noise performance of their CT sub-systems, overall they are well-suited in terms of cost and performance to addressing the needs of attenuation correction and low-resolution anatomical localization and provide useful information that improves diagnostic accuracy compared to SPECT scans alone. SPECT/CT systems with advanced CT capabilities were introduced in 2004 and now are being adopted in clinical practice. These systems, such as the Siemens Symbia and the Philips Precedence, typically match a dual-head SPECT system with a multi-slice CT scanner having performance similar to that obtained with conventional diagnostic CT. The Siemens Symbia is also available with a single-slice lower resolution CT scan for attenuation correction and anatomical mapping or with a diagnostic 2-, 6-, or 16-slice CT. Similarly, the Precedence SPECT/CT system from Philips is available with a 6- or 16 slice CT capability. Both the low- and high-power CT systems available from the commercial vendors can be used to perform attenuation correction and anatomical localization of the radionuclide data suitable for myocardial perfusion measurements, tumor imaging, and other radionuclide studies. However, the improved signal-to-noise characteristics and multi-slice capability of the higher-power CT systems offer detailed anatomical information with improved spatial resolution, excellent soft-tissue contrast resolution, and sufficiently fast scan speed for applications with intravenous iodine contrast enhancement. These characteristics are especially suitable for oncology where detailed anatomical localization is needed. Other investigators have reported using the higher-performance SPECT/CT systems for applications in orthopedics, infection and inflammation, pulmonary function, and endocrinology, where the improved anatomical localization helps identify areas of disease that can be difficult to discriminate with SPECT alone. As



previously mentioned, high-resolution CT performance can be used to define target anatomy to improve the quantitation of absolute radionuclide uptake in small lesions such as tumors or in the myocardium. Finally, a SPECT/CT system with cardiac and coronary CT capability is likely to be well matched to myocardial perfusion radionuclide measurements, which still account for almost 50% of SPECT imaging. SPECT/CT systems are now available with 64-slice CT sub-systems, capable of ultra-short scan times which "freeze" cardiac motion as required for CT coronary angiography and calcium scoring. The high performance SPECT/CT systems also have the potential for absolute quantitation of radionuclide content with corrections for photon attenuation, scatter radiation, and partial-volume errors in a way that could offer accurate non-invasive assessment of regional myocardial blood flow and coronary flow reserve. These capabilities are just beginning to emerge, but are likely to be developed and tested as the capabilities and performance of SPECT/CT mature.

Future Developments in SPECT/CT

The scintillation camera technology currently in use for clinical studies still relies on the technology invented by Hal Anger in 1957. Nevertheless, SPECT and SPECT/CT is continuing to evolve with the introduction of new technologies that have the potential to improve performance beyond that possible with Anger's pioneering approach. Recent advances in detector technology that incorporate silicon photodiode or solid-state materials offer the potential for improved spatial resolution and energy resolution, with greater stability and more compact size, compared to conventional camera designs based on photomultiplier tube technology. At this early stage in their development, the use of solid-state and semiconductor detectors has focused on imaging of the heart, breast, and other small organs. Nevertheless, it is likely that as these newer detector technologies will mature, they will become more robust in performance and cost effectiveness and therefore eventually replace the photomultiplier tube in radionuclide imaging detectors.

Innovative SPECT/CT Designs for Cardiac Imaging

A SPECT protocol for myocardial perfusion imaging can consume 2.5 hours or more in procedure time, including 40-50 minutes of camera time, (longer if soft-tissue attenuation is suspected and the patient is imaged with prone positioning). Recently, myocardial perfusion cameras have been developed with novel detector and collimator geometries that significantly improve detection efficiency while maintaining or improving spatial resolution for myocardial perfusion imaging in comparison to conventional scintillation camera designs. For example, dedicated nuclear cardiology cameras have been developed by Spectrum Dynamics, Ltd.2 (Caesarea, Israel) and by Cardiac, Inc.3 (Canton, MI) and are designed to acquire myocardial perfusion images in only 2 to 3 minutes versus the 10 to 15 minutes needed with conventional dual-head SPECT systems. Similar performance now is being reported as a works-in-progress (as of 2007) with a new myocardial SPECT camera developed by GE healthcare. These new instruments offer significant advantages over conventional SPECT/CT systems in which an expensive CT scanner remains idle while the slow SPECT scan is completed. The inclusion of a highly efficient SPECT system can decrease the scan time of the SPECT study, and in doing so also increases the utilization of CT and patient throughput compared to conventional SPECT/CT systems. The clinical procedure includes 5-6 minutes needed to acquire the correlated radionuclide and x-ray data with an efficient SPECT camera plus a modern multi-slice CT system versus the 20-25 minutes required with conventional SPECT technology. The total procedure will be lengthened for acquiring both rest and stress myocardial perfusion data between which the patient typically leaves the imaging system for administration of the radiopharmaceutical for the second perfusion scan. However, significant reductions in scan time would be obtained if the rest/stress images were obtained with simultaneous dual isotope imaging in which, for example, the patient first was administered 201Tl at rest followed immediately by exercise or pharmacological stress after which the patient would be injected with the 99mTc perfusion agent for the stress perfusion study. If the imaging system included a high-performance CT scanner, the radionuclide imaging studies could be followed immediately by CT coronary angiography and assessment of coronary calcification. It is conceivable that the volumetric CT data also could quantify myocardial thickness to improve the measurement of radionuclide uptake in the myocardium. Both CT coronary angiography and quantitation of myocardial perfusion are illustrative the potential for a high-performance myocardial SPECT/CT with a fast and cost-effective acquisition protocol.

Innovative Breast Imaging with SPECT/CT

Tornai et al at Duke University are developing a compact dual-modality SPECT/CT system for dedicated tomographic imaging of the pendant, uncompressed female breast. A prototype system is designed to perform SPECT with a 1.620-cm² CZT-based compact gamma camera having 2.5-mm pixels that allow flexible angular positioning with a goniometer. This dual-modality breast imager also includes a flat-panel digital detector coupled to a CsI(Tl) phosphor to perform CT with a quasi-monoenergetic x-ray cone-beam produced with a heavily-filtered tungsten anode. The CT system has a stationary polar orientation and is laterally offset from the center of rotation for imaging pendant, uncompressed breasts that are larger than the detector's field of view. Both the x-ray and radionuclide sub-systems are coupled to a common rotation stage and have a common field of view. As independent systems, both dedicated SPECT and CT have yielded visualization of small lesions in the breast, including those located close to the chest wall. Results from the combined system show that emission projection images can be contaminated by x-ray scatter



photons that artifactually increase the apparent signal in reconstructed emission images. Emission contamination also can increase noise in the transmission image resulting in reduced signal-to-noise ratios in reconstructed CT images. Nevertheless, measurements with the combined system components show that optimal placement of the SPECT and CT sub-systems is limited by physical constraints rather than signal cross-contamination that can occur with a SPECT/CT system that shares a common field of view. Overall, integrating both modalities on a single gantry is designed to simplify data acquisition, SPECT-CT image registration, and necessary image corrections with the goals of correlating radionuclide uptake with anatomical structure, improving detection and staging of cancer, monitoring treatment response, and improving selection of surgical biopsy sites.

Quantitative SPECT/CT imaging

Absolute quantification in terms of image units in Bq/mL or SUV is the standard in PET imaging. Although some reports suggested that SPECT is not a quantitative modality, technological advances have led to an increase in the number of papers reporting high quantitative accuracy with SPECT, mainly evaluated in phantom or simulation studies. For example, Shcherbinin et al. reported errors of between 3% and 5% in a study on a torso phantom using the isotopes Tc-99m, I-123, I-131 and In-111. Du et al. achieved a 2% error for I-123 in a brain phantom. Vandervoort et al. performed simulation studies on the Mathematical Cardiac Torso phantom and on a Tc-99m filled torso phantom and reported 8% error for the simulation and within 4% error for the phantom study. Da Silva et al. reported 8% error in an anthropomorphic phantom with cardiac insert, for the isotope Tc-99m. For the in vivo quantification of Tc-99m in 16 patients, Zeintl et al. applying corrections for point spread function, attenuation and scatter, found average deviations of 6.8% between the activity concentration obtained on SPECT and a well counter measurement of the activity concentration in the bladder. Using the same methods, Cachovan et al. reported uptake of Tc-99m-bisphosphonate in the lumbar spine in 50 patients. The quantification of diagnostic tracers is of great interest if one's aim is to evaluate the course of a disease. Another potential application in this field is the quantification of therapeutic radionuclides for dosimetric purposes. In this regard, Shcherbinin et al. reported a 14.2% overestimation of the activity concentration of a 70 mL container filled with Lu-177. Similarly, Beauregard et al. obtained a deviation of 79% for Lu-177 in a phantom with cylindrical compartments, applying corrections for PSF, attenuation, scatter and dead-time. For the in vivo quantification, they reported an average error of 3.1% for six patients. Unfortunately larger studies that evaluate the quantitative accuracy of today's SPECT systems for therapeutic tracers are still lacking. Nevertheless, some manufacturers have recently started offering SPECT systems that generate quantitative images for a limited number of isotopes.

Conclusion

As we emerge from the first decade of the clinical use of SPECT/CT, several challenges still remain. First, unlike PET/CT, which has essentially replaced PET-only systems commercially, SPECT/CT has not achieved comparable commercial dominance over conventional SPECT. This likely is due in part to the clinical flexibility of SPECT, which is used for a wide spectrum of clinical applications with different radiopharmaceuticals. This is a decidedly different situation than that with PET and PET/CT, which are used predominantly for tumor imaging with 18F-fluorodeoxyglucose. Secondly, as noted above, SPECT/CT suffers an imbalance in cost-effectiveness due to the differences in acquisition time between SPECT and modern CT. However, as also noted above, advances in SPECT instrumentation, CT technology, and radiopharmaceutical development have the potential to advance SPECT/CT beyond its current level of performance. Potential clinical applications of SPECT/CT are numerous and include more efficient studies of myocardial perfusion imaging with the potential for correlation with CT coronary angiography. CT also has the potential to provide anatomically guided partial-volume correction for absolute quantitation of tumor uptake and dosimetry of tumor-specific agents with an accuracy not achievable using SPECT alone. SPECT/CT also has the potential to advance imaging application in infectious diseases, orthopedics, neurology, and breast cancer. Finally, on the horizon, is the potential for SPECT imaging with new tumor-specific agents now entering clinical trials. Given these characteristics and potential applications, it is likely that the clinical use of SPECT/CT will expand, becoming an increasingly important tool in diagnostic imaging for a wide spectrum of disease. Another important aspect of SPECT/CT is the fact that the technique, like PET, allows quantification of the amount of tracer in terms of Bq/mL or as a SUV. Numerous publications have shown that absolute quantification is feasible. This can be expected to further boost diagnostic confidence, e.g. for judging the efficacy of a treatment through follow-up acquisitions from the same patient or for improving dosimetry for radionuclide therapy.

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Image Reconstruction Techniques & Concept in Nuclear Medicine Imaging Systems

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PREAMBLE:

Image reconstruction is a mathematical process that generates tomographic images from projection data acquired at many different angles around the patient. Image reconstruction has fundamental impacts on image quality and provides significant technical challenges for the nuclear medicine personal.

PET/SPECT images are formed by acquiring gamma photons **emitted** from the body whereas CT images are by acquiring X-ray **transmitted** through the body. Only acquisition technique of each modality is different, otherwise reconstruction technique is common in all the modalities e.g. SPECT, PET, CT and MRI.

The basic principle of tomography is to reconstruct the image of a slice of activity in the body based on the measured images at different angles. A set of images around the patient are acquired (called forward projections), then consider only the single lines on these images that correspond to the acquired counts from a single slice. The reconstruction is done by commonly either back projection or iterative reconstruction algorithms.

Filtered back projection (FBP) and the associated filtering necessary to reconstruct data in emission tomography are very simple and mostly used. However, FBP has some limitations, particularly when there is need to incorporate attenuation correction. The alternative is to adopt an iterative reconstruction technique, which more readily can incorporate accurate attenuation correction as well as having attractive noise properties. The basic concepts of each reconstruction techniques with some emphasis on iterative-maximum likelihood reconstruction will be discussed. The later technique is time consuming but the availability of faster computers has enhanced the applicability of iterative techniques in clinical practice.

Simple back projection reconstruction Technique:

In tomography, the data acquired at different angles (called forward projections) is back projected for reconstruction. Back projection involves taking the projection counts and projecting these, back along the direction from which the counts originate. For a parallel hole collimator this is assumed in a direction at perpendicular to the detector (assuming all detected photons have travelled in straight lines and are well collimated). Since we do not know the exact location from which counts originated, the best we can do is to allocate counts equally along this line as shown in Fig. 1 (a, b).

Filtered back projection (BP):

Though the back projection reconstruction technique is very simple to use but it has several drawbacks: First, it produces an image, which has a high density in the center (PI see above figure). This is due to the fact that many different images are being overlapped in this area. Secondly, the resulting image is severely blurred and we end up with counts streaked (star artifact) all over the image (Fig 2a, 2b). We have to find a solution to correct this problem that has been introduced by the back projection process. The way this is done is to add a filter to correct the problem and perform **filtered back projection**. The purpose of the digital filter is to correct for the star artifact in the back projection process. The correction can be done on the final image, but it happens that one can apply the correction to the original projections, before back projection, which can be done by Fourier Transform.

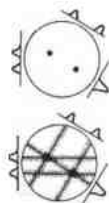


Figure 2a-b.

(a) Distribution of radioactivity from two points sources acquired at different angles shown

(b) Back projections of these point sources by superimposition at various angles to reconstruct images (to get back two point sources). The drawback is it introduces star artifacts.



Filtered back projection always involves a Ramp filter. However a second smoothing filter (or combined smoothing/Ramp filter) is necessary to control the noise. For that the question is always comes in mind that which second filter one should use to control noise in filtered back projection and for that the complete knowledge of digital filtering is required

The window of filter is chosen in such way that it retain true signal at the low frequencies, but remove statistical noise at both the lowest and highest frequencies. Therefore, filtering is accomplished through multiplication of Ramp reconstruction filter with a low pass frequency and it may be expressed as follow:

$$H(f) = f \cdot L(f)$$

Where $H(f)$ is the modified reconstruction filter at frequency 'f' and $L(f)$ is a low pass frequency filters of choice. Pl note that Ramp filter is a linear filter, that is why we use Ramp filter ($\text{Amp} = \text{freq}$), whose amplitude increases with frequency and after multiplication result is always equal to 1 (i.e. $1/f \times f = 1$)

The various filters which are generally used along with Ramp are low pass filter (allows low frequencies and cut-off higher noisy frequencies) viz. Butterworth, Hann (often misnamed as the Hanning), Shepp-Logan, Parzen, Gaussian, etc. These are all smoothing filters, which can be combined with the Ramp. These different named filters simply refer to the shape of the filters that are all slightly different. Normally choose parameters that further modify the shape of these filters so the final result will depend not only on the filter chosen but also the parameters chosen.

It is worth to mention here that amongst all filters, the **Butterworth** filter is the main filter since it is widely used as its shape is particularly well suited to SPECT filtering. It has a specific shape with a plateau at low frequencies (this means that the filter has no effect on low frequencies (multiplying by 1) but only affects high frequencies).

In addition, Image **Smoothing** is necessary since the Ramp filter also **amplifies high frequency noise**. Since smoothing involves multiplication (in the Fourier domain) it can be performed **before, during or after Ramp Filtering**. In all cases if the same filter is applied the result is same. However smoothing can be improved if you smooth in as many directions (x, y, z) as possible. In short, it does not make any difference whether we apply filter i.e. before or after reconstruction. On some systems one has a choice of exactly when to apply filter either as a pre-reconstruction filter or post-reconstruction filter. Infact it can be demonstrated that one can achieve exactly the same results by a number of approaches.

Each filter has some advantages and disadvantages. One must decide what is more necessary: less noise, clear image, or faster results when deciding which filter to use.

Iterative Reconstruction:

Although FBP gained popularity as a very fast reconstruction technique there are limitations in the image quality produced. To a large extent this is due to the back projection process and the necessary filtering, which accentuates noise and can result in streak artifacts and degrade the image quality, especially when projection is having low counting statistics. Also, filtered back projection is not suitable, particularly when there is need to incorporate accurate non-uniform attenuation correction, scatter, quantitative imaging and other physical factors. An alternative to FBP is to use iterative reconstruction technique [4, 5, 6] and can incorporate attenuation correction and helps to remove noise. However, limitations exist for the routine application of this technique due to the higher computational demand and the slow convergence of the algorithm. Therefore, the iterative reconstruction was mainly limited to faster computer systems. Due to the availability of new powerful PC systems; the iterative reconstruction can now be implemented on PC based workstation also. The iterative reconstruction algorithms are now commonly available from commercial suppliers and therefore familiarity with iterative reconstruction techniques is required.

Basic of Iterative Reconstruction Technique:

Iterative reconstruction technique is nothing but guess work by taking progressively smaller steps that gradually get closer to the correct (difference between guess and actual approach to zero) solution. It is also called hit and trial method so that the difference between object and image is minimal small. For PET scanner, a common iterative reconstruction technique is maximum likelihood reconstruction in which projections estimated from the current solution are compared with the measured projection and the current solution is modified to minimise the difference.

In SPECT study, by using the guess to estimate, what the projections would look like i.e. what the gamma camera would have seen if the guessed object was imaged. It would be similar to what was measured but would not be the same. One can therefore compare the estimated projections, based on your guess, with the real measured projections and use this comparison to alter the result, which is illustrated in the flow chart (Fig. 3)



Fig. 3 Flow chart of Iterative Reconstruction Technique

There are many ways in which iterative reconstruction can be performed but all have similar approaches. Probably the most commonly used method is called **maximum likelihood (ML) reconstruction**, often referred to as expectation maximisation (EM) or OSEM (Ordered Subset Expectation Maximisation) reconstruction. ML reconstruction usually is performed using the (EM) algorithm, whose abbreviation is commonly used.

There are many types of Iterative Reconstruction methods available. All the early CT reconstructions were iterative before FBP became standard for SPECT and PET studies most widely recommended type is the: **Maximum Likelihood family** [8, 9], using the **Expectation Maximization algorithm (ML-EM)**. A major attraction of this algorithm is its simplicity.

In summary, the filtered back projection (FBP) algorithm and statistical model based iterative algorithms such as the maximum likelihood (MLEM) reconstruction are the two major classes of tomographic reconstruction methods. Analytic reconstruction algorithms, for example the filtered back projection algorithm, are simple, faster and elegant, but they are unable to handle complicated factors such as scatter, attenuation corrections, etc. Iterative reconstruction algorithms on the other hand are more versatile and produce accurate images without star artifacts as in the FBP. They allow important corrections for image degrading effects, such as attenuation, scatter and depth-dependent resolution. Earlier, the main limitation for introducing iterative algorithms in nuclear medicine was computation time, which is much longer for iterative techniques than for FBP. Many new iterative algorithms are currently under development, which will reduce the reconstruction time. With the advent of faster computer, it is possible to reduce the iterative processing time to minimum and will enable more quantitative reconstructions.

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Quality control of PET/CT as per NEMA Guidelines: From reference manual to Manoeuvre into practice.

Mr Ankit Watts , PGIMER, Chandigarh

The introduction of PET more than 2 decades ago has revolutionized oncologic imaging and fostered a new understanding of molecular alterations of cancer cells. Interest in PET especially increased after the introduction of PET/CT scanners, which allowed for the collection of both anatomic information and metabolic or functional information in vivo in one scanning session. Diagnostic capability of a PET/CT is dependent upon on the accurate, reproducible performance of the instrument. The complexity of a combined PET/CT system needs to be balanced with rigorous quality control (QC) procedures. An extensive series of parameters has been developed over the years for acceptance testing and performance characterization of PET/CT scanner. National Electrical Manufacturers Association (NEMA) has promulgated the detailed data acquisition and analysis protocols for this purpose. However,



the settings, procedures and phantoms to be used are, normally, manufacturer specific. The performance characteristics (specifications) are provided together with the equipment and should be checked during acceptance testing of the equipment. Daily and periodic test results should be recorded and monitored continuously, so that any significant deviation from the reference values can be detected and corrected for, before affecting clinical results. Both the PET and the CT components should be tested separately as recommended and each parameter's working limits should be considered. The NEMA has revised standard document for PET scanner with the first being NU2-1994 followed by Nu2-2001 to specifically cater for 3-D scanning and the effects of out-of-field radioactivity. In year 2007, then Nu2-2007 document was made to cater for the introduction of PET scanners with intrinsically radioactive components & latest being Nu2-2012 amended to include the time of flight and nontime of flight coincidence systems, discrete and continuous detector designs, single and multiple slice devices and multi-planar and volume reconstruction models.

Before planning a QC procedure it is advisable to prepare a schedule of testing and radioactivity requirements in advance of testing. Depending on the scanner, acceptance testing & complete yearly / scheduled quality controls can be completed in three to five days. Some of the essential tests as recommended by NEMA are:

- Spatial resolution
- Sensitivity
- Scatter fraction, count losses and randoms measurements
- Energy resolution
- Image quality and accuracy of attenuation, and scatter correction and quantitation
- Coincidence timing resolution for TOF

Once the instrument that is being tested passes all of the acceptance tests, 'benchmark tests' must be performed. These tests are a set of quality control (QC) tests that are performed in the same way as the routine QC procedures. The benchmark tests serve as a baseline for instrument performance and are used to evaluate subsequent QC tests. The tests should also be used to evaluate instrument performance after major services and updates in software, and must be repeated after upgrades in hardware & as required by the competent authority of the country.

Practical Experience in operations of Medical Cyclotron

Dr Rajeev Kumar, AIIMS, New Delhi

Cyclotron is a type of particle accelerator which is invented by Ernest O. Lawrence^[1] in 1934. In this charged particles accelerate outwards from the centre along a circular pathway. Lawrence was awarded the 1939 Nobel prize in physics for this invention. There are approximately over 1200 cyclotrons used in nuclear medicine worldwide for the production of radionuclides.

Our facility has a self-shielded medical cyclotron RDS 111 from Siemens Ltd. located in the basement with an 11MeV proton beam in use for the past 10 years to produce positron emitters (18F, 13N, 11C, 15O and 18F-2) for PET imaging. It is a negative ion Cyclotron with 8 targets each side having 40 micro ampere target current.

During the routine operation of cyclotron, it is mandatory to measure the radiation levels in and around the cyclotron. This helps to keep the radiation exposure to a level of minimum and also helps the radiological safety officer (RSO) and medical physicist (MP) to identify the high radiation level around cyclotron. During 18F production, we follow a set protocol comprising the following: monitoring target pressure, rinsing the target with 16O water just immediately after bombardment, ion source feedback, radiofrequency (RF) feedback, and recording any unusual events that occurred during the operation. Besides this, enrichment of 18O water, target volume, target current, energy of the beam, variation in argon pressure on the target, bombardment duration, target status (new or old target or total number of previous bombardments on the same target), status of the delivery lines from target to the radiochemistry module (old or new) are also recorded. We share our ten years of operational experience of medical cyclotron. This experience has helped us gain working knowledge on cyclotron operation with practical points, which may help in improving 18F yield, minimizing the breakdown time, and help in the prevention of the occurrence of unusual events.



Clinical Importance of Quality Control in Nuclear Medicine

Subhash Chand Kheruka

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Nuclear medicine is critically dependent on the accurate, reproducible performance of clinical radionuclide counting and imaging instrumentation. Quality control (QC), which may be defined as an established set of ongoing measurements and analyses designed to ensure that the performance of a procedure or instrument is within a predefined acceptable range, is thus a critical component of routine nuclear medicine practice. An extensive series of parameters has been developed over the years for acceptance testing and performance characterization of γ -cameras, SPECT and PET scanners, and other nuclear medicine instrumentation. And detailed data acquisition and analysis protocols for this purpose have been promulgated by the National Electrical Manufacturers Association (NEMA), the American Association of Physicists in Medicine (AAPM), IAEA, IEC and other regulatory, advisory, and professional organizations.

Proper record keeping greatly facilitates detection of gradual deterioration of performance over an extended period of time, by analyzing the results for degradation and initiating corrective action when necessary.

A baseline set of quality control results should be recorded, after a thorough evaluation of the system at installation and acceptance testing, to serve as a reference for the life of the equipment. These can be used as a basis for developing detailed protocols for individual systems and models of equipment.

As advances in medicine occur at a rapid rate, the review and update of guidelines, such as these, should take place at regular intervals and should be considered to be part of the quality assurance process.

Molecular Imaging

Current Trends in Molecular Imaging and Radionuclide Therapy"

Dr. Baljinder Singh

Dean-Indian College of Nuclear Medicine & Professor, Department of Nuclear Medicine
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In the current era of providing personalized medicine especially in cancer, functional PET-molecular imaging using both 18-fluorodeoxyglucose (FDG) and non-FDG tracers and providing accurate information about tumor biology and cellular characteristics play an important role. This 'state of the art' PET molecular imaging has undoubtedly established its strength in demonstrating the inherent heterogeneity of cancer cells with their varied cellular biology and metabolic and receptor phenotypic expression in cancer patients through the use targeted PET/SPECT radiopharmaceuticals. During the last two decades, we have witnessed a significant improvement of oncological imaging through CT, MR imaging, PET, subsequent movement through hybrid or fusion imaging with PET/CT and single-photon emission computerized tomography (SPECT-CT) and now moving ahead towards the evolving PET/MR imaging.

These technological and radiopharmaceuticals advancements have been able to enhance oncology care and have the potential to help image the tumor biology at the cellular level, followed by providing a tailored treatment. Molecular imaging, integrated diagnostics, biology-driven interventional radiology and theranostics, all hold immense potential to serve as a guide to give "start and stop" treatment for a patient on an individual basis. This will likely have substantial impact on both treatment costs and outcomes.

I shall be discussing current trends in molecular imaging and targeted radionuclide therapy through the practice of established and experimental techniques (PET/CT) with particular emphasis on newer SPECT/PET molecules and newer beta/alpha radionuclides Theranostics. The molecular imaging and translation research and its role in drug development shall be discussed.



Mathematical Modeling of Molecular Imaging Using Lattice Boltzmann Method

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Abstract

Molecular imaging (MI) is a new biomedical research discipline which enables the visualization, characterization and quantification of biologic processes that take place at the cellular and subcellular levels within intact living subjects including patients. MI includes the field of nuclear medicine along with various other fields that together offer an array of different strategies to produce imaging signals. Whereas nuclear medicine uses radiolabeled molecules (tracers) that produce signals by means of radioactive decay only, molecular imaging uses these as well as other molecules to image via means of sound (ultrasound), magnetism (MRI or magnetic resonance imaging), or light (optical techniques of bioluminescence and fluorescence) as well as other emerging techniques. The images produced with MI reflect cellular and molecular pathways and mechanisms of disease present in the context of the living subject. MI is a new paradigm, in the sense that the molecular imaging itself encompasses a new imaging paradigm that includes multiple image-capture techniques, cell/molecular biology, chemistry, pharmacology, medical physics, biomathematics, and bioinformatics. MI is in contrast to the classical form of diagnostic imaging where documented findings show the end effects of these molecular alterations typically via macroscopic and well-established gross pathology.

Applications of MI techniques will benefit various clinical practices including classification and tracking of chemotherapy and treatment planning of radiotherapy, as well as drug discovery and development. MI typically includes two or three dimensional imaging with quantification over time, and is often applied on molecular imaging modalities, such as Positron Emission Tomography (PET), Single Photon Emission Computed Tomography (SPECT) etc. According to the definition from the Society of Nuclear Medicine and Molecular Imaging (SNMMI), molecular imaging is the visualization, characterization, and measurement of biological processes at the molecular and cellular levels in humans and other living systems. Molecular imaging usually involves two- or three- dimensional images and conducts quantitative analysis over the time. Molecular imaging modalities include Positron Emission Tomography (PET), Single Photon Emission Computed Tomography (SPECT), Optical imaging, Magnetic Resonance Imaging (MRI), Computed Tomography(CT), and Ultrasound(US).

Lattice Boltzmann computational Scheme can be applied to model the molecular imaging mathematically. Lecture will finally address the knowhow of this new computational scheme for addressing the molecular imaging.

Keywords: Molecular imaging, PET, SPECT, biomedical, nuclear medicine, radiotherapy

"Contrast in PET/CT with emphasis on different protocol and management of its allergic reaction"

Dr Punit

State-of-the-art diagnostic positron emission tomography/computed tomography (PET-CT) with intravenous or oral contrast gives excellent anatomic details as well as information on tumor vascularization and reduces the need for additional contrast-enhanced diagnostic imaging modalities. It has now become the standard of care in most of PET-CT centers. While intravenous contrast agent are usually sub grouped as ionic and non-ionic agents, oral contrasts are sub grouped as positive or negative oral contrasts. Contrast agents (especially positive oral contrast agents) in PET/CT may lead to overestimation of PET attenuation factors; however, this increase/overestimation of standardized uptake value is clinically insignificant. Use of positive oral contrast agents should be limited to patients in whom the pathologic abnormality or site of suspected disease is in the gastrointestinal tract or abdomen. Use of contrast especially intravenous contrast is associated with various adverse reactions. These can be divided into mild, moderate, and severe. Mild reactions are the most common and include itching, flushing, pallor, rashes, and so on and usually require observation and reassurance. Moderate reactions like tachycardia, hypotension, bronchospasm, laryngeal edema, and others require prompt treatment and close observation. Rarely, severe, life-threatening reactions may occur like progressive laryngeal edema, profound hypotension, cardiopulmonary arrest, convulsions, and so on that require hospitalization and prompt intervention.

Short Biography

CURRENT POSITION: Working as Consultant, Department of Nuclear Medicine and PET/CT, Apollo Gleneagles Hospitals, Kolkata, India



PROFESSIONAL QUALIFICATIONS

- MBBS (Cal)
- MD (Nuclear Medicine-AIIMS, Delhi)
- FANMB (Fellow Asian Nuclear Medicine Board)
- FEBNM (Fellow European Board of Nuclear Medicine)
- Member Indian College of Nuclear Medicine (MICNM)
- Young Professional Committee Award in Clinical Sciences, 2013, Awarded by Society of Nuclear Medicine and Molecular Imaging's Young Professionals Committee
- Asian Young Investigator Award, 2013, Awarded by the Japanese Society of Nuclear Medicine

Publications:

About 160 publications in reputed International and National Journals

Translational Preclinical Imaging and Drug Discovery Research

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Abstract

Translational imaging is becoming very important in clinical and preclinical drug development apart from its diagnostic potential. There are several steps in the process of drug discovery, which starts with *in silico* tests and involves several *in vitro* and *in vivo* assays till clinical trials. *In vivo* tests are performed in suitable animal model system. Conventionally *in vivo* evaluation is done in large number of animals, but presently by introduction of imaging technologies the number of animals has been reduced. Besides the data obtained is more accurate and reproducible. The precision data can be obtained with advanced imaging technologies such as PET, SPECT, CT, MR and optical imaging. PET, SPECT being nuclear medicine modalities involves use of suitable radioisotopes. The animal model validation is also done using imaging and then once model is ready the drug efficacy is also evaluated using imaging.

In last decade interest in preclinical imaging technologies has increased manifold. The instrumentation used in these modalities is based on similar detector material, signal recognition criteria and data analysis algorithms used in clinical instruments. The biomarkers used in preclinical and clinical stage evaluations are same, which makes translation more comparable, faster and allows us to take go or not to go decisions about new molecules quickly. Combination imaging is also getting popular in preclinical setup due to its advantages such as accurate information about molecular event and its localization. This talk deals with our experiences in setting up of first preclinical nuclear medicine imaging laboratory and its utility in drug discovery as well as other multidisciplinary research area.

The Role of Positron Emission Tomography-Computed Tomography (PET-CT) with Elevated Tumor markers in Better Diagnosis, Prognosis and Treatment of Cancer Patients with Suspected Recurrence.

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Keywords: PET-CT, Tumor Markers, Cancer Recurrence

Introduction:

Early detection of cancer recurrence is clinically important and can improve the prognosis and survival of patients. Computed Tomography (CT), considered the primary method of investigation because of its low cost and widespread availability, provides anatomic details but may underestimate small tumor clusters in areas of distorted anatomy after treatment. 18F-FDG PET-CT is an effective whole-body imaging technique which provides fused images that demonstrate the complementary roles of functional and anatomic assessments in the diagnosis of cancer recurrence through the precise localization of suspected 18F-FDG foci. In addition to this PET-CT has an impact on patient management because it can assist in defining potential candidates for surgery for cure, planning the appropriate surgical or radiotherapy approach, and referring patients with unresectable disease to other therapeutic options. Tumor markers are substances that are produced by cancer or by other cells of the body in response to cancer. Higher



levels of tumor markers are indicative of the presence of cancer in the body. Elevated levels of tumour markers like CA 15.3 for Ca Breast, Ca 125 for Ca Ovary, CEA for Colorectal Ca, PSA for Ca Prostate are frequently registered in the follow-up of cancer patients.

Method:

Standard protocol of whole body F-18-FDG PET/CT imaging is followed. 10mCi dose of F18-FDG is injected I/v, after overnight fasting and scan is taken 60min post injection. Oral and I/v contrast agents are administered in patients who present clinical system regarding the same to ensure diagnostic CT data. Levels of serum creatinine is monitored before giving I/v contrast in order to avoid kidney impairment. In case of diabetic patients levels of their blood sugar is checked before injecting the dose. It should be below 150 mg/dL.

Discussion:

Colorectal Cancer is one of the most frequent malignancies in the world. Approximately one third of patients with newly diagnosed colon cancer will develop liver metastases. The overall PET-CT performance for recurrent colorectal cancer in the abdomen, the liver, and extra abdominal sites showed a sensitivity of 89%, a specificity of 92%, and an accuracy of 90%. The metabolic information provided by PET and superimposed on topographic CT landmarks optimized subsequent surgical and radiation treatment planning by differentiating surgical scar from recurrence. Further, CEA levels may be useful in the cancer prognosis or post-operative surveillance of colorectal cancer patients.

Ovarian Cancer,

PET-CT is very helpful for the early diagnosis of recurrent ovarian malignancies. Hybrid imaging differentiates between adjacent sites of physiologic and malignant 18F-FDG uptake and defines the pattern of metastatic peritoneal seeding sparing unnecessary invasive diagnostic and therapeutic procedures in patients with extensive disease. CA-125 antigen remains the only serum tumour marker routinely used in epithelial cancer of the ovary for patient prognosis, disease progression, and response to chemotherapy.

Breast Cancer, is the most frequent malignancy in women. It can recur at any time, but most recurrences occur in the first three to five years after initial treatment. Following the increased clinical use of CA 15.3 serum tumor marker measurements, non invasive PET-CT can decrease the time lag between diagnosis and treatment of relapsing breast cancer and therefore increase the chances for cure or long-term palliation.

Prostate Cancer, Prostate Specific Antigen (PSA) is present in small quantities in the serum of normal men, and is often elevated in the presence of prostate cancer and other prostate disorders. Although other imaging techniques such as bone scan, MRI can also help in detecting recurrence but whole body PET-CT imaging in one shot can scan chest, abdomen including bones to look for cancer recurrence.

Thyroid Cancer, is monitored mainly with measurements of serum thyroglobulin. The next step is whole body radioiodine imaging. Patients with noniodine-avid recurrent thyroid cancer pose a therapeutic dilemma because they will not respond to 131I treatment. In that case 18F-FDG is taken up by metastatic noniodine-avid thyroid cancer as a result of a tumor dedifferentiation process, and PET-CT therefore provides important prognostic information.

Conclusion:

Recurrent cancer can pose considerable diagnostic and therapeutic challenges for the oncologic team. PET-CT, a single-step metabolic and structural whole-body imaging procedure, is being advocated as a useful tool for early detection of cancer recurrence. Tumour markers may be used to help diagnose cancer, predict and monitor response to treatment and determine whether cancer has recurred after treatment. In general, tumour markers alone cannot be used to detect cancer recurrence alone, they must be combined with other investigations such as PET-CT in order to decrease the time lag between diagnosis and treatment of relapsing cancer and therefore increases the chances for cure or long-term palliation.



Utility of Attenuation Corrected and Non Attenuation Corrected images in Cardiac SPECT/CT study

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MPS has become an indispensable tool in the assessment of patients with known or suspected coronary artery disease, presenting great diagnostic and prognostic utility. Although the sensitivity of cardiac SPECT is high, the specificity remains low because of the image artefacts resulting from the nonuniform reduction of photon activity caused by attenuation, which causes apparent perfusion defects. To better discriminate perfusion defects from artifacts, several methods have been proposed such as integrating findings from gated SPECT, scanning patients in the prone position, and using an external source of irradiation, either a line source or CT. CT-AC has several advantages over external radionuclide sources for AC, such as higher photon flux and hence no influence by cross-talk from the SPECT radionuclide, no decay of transmission source, and shorter scan times. Use of CT-AC has demonstrated to increase the specificity, sensitivity and accuracy of MPS. However, sometimes it may overcorrect the attenuation and cause a decrease in sensitivity of MPS. Also, if there is misalignment between SPECT and CT, then it becomes a major source of artifact in corrected images. Thus a judicious use of AC is proposed for better diagnostic accuracy in MPI SPECT/CT.

Radiation Safety & Dosimetry

¹⁸F-DG PET/CT Dosimetry using Dynamic PET Scan Protocol

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There is a growing concern over the radiation exposure of patients from undergoing ¹⁸F-DG PET/CT (¹⁸F-fluorodeoxyglucose positron emission tomography/computed tomography) whole body investigations. The aim of the present study was to study the kinetics of ¹⁸F-DG distributions and estimate the radiation dose received by patients undergoing ¹⁸F-DG whole body PET/CT investigations.

Dynamic PET scans in different regions of the body were performed in 49 patients so as to measure percentage uptake of ¹⁸F-DG in brain, liver, spleen, adrenals, kidneys and stomach. The residence time in these organs was calculated and radiation dose was estimated using OLINDA software. The radiation dose from the CT component was computed using the software CT-Expo and measured using computed tomography dose index (CTDI) phantom and ionization chamber. As per the clinical protocol, the patients were refrained from eating and drinking for a minimum period of 4 h prior to the study.

The estimated residence time in males was 0.196 h (brain), 0.09 h (liver), 0.007 h (spleen), 0.0006 h (adrenals), 0.013 h (kidneys) and 0.005 h (stomach) whereas it was 0.189 h (brain), 0.11 h (liver), 0.01 h (spleen), 0.0007 h (adrenals), 0.02 h (kidneys) and 0.004 h (stomach) in females. The effective dose was found to be 0.020 mSv/MBq in males and 0.025 mSv/MBq in females from internally administered ¹⁸F-DG and 6.8 mSv in males and 7.9 mSv in females from the CT component. For an administered activity of 370 MBq of ¹⁸F-DG, the effective dose from PET/CT investigations was estimated to be 14.2 mSv in males and 17.2 mSv in females.

The present results did not demonstrate significant difference in the kinetics of ¹⁸F-DG distribution in male and female patients. The estimated PET/CT doses were found to be higher than many other conventional diagnostic radiology examinations suggesting that all efforts should be made to clinically justify and carefully weigh the risk-benefit ratios prior to every ¹⁸F-DG whole body PET/CT scan.

Challenges and Advances in Development of Medical Countermeasures against Radiation

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Twenty first century can be considered as a century for advanced translational research in radiobiology. Over the past few decades, there has been tremendous increase in our understanding about the biological effects of low as well as high linear energy transfer (LET) radiations. The health effects of radiation are governed by the type of radiation, dose, dose rate, duration of exposure and nature of exposure such as internal or external. Certain organs and systems such as immune system, hematopoietic system, gastrointestinal tract are understood to be at greater risk. In situations where large doses (acute) are absorbed, multiple tissues and body cells are affected, the acute radiation syndromes



(ARS) are experienced. During ARS, either multiple organ failure (MOF) or multiple organ dysfunction (MODF) results leading to death of individuals in days or weeks after the radiation exposure. The ARS has been witnessed in large populations during WWII atomic bomb explosions, and more recently during radiation accidents such as Chernobyl accidents in year 1986 and Fukushima accidents in year 2011. The manifestation of radiation injuries is a complex process. The tissue reactions appear either early or late after the absorption of radiation doses above a threshold limit. The latency time before manifestation is related to cell turnover rates, structural organization of tissue and its proliferative behavior.

Development of medical interventions to seek protection from radiation injuries has been of paramount importance on human mind after WWII. Despite decades of intense research in this field world over, availability of medical countermeasures for prophylactic use, which are safe and effective for human use, remains an unmet demand globally; although some agents, meant for mitigation and/or treatment of radiation injuries, have reached the penultimate stages. Undertaking newer goal oriented, research to fill the knowledge gaps and meet the societal expectations is important and requires collective wisdom. It calls for refreshing and reinforcing the understanding of key radiation biology and protection principles. It also compels us to revisit the approaches tested so far, and dwell on the concepts arising from newer researches in various allied areas. Some of our recent understandings and approaches used in the field of development of medical countermeasures will be highlighted.

Neutron dosimetry by superheated emulsion

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Superheated emulsion detector consisting of the droplets of superheated liquid is a promising neutron detector that has been using since 1979 [1]. Superheated droplet neutron dosimeter is used for measuring the neutron dose equivalent in and around the radiotherapy beam and in patients in the presence of large background of photon flux (three to four orders of magnitude larger than neutrons) [2].

Superheated emulsion detector consists of the droplet of superheated liquids which undergoes phase transitions to vapour bubbles upon irradiation with the release of acoustic waves and these bubbles as well as the acoustic pulses are detected for the measurement of the radiation. If the Linear Energy Transfer (dE/dx) by a particle is greater than critical energy (W) deposition ($W > krc$), nucleation occurs, where k is the nucleation parameter and rc is the critical radius. The threshold energy for such detector depends on temperature and pressure and the types of the sensitive liquid used in the detector. Thus the detector can be made insensitive to gamma rays while being sensitive to neutrons by varying the ambient temperature and pressure of the liquid. This property of the detector makes it a very useful tool in neutron dose measurement in a strong background of gamma rays. Superheated emulsion detector along with the required instrumentation has been developed in our laboratory for neutron measurement.

Out-of-field dose measurements in radiotherapy have been done with superheated emulsion by the EURADOS Working Group 9 (WG9). WG9 research aims at estimating the risk of second cancer induction due to radiation therapy [3,4]. Position sensitive superheated emulsion chamber for 3D brachytherapy dosimetry has also been developed [5]. The neutron energy spectrum has been measured with superheated emulsions by varying the operating temperature and applied pressure, in presence of neutrons generated by the $Pb(\gamma, n)Pb$ from 45MeV electron LINAC at Hokkaido University, Japan [6]. The neutron bubble detector is so far the only personal neutron dosimeter satisfying the energy response criteria of the International Committee of Radiation Protection 60 (ICRP 60) [7]. It has turned out to be a reliable and cost effective dosimeter for medical applications.

The intrinsic background of the detector makes it less sensitive as a dosimeter. The main intrinsic background of this detector is alpha particles coming from the contamination of both detector polymer and the active liquid and that needs to be investigated. The simulation of the response for alpha-particles to superheated emulsion detector using GEANT 3.21 simulation toolkit has been carried out. The simulation is done for 241Am spiked detector where the contamination is in polymer and 226Ra spiked detector where the contamination is both in the polymer and in the droplets. In both cases, the simulation results are reasonably well matched to the experimental results [8] This result implies that the alpha particles is not responsible for the shift of the threshold to lower temperature. Unlike 241Am spiked detector, in case of 226Ra spiked detector various recoiling nuclei from the decay chain of 226Ra are present inside the droplet and the calculation of LET shows that 208Pb of energy 146 keV in particular has a higher value of LET compared to that of alpha-particles, which could trigger nucleation events at a lower threshold temperature. It is observed from experiment that the nucleation events due to alpha particles are smaller than that of neutron for the droplets of 2-3 μm radii. Therefore, for neutron detection, most of these background events due to alpha particles can be well separated from neutron signals.



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New Concept of Radiation Burden in Medical Imaging: Shift from LNT model

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The linear no-threshold model (LNT) is a model used in radiation protection to quantify radiation exposure following medical procedures and thus set regulatory limits. It assumes that the long term biological damage caused by ionizing radiation (essentially the cancer risk) is directly proportional to the dose. This allows the summation of all radiation exposures, without considering dose levels or dose rates. In this 70 year old model, radiation is always considered harmful with no safety threshold. The model promotes a liner relationship between radiation exposure and risk of carcinogenesis.

The LNT model was introduced as a concept to facilitate radiation protection. But the use of this model led to the claim that even the smallest dose may initiate carcinogenesis for instance, from diagnostic x-ray sources. This claim is highly hypothetical and has resulted in medical, economic, and other societal harm. There are recent studies being published in radiation physics and medical journals which have questioned the authenticity and validity of such models. They have even highlighted the flawed assumptions of this model leading to "radiophobia". These studies have also established the fact that low dose radiation in fact does have some protective beneficial effect in the long run.

The concept of ALARA (as low as reasonably achievable) is a natural deduction of LNT model and as shown by recent studies this concept too is fatally flawed, focusing only on molecular damage ignoring protective, organismal biologic responses.

As a whole the medical imaging community has long remained concerned about radiation risk and developed a radiophobia-centered, not scientific, approach. The purpose of medical imaging studies is to provide diagnostic information and should be governed by the highest science-based principles and policies. The recent works have called for ending the radiophobia. This concept needs to be changed and the concept of LNT-ALARA-radiophobia needs to be changed. The mindset of the imaging experts and radiation personnel as well as regulatory authorities should also change. The image wisely and image gently campaign might have started with great intent but they should not promote radiophobia and suboptimal imaging studies obviating the benefits of medical imaging.



Regulatory Framework for Nuclear Medicine Facility in India

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Introduction

Radioactive materials and the radiation generating equipment have many applications in medicine, industry, agriculture and research. Radioactive materials are used either as sealed radioactive sources or unsealed radioactive sources. One such use of unsealed radioactive source is in nuclear medicine for diagnostic and therapeutic purpose. In nuclear medicine, mostly short-lived radionuclides in unsealed form are used. Iodine-131 and Technetium-99m are used in more than 90% of the Nuclear Medicine Procedures and Thallium-201 and Ga-67 in very few cases in India for diagnostic procedures. Radionuclides such as P-32, Sr-89, Y-90, Re-186 and I-131 are used for therapy procedures.

Single Photon Emission Computed Tomography (SPECT) and Positron Emission Tomography (PET) scans are the two most common imaging modalities in nuclear medicine. In nuclear medicine imaging, radiopharmaceuticals are taken intravenously or orally. Then, external detectors (gamma cameras) capture and form images from the radiation emitted by the radiopharmaceuticals. This process is unlike a diagnostic X-ray, where external radiation is passed through the body to form an image. Nuclear medicine scans differ from radiology as the emphasis is not on imaging anatomy but the function and for such reason; it is called a physiological imaging modality.

In view of the potential hazard associated with use of unsealed radioactive sources in nuclear medicine, the procedures related to nuclear medicine need to be controlled by appropriate measures to ensure that adequate safety is provided to the staff concerned with nuclear medicine, the patient, the general public as well as the environment. In order to enforce the regulatory control over the use of radioactive materials and radiation generating equipment, Government of India has promulgated the Atomic Energy Act. Under the provision of the Act, Radiation Protection Rules were issued as well as the competent authority was appointed to enforce of the provisions of the Rules.

Principal Legislations For Nuclear Medicine Facility

A. The Atomic Energy Act -1962

The Atomic Energy Act, 1962 provides the basic regulatory framework for all activities related to atomic energy programme and the use of ionising radiation in India. This is "an Act to provide for the development, control and use of atomic energy for the welfare of the people of India and for other peaceful uses and for matter connected with. This Act consists of many sections. Section 16 is related to control over radioactive substances whereas section 17 pertains to safety related issues involved and identifies the areas of concern and responsibility for those engaged in the applications of radioisotopes and use of radiation generating plants. Sections 24, 25 and 26 deal with penalties prescribing fine, imprisonment, or both, depending on the offence. Section 27 deals with power to appoint the Competent Authority to enforce the rules framed under the provision of the Act. Section 30 deals the power of the government to make appropriate rules to enforce the provision of the Act.

Rules under the Atomic Energy Act -1962

Under section 30 of the Atomic Energy Act-1962, following rules have been framed for control of radioactive substances:

- i) Atomic Energy (Working of the Mines, Minerals and Handling of Prescribed Substance) Rules, 1984
- ii) Atomic Energy (Radiation Protection) Rules, 2004
- iii) Atomic Energy (Safe Disposal of Radioactive Wastes) Rules, 1987
- iv) Atomic Energy (Control of Irradiation of Food) Rules, 1996
- v) Atomic Energy (Factories) Rules, 1996 (under the Factories Act, 1948)

Chairman, Atomic Energy Regulatory Board (AERB) is designated as the Competent Authority to enforce the above Rules. Chairman, AERB may issue Surveillance Procedures, Codes, Standards, and Guides which elaborate the provisions of the Rules for implementation.



B. Atomic Energy (Radiation Protection) Rules-2004

According to Rule 3 of the Atomic Energy (Radiation Protection) Rules 2004, a license is required for siting, design, construction, commissioning, operation and decommissioning of a radiation installation. License may be in the form of license, authorization or registration based on the hazard potential of the radiation installation. A license in the form of authorization is required for operation of a nuclear medicine facility. Rule 9 specifies validity of the license as five years whereas Rule 10 talks about suspension, modification or withdrawal of the license. Rule 14 specifies that radiation symbol and warning sign needs to be displayed conspicuously and prominently at various locations of the radiation installation. Accordingly to Rule 15, licensee needs to comply with the dose limits and other regulatory constraints specified by the competent authority time to time. As per Rule 16, competent authority may issue safety codes and safety standard prescribing various requirements related to a radiation installation. Under rules 19, every employer shall designate with the approval of the competent authority, a person having appropriate qualification as radiological safety officer (RSO). The responsibilities of the employer, the licensee and the RSO have been specified in rule 20, 21 and 22 respectively. Responsibilities of the worker have been specified in Rule 23. As per Rule 26, in case of diagnostic or therapeutic work using radiation generating equipment, sealed or unsealed sources, performance of the equipment needs to be verified periodically by appropriate quality assurance tests by the licensee for optimizing medical exposure. Rule 30 provides power for inspection of radiation installations and Rule 31 to investigate, seal or seize radiation installation or radioactive material in case of contravention of any of the provisions of the rules. Rule 33 talks about preparation of emergency preparedness plan by the facility.

C. Atomic Energy (Safe Disposal Of Radioactive Waste) Rules- 1987

These Rules are also framed under Section 30 of the Atomic Energy Act -1962. These Rules cover restriction on the disposal of radioactive material without valid Authorisation issued by the Competent Authority. **As per Rule 15 of the AE (SDRW)-1987**, Persons using small amounts of radioisotopes of very short effective half life for medical purpose may submit their application for authorisation to dispose of radioactive waste. Any authorised person may dispose of wastes containing short lived radioisotopes, contaminated materials and contaminated effluents, in accordance with the procedures and conditions laid down in the authorisation.

AERB's Safety Directive Applicable to Nuclear Medicine Facility

i) Directive No. 01/2011

It is necessary to monitor and control the dose received by the radiation workers during the work. It is the responsibility of the licensee of NM facilities to ensure that the radiation workers of the facility comply with the dose limits and regulatory constraints as specified by the Competent Authority. In exercise of rule 15 of the Atomic Energy (Radiation Protection) Rules, 2004, the Chairman, Atomic Energy Regulatory Board, being the Competent Authority under the said rules, has issued an order prescribing the dose limits for exposures from ionising radiations for workers and the members of the public, which needs to be adhered to by the facility. The directive talks about dose limit for occupational workers, apprentice & trainees and members of the public.

ii) Directive No. 02/2011

In exercise of rule 14(3) of the Atomic Energy (Radiation Protection) Rules, 2004, Chairman, Atomic Energy Regulatory Board, being the Competent Authority under the said rules, has issued an order prescribing the specifications for the radiation symbol and warning sign. Appropriate radiation symbol and warning sign needs to be displayed conspicuously and prominently at various locations of a nuclear medicine facility.

Safety Document for Nuclear Medicine Facility

AERB has published a Safety Code for Nuclear Medicine Facilities (AERB Safety Code No. AERB/RF-MED/SC-2 (Rev. 2), 2011) which stipulates radiation safety requirements in handling radioactive materials for nuclear medicine applications. The Code covers aspects like qualifications, role and responsibilities of employer, licensee, nuclear medicine physician, nuclear medicine technologist, radiological safety officer, radiological safety requirements, management of radiation emergencies and accidents, regulatory control, criteria for discharge of patients from hospitals and different forms for consent.



Guidelines for Setting Up of Nuclear Medicine Facility

In Nuclear Medicine (NM), the diagnostic and therapeutic procedures using unsealed radioisotopes needs to be done only in a facility approved by the Atomic Energy Regulatory Board (AERB). The approved nuclear medicine facility should not be located in the residential building and shall comply with all the regulatory requirements as specified in the AERB safety code on nuclear medicine facilities AERB/RF-MED/SC-2 (Rev. 2), 2011.

The various stages of approval of nuclear medicine facility by AERB are given as follows:

1. Site and Layout Plan Approval
2. Application for Authorization for Commissioning of the Facility
3. Pre-commissioning Inspection.
4. Approval for Commissioning / Routine Operation.
5. Decommissioning.

e- Licensing of Radiation Application (e-LORA) for Nuclear Medicine Facility

AERB has launched e- LORA (e- Licensing of Radiation Applications), an e-governance application system to facilitate online submission of applications for regulatory consents and establish channel of communication with AERB for other regulatory requirements. All Nuclear Medicine user Institutes are required to use e-LORA for obtaining relevant consents and approvals from AERB.

All the application forms pertaining to various stages of consenting of nuclear medicine facility can be submitted for approval through **web-based application named e-Licensing of Radiation Applications (e-LORA)**. General guidelines for regularizing of existing as well as new nuclear medicine facilities through e-LORA are (i) registration of the institute (ii) General requisite -General details of the facility has to be recorded in the system like declaration of different types of employees and approval of RSO (iii) adding of different instruments consisting of measuring, monitoring, safety and QA tools. Information to be provided or approval required through e-LORA for existing and new nuclear medicine facility is as follows:

A. Existing Nuclear Medicine Facility

Already existing Nuclear Medicine facilities have to regularize their Layout Approval and License of the equipment / installation in e-LORA. The following procedure needs to be adopted:

- (i) Approval of layout plan
- (ii) Application for Intimation of available equipment (PET/SPECT-CT/Gamma Camera/PET-CT / High Dose Therapy)
- (iii) Application for license
- (iv) Submission of QA/QC report and radiation survey report
- (v) Application for Decommissioning/Disposal
- (vi) Application for intimation of Decommissioning/Disposal

B. New Nuclear Medicine Facility

Guidelines for licensing procedures of New Facilities through e-LORA are as follows:

- (i) Approval of layout plan
- (ii) Intimation of available equipment (PET/SPECT-CT/Gamma Camera/PET-CT/High Dose Therapy)
- (iii) Application for source procurement
- (iv) Intimation of source procurement
- (v) Application for license
- (vi) Submission of QA/QC report and radiation survey report
- (vii) Application for Decommissioning/Disposal
- (viii) Application for intimation of Decommissioning/Disposal



Waste Disposal

In India, radioactive waste management is governed by the Atomic Energy (Safe Disposal of Radioactive Wastes) Rules, 1987, GSR-125 issued under the Atomic Energy Act, 1962. Radioactive waste needs to be managed safely because it is hazardous to human health and the environment. Through good practices in the production and use of radionuclides, the amount of waste may be significantly reduced but not fully eliminated. Radioactive waste in hospitals may be in solid, liquid, or gaseous form. Moreover, some of the wastes are mixed with biological substances, such as blood and may be infectious. Also, special precautions must be taken for disposing items, such as needles used for injection. All these aspects must be accounted for in the planning of waste treatment in a hospital.

The main radioisotopes used in hospitals are technetium-99m (Tc-99m), Iodine-131(I-131), Fluorine-18(F-18), Tritium (H-3) and Carbon-14(C-14). The bulk of the hospital radioactive waste gets generated in the department of Nuclear Medicine. Most of the radioactive waste is liquid, with lesser amount of solid and gaseous. Syringes, needles, cotton waste, vials, contaminated gloves and absorbent materials are the solid wastes containing traces of radioactivity. Clothing and utensils of patients administered high doses of radioisotopes also constitute the solid radioactive waste material. The radioactive waste should be identified and segregated. Foot operated waste collection bins with disposable polythene lining should be used for collecting solid radioactive waste and polythene carboys for liquid waste. Each package is monitored and labeled for the activity level before disposal.

All the labels on the containers having contaminated radioactive material should be removed, defaced prior to disposal. There are two main approaches to the disposal of radioactive waste. One is characterized as "dilute and disperse" and the other as "concentrate and contain." By the "dilute and disperse" concept, radioactive material, in aqueous or gaseous form, is released into the environment in such a way that the material is diluted and distributed over a large volume so that the final concentration of radionuclides is acceptably low. In the "concentrate and contain" approach, the waste is collected and converted into a form such that, when placed in a repository, it will retain the radionuclides until the activity has decayed, or at least will ensure that the leakage of radionuclides from the repository does not give rise to unacceptable concentrations anywhere in the environment. This approach is always used for longer-lived solid radioactive waste and spent sources, which are negligible in the PET-CT facility.

Regulatory Inspection & Periodic Review

According to Rule 30 of the Atomic Energy (Radiation Protection) Rules, 2004, any person duly authorized under sub-section (4) of Section 17 of the Atomic Energy Act, 1962 may, for the purpose of enforcement of these rules, inspect any premises, or radiation installation. In case of new nuclear medicine facilities, pre-commissioning inspection is carried out to ensure whether the construction of nuclear medicine facility is as per the approved plan, to verify whether all information provided in the application form for obtaining license of commissioning are correct and whether all the facilities for operation are available. The facility may be required to perform the QA tests as per the NEMA protocol in front of the AERB inspector during inspection. In addition, routine as well as surprise regulatory inspection are also carried out by AERB to physically verify radiological safety status of nuclear medicine practices. Facility also needs to submit safety status report of the facility annually. The same is reviewed and if any non-compliance is noted, the same is communicated to the facility for immediate compliance.

Personnel Monitoring Services & Dose Records

Every staff member, involved in radiation work, such as radio-pharmacy, radiochemistry, dispensing of radioactivity, radio-pharmaceutical dose administration, patient imaging, and others, should be provided with personnel monitoring services. For availing this facility, one may approach RP and AD, BARC, Anushakti Nagar, Mumbai - 400 094, or the respective accredited laboratory in their zone for the service. Presently, four such laboratories are accredited as given below:

Sl.	Name of Accredited Laboratory	States covered
1	M/s. Avantec Lab. Private Limited, 76, 7th street, ground floor, Ponur Garden, Phase-1, Chennai, Tamil Nadu, Pin-600095	Andhra Pradesh, Tamil Nadu, Karnataka, Kerala, Puducherry (Southern Region)
2	M/s. Renentech Lab. Private Limited, C-106, Synthofine Industrial Estate, Off Aarey Road, Goregaon (E), Mumbai, Pin-490063	Maharashtra, Gujarat, Rajasthan, Goa (Western Region)



3	M/s. Ultratech Lab. Private limited, Cloth Market, G.E. Road, kumhari, Bhilai, Durg, Chhattisgarh, Pin-490042	All other states in the Central, Northern and North Eastern parts of the country
4	Defense Laboratory, Jodhpur	All Defense institutions of the country

Up to date dose records of all the radiation workers needs to be maintained by the facility and information should be given to the radiation workers about their monitoring results. As per the Directive issued by the Competent Authority vide notification ref. no. CH/AERB/ITSD/125/2011/1507 dated April 27, 2011, investigation to ascertain genuineness of the dose received is done by a committee constituted by the Competent Authority, AERB in case dose received by radiation worker in a single monitoring period exceed any of the following:

- The cumulative effective dose over a block of successive five years shall not exceed 100 mSv (i.e. average 20 mSv for every year of this five year block) and
- The effective dose in any calendar year during a five year block shall not exceed 30 mSv.
- To investigate over-exposure cases (a) the dose reported in a given monitoring period exceeds the limit. That corresponds to 10 mSv and (b) the annual individual dose exceeds 30 mSv.

Conclusion

Documents in the form of Act, Rules, Safety Directives, Safety Code etc exist for safe operation of a nuclear medicine facility in India. Atomic Energy Regulatory Board (AERB) issues authorization for operation of nuclear medicine facility after appropriate review and inspection. The licensee needs to keep himself updated on the regulatory requirements and apprise the concerned staffs regarding the same. RSO has the key role to ensure the radiation safety in the institution, though the ultimate responsibility for the same rests with the licensee. Web based E-Licensing of Radiation Application (e-LORA) system needs to be used fully by the facility for getting required consent and also to submit periodic status report.

- References:
- Atomic Energy Act -1962 & Rules framed under the Act
 - AERB's Directives
 - e-LORA Guidelines for Nuclear Medicine Facility
 - AERB's Safety Code on Nuclear Medicine Facility

Manas Kumar Pathak, a Post-Graduate Engineer with more than 22 years experience is at present working as Officer-In-Charge of Eastern Regional Regulatory Centre (ERRC), Atomic Energy Regulatory Board (AERB). He is involved in safety review and regulatory inspection of Nuclear & Radiation facilities. He is serving as a membersecretary, Excessive Exposure Investigation Committee for Eastern Region. He has delivered many lectures related to industrial, fire and radiation safety in different forums. He was one of the authors of the Monograph titled "Construction Safety" published by AERB. He has also written several papers related to safety. His area of interest is probabilistic safety analysis, lay out optimization, fire hazard analysis etc. Currently, he is pursuing "Post Graduate Diploma in Nuclear Law". He has also registered for Ph. D programme on Layout Optimisation of Radiation Facilities.



Radionuclide Therapy

Bench to bedside experience using the iodine pump protein for radio-iodine therapy in breast cancer

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Background:

Sodium iodide Symporter (SLC5A5 or NIS) or the iodine pump protein is known for its crucial role of delivering iodide ions inside cells primarily in thyroid follicular cells. In recent years, aberrant expression of this protein in breast malignancies has raised hope of utilizing this as target candidate of radio-iodine based detection and therapy. Despite the potential utility of this protein target, its expression and ambiguous cellular localization is found to be the probable cause of this pump protein's dis-function, which remained as the main bottleneck for clinical use of this rather simple targeted therapy approach in breast cancer.

Results:

Challenging this daunting task, we have conducted multi-dimensional studies using in vivo cell and animal model. First, we have attempted modulation of NIS gene expression and function in BC cells by modulating transcriptional control switches of the cells. Our results show that a brief sub-lethal pre-treatment with HDAC inhibitors can immensely improve the therapeutic efficacy of this endogenous target upon I^{131} exposure in vivo. Significant induction ($P < 0.005$) of hNIS endogenous mRNA is observed in cells tested with prominence in ER positive cell types. Sidewise, regulatory roles of cancer relevant transcription factors such as p53 was studied, which shows for the first time that NIS based therapy may be more efficacious in p53 mutant cases as the wild type p53 suppresses NIS expression. Finally, understanding the intracellular trafficking and glycosylation of NIS protein to improve the functional deficiency of this protein, we have developed a unique cellular model, where the protein is differentially expressed either on the plasma membrane or the cytoplasm. Cluster analysis the glycosylation specific qRT-PCR profiler array data on 80 gene signatures has helped to identify key glycosylation enzyme candidates, which can be targeted to rectify the differential expression pattern of these clones.

Conclusion:

Our investigation has establishes that HDACi pre-treatment mediated transcriptional regulation of NIS as a novel strategy to turn radio-iodine therapy efficacious in breast cancer. A clinical protocol has now received approval for further feasibility test in our breast cancer clinic.

Re 188 Lipiodol therapy in inoperable HCC and hepatic metastases- a work in progress-

Dr Ajit Shinto, KMCH, Coimbatore, India

Hepatocellular carcinoma (HCC) is caused by a malignant transformation of the epithelial cell lining in the hepatocytes and is the most common primary liver cancer. Although not very common in the western population, it still causes >500,000 deaths worldwide annually, making it one of the top 5 cancers causing death. The highest prevalence of HCC in the world is in Asia, especially China and Southeast Asia. Other regions with high incidence are Sub-Saharan Africa and Japan. The incidence of HCC is being increasingly reported in European countries and USA also, which could be due to the increasing incidence of chronic viral hepatitis and alcohol consumption, both considered to be definite risk factors for cirrhosis and HCC. The incidence of HCC is much higher in cirrhotic patients, which further decreases the amount of hepatic reserve in these patients and limits the therapeutic possibilities. Surgical intervention, if possible, either by means of hepatectomy or liver transplantation, is the mainstay of curative treatment. Overall, if the degree of liver dysfunction and the tumor load are taken into consideration, most patients are not eligible for surgery.

Other locally applicable therapies such as percutaneous ethanol injection (PEI), radiofrequency ablation (RFA), and trans arterial oily chemoembolization (TOCE) and trans arterial chemo or radio -embolization (TACE /TARE) have proven to be useful in selected patients and are mainly palliative in intent or serve as a bridging strategy in patients awaiting liver transplantation. Multiple reports have proven survival advantages with TACE in well-selected patients and it is considered as well as approved in the clinical treatment algorithm for inoperable HCC. Other locally applied treatment modalities producing reasonable response rates are the use of lipiodol alone, or loaded with chemotherapeutic agents or radiolabeled lipiodol with a therapeutic beta emitting isotope.

Radionuclide therapy provides yet another interesting option for the treatment of unresectable HCC, as shown by studies using radionuclides such as iodine-131, yttrium-90 microspheres, holmium-166 and rhenium-186 or 188 conjugated to monoclonal antibodies, lipiodol or chemical



Compounds. For unresectable HCC, hepatic intra-arterial radio conjugates aim to deliver a high radiation dose to the tumor, while at the same time limiting the radiation dose to normal liver, lung and bone marrow to within the maximum tolerated dose. This approach is possible because the blood supply to HCC is mainly from the hepatic artery, while normal liver parenchyma obtains 80% of its blood supply from the portal vein. Y-90 labelled glass spheres or micro spheres are commercially available and have been approved for patient use in many of the developed countries. However, it is very expensive for a palliative procedure and not practical to use it as standard of care in countries, where there is no universal insurance coverage and patients have to pay from personal resources. Lipiodol localizes in hepatic tumors when administered via the hepatic artery, and is retained by HCC for many weeks, while it is cleared from normal hepatocytes within 7 days.

Over the last 2 decades, there have been multiple reports of the use of ^{131}I and ^{188}Re radio labelled lipiodol for the treatment of HCC. Considering the cost, physical characteristics and from radiation protection point of view, ^{188}Re presents several advantages for radionuclide therapy compared to ^{131}I . The main problems with ^{131}I is its long physical half-life of 8.03 d and emission of a highly energetic gamma-ray of 364 keV at an abundance of 82%, necessitating delayed hospitalization for radioprotection purposes. In comparison, ^{188}Re emits a gamma-ray of 155 keV at an abundance of 15%, which allows for imaging and at the same time limits radiation protection problems. The next major factor is the relatively soft beta emission of ^{131}I which is only 606 keV, whereas, in ^{188}Re , the Beta-particles are emitted with a maximal energy of 2.1 MeV. Thus, the effective range of therapeutic effect with the ^{188}Re Beta-emission is about 3 times longer than that with ^{131}I , which would be very useful in treating intermediate to large sized tumors, commonly seen in HCC patients. However, the most influential factor, especially in developing countries, is that ^{188}Re is eluted from a relatively inexpensive $^{188}\text{W}/^{188}\text{Re}$ generator, which has a long useful shelf life of several months and routinely provides a good yield of carrier-free ^{188}Re . Further developments in ^{188}Re generator technology have introduced new and larger generators which require no post elution concentration and are capable of producing radioactive concentration of upto 1 Curie in 5-8 ml elutions.

The first clinical results using ^{188}Re -4-hexadecyl-1,2,9,9-tetramethyl-4,7-diaza-10,10-decanethiol/lipiodol (^{188}Re -HDD/lipiodol) were reported by Sundram et al. The radiopharmaceutical was administered as close to the tumor feeding artery as possible and the tolerance as well as results were very encouraging. In a trial conducted by Lambert et al., a fixed activity of 3.6 GBq ^{188}Re -HDD/lipiodol was used in patients with well compensated cirrhosis, which again was well tolerated and further escalation of the activity seemed feasible provided a super selective injection technique was followed. This was borne out by the large multinational, multi-centric study conducted by the IAEA, which had patients treated with 50-206 mCi (upto 7.4 GBq) of the radio conjugate and showed that ^{188}Re -lipiodol is a safe and cost-effective method to treat primary HCC via the transarterial route. In terms of efficacy, it was considered a good alternate therapeutic approach needing further evaluation by treatment of larger numbers of patients. At present, in KMCH we use selective intra-arterial administration of an empirically calculated dose based on tumor volume of the same radio conjugate mentioned above in the treatment of inoperable or advanced HCC's. We have also developed the therapeutic use of ^{188}Re to encompass bone pain palliation, joint synovectomy as well as V-DMSA therapy. We are in the process of initiating SSTR and PSMA labelling enabling ^{188}Re to act as the work horse of a therapeutic NM programme.

NET management through NM: Fundamentals & Advances

Dr Sandip Basu

Radiation Medicine Centre, BARC, Tata Memorial Centre Annexe, Parel, Mumbai: 400012

Clinical diagnosis and treatment of the neuroendocrine tumors have undergone a revolution with the improvements in radioisotope based diagnostic scan and treatment. Somatostatin receptor imaging and peptide receptor radionuclide therapy (PRRT) are now integral parts of NET management. In several active therapy centres, NET service has now developed almost parallel to thyroid carcinoma services. In this presentation, we shall discuss the fundamentals involved in radionuclide based diagnosis and therapy. We shall also look at the various avenues where Nuclear Medicine imaging & therapies are playing potentially useful role in combination with standard histopathological grading system in advancing the science of NET clinical management.

Radiopharmacy & Chemistry

Chemistry in Imaging: Tracers for Hyphenated Imaging Tools

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In life imaging, the ongoing efforts to enhance diagnostic accuracy and optimize treatment strategies have led us to design chemical entities loaded with EMR tracers having an excellent physical properties. Mostly, exploited Positron Emission Tomography (PET) and Computed Tomography (CT) is a hyphenated imaging existing for many years. The high spatial and contrast resolution of magnetic resonance imaging (MRI) and the high sensitivity lacking with specificity due to specific contrast agents or chemical shift imaging agents which is being covered by designing novel tracers (hybrid molecules) combined with molecular information from PET imaging are going to rule the life imaging to



personalize treatment planning using hyphenated imaging tools . To create a hybrid contrast agent for PET-MRI device, a PET radiotracer needs to be combined with an MRI contrast agent. The most common approach is to develop cocktail molecules having different linkable arms to biological vectors and loading multinuclei without compromising biological behaviour of entire conjugates.

The resulting agents offer a wide range of applications, Diagnose disease before structural changes become detectable with anatomical imaging techniques, potentially improving the understanding of disease at molecular level leading to prevention of pathology, evaluate suspicious lesions detected on other exams, helping predict whether those lesions are benign or malignant thus improving the prognosis, identify distant, occult metastases that may affect the course of treatment and, therefore, change patient management and hence making it cost effective, in some cases, replace multiple diagnostic procedures with a single exam, Help predict the potential benefit of planned surgical procedures, to eliminate those that won't benefit the patient, thus significantly reducing the cost of healthcare delivery and minimizing unnecessary morbidity for the patient, manage patient therapy by monitoring response to a given regimen and providing early feedback on its efficacy, helping to reduce or avoid the cost and potential complications of ineffective treatments or unnecessary hospitalization. The aim is to combine high spatial resolution, high sensitivity, morphological and functional information. Future prospects include the use of specific cocktail molecules and hybrid multimodal PET-MRI-ultrasound-fluorescence imaging with the potential to provide overall pre-, intra- and postoperative patient care.

Dr. Anil Kumar Mishra, PhD

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Team: Molecular imaging and Nuclear Medicine

Dr. A.K. Mishra is working as a Scientist at Institute of Nuclear Medicine and Allied Sciences, Defence Research and Development Organization, Ministry of Defence, Govt. of India. He obtained his M.S. (Chemistry) in 1984 from Gorakhpur University, Gorakhpur, India and Ph.D. (Chemistry) in 1988 from Banaras Hindu University, Varanasi, India. During his career, he held positions as Post-doctorate fellow at Université de Bourgogne, Dijon, France; Research Scientist at University of California, Davis, USA; Senior Scientist at INSERM U-463, Nantes, France, and Visiting Professor at Max-Planck Institute, Germany. Dr. Mishra has published more than 264 papers, in various journals. Dr. Mishra is granted US, European and Indian patents. He has received several awards and most prestigious one is DRDO-Young scientist by Prime Minister of India in 1999.

Research Interest:

- Molecular Imaging agents, Radiochemistry
- Specific MR contrast agents
- Optical Imaging agents
- Coordination chemistry
- Synthetic chemistry
- Radiopharmaceuticals
- Bioconjugate chemistry

Scientific expertise:

- Design and synthesis of molecular imaging agents for non-invasive imaging

Projects:

My research activity is centered on the development of molecular imaging agents for MR/NM/optical imaging tools. We have been creating molecular imaging agents to identify a molecule that is specific for a target associated with the disease being studied. We labeled these molecules with a radioactive/ paramagnetic/fluorescent substance or other modality that allows detection by an imaging device. We are heavily involved in developing Specific MR Contrast agents (SCAs) and PET-MR imaging probes for neuroimaging.



Trends in the use of Radionuclides for Radiopharmaceuticals and their Impact

N. Ramamoorthy

Retiree from BARC/DAE-Mumbai, and from IAEA-Vienna (nramasta@gmail.com)

Extended Abstract - Synopsis

Sustainable services and growth of nuclear medicine (NM) are strongly dependent upon the availability and affordability of the appropriate radiopharmaceuticals (RPh), and in turn, of their constituent radionuclide (RN). As regards the imaging instrumentation in diagnostic procedures, tomographic imaging is established as the well-accepted modality, with both SPECT and PET (PET/CT) in extensive use. Since the early days of NM, ^{131}I (8 d, b.g; Eg 364 keV) products have been in wide use, and they continue to play vital roles currently too. The next major impact is obviously attributable to $^{99\text{m}}\text{Tc}$, which has become an omnipresent item in NM centres since five decades. It is common knowledge that diagnostic imaging in NM has been almost singularly dominated by the use of $^{99\text{m}}\text{Tc}$ (6 h; IT decay; Eg 140.5 keV) during 1980s and 1990s - aided by developments in RPh and by the transition from analog to digital gamma cameras, supplemented by quantitation capability, and later transformation to SPECT and SPECT/CT. $^{99\text{m}}\text{Tc}$ is invariably obtained from its precursor RN, ^{99}Mo (66 h; b.g; Eg 740 keV), while in recent times, its direct production in 20-30 MeV proton cyclotrons (using highly enriched ^{100}Mo target) has been gaining attention. The era of ^{201}Tl (73 h; EC decay; Eg 137 & 165 keV, and X-rays 69-80 keV) began nearly four decades ago, due to the vital need for a good marker of myocardial perfusion. Its use has however come down considerably during the past two decades, due to the use of ^{201}Tl products, and in recent times, due to the use of also some PET tracers. The growing adoption of PET imaging and wide use of PET tracers, mainly ^{18}F (110 min; 511 keV annihilation radiation) products, marked another important trend, mainly beyond the year 2000. The increasing use of medical cyclotron produced organic PET tracers has also led to the demand for the use of other PET tracers - mostly metallic RN - such as, ^{68}Ga , ^{64}Cu , ^{89}Zr among others - ^{68}Ga is obtained from ^{68}Ge - ^{68}Ga generator (68 min; 511 keV annihilation radiation); ^{64}Cu (12.4 h; 511 keV annihilation radiation) can be produced in medical cyclotrons as well as in reactors.

Meanwhile, RN therapy (RNT) has also been growing in parallel, moving beyond ^{32}P (14.3 d; b). Pure beta emitters as well as beta-gamma emitters have contributed to the growth of RNT, starting from ^{90}Sr (50 d; b 1.5 MeV) used for metastatic bone pain palliation, and its alternate, ^{153}Sm (46.5 h; Eb 0.8 MeV, Eg keV 103 (28%)) as phosphonate complex (Sm-EDTMP), and its ^{177}Lu analog (Lu-EDTMP) in more recent times. The subsequent entry of the alpha emitter ^{223}Ra (11.4 d; Ea 5.78 MeV, Eg keV 269 (13.6%), 154 (6%), 324 (3.9%)) as RaCl_2 for use in RNT of bone metastases, following very significant clinical findings of its high efficacy, marks yet another major impact of RN-RPh in NM. Above all, the RN pair of ^{177}Lu (6.7 d; Eb 0.5 MeV, Eg keV 208 (11%), 113 (6%)) and ^{177}Lu (66 h; b 2.27 MeV) have attracted much attention for use in a variety of RNT procedures, especially in targeted therapy, like receptor based procedures called PRRT using suitable peptides. They will remain relevant in Indian context due to evident scope for their indigenous accessibility. The use of ^{186}Re has been also doing the rounds in limited number of NM centres, due to similarity of chemistry with $^{99\text{m}}\text{Tc}$ products, while their sustainable, affordable availability will remain debatable. As these trends have emerged, there has been a strong reorientation to addressing the associated physico-chemical aspects of the RN products. The long-standing mind-set due to 140 to 364 keV emissions being the common ones in NM centres - be it for imaging aspects, or from shielding point of view, or for radioactive waste management, or for tackling accidental situations due to radioactive contamination (during technical operations and/or coming from (sick) patients) - had to undergo a paradigm-shift with 511 keV emissions of PET tracers, and relatively longer-lived RN in much large quantities used in RNT. Furthermore, PET tracers ushered in the era of hospital-based medical cyclotrons in several centres, and in turn, shifting RN production role, and attendant responsibility, to end-user entity (cf. handling by commercial suppliers, professional service providers). Due to the very short half-life of most PET tracers in regular use, considerable decay losses are inevitable, apart from the much higher radiation dose burden during handling and transport. In addition, in RNT, the use of low-abundance gamma emitting RN like ^{153}Sm , ^{177}Lu etc. warrants additional considerations, compared to the case with pure beta emitters like ^{32}P , ^{90}Sr , ^{89}Y . While most of the RNT procedures of early days involved oral administration (of mostly ^{131}I solution or capsules), the subsequent trends have moved over to systemic administration (including slow infusion in the case of MIBG- ^{131}I), local instillation (e.g. for radio-synovectomy), etc. It is also known that certain long-lived RN traces would be invariably present (within permissible levels) in some therapeutic RN - e.g. ^{177}Lu (160.4 d) in ^{177}Lu ; ^{147}Sm (8.6 y) in ^{153}Sm - due to their inevitable, concomitant production during reactor irradiation. This adds to the complexity in waste management. Thus, many NM procedures would pose challenges to the NM team tasked with ensuring safe and efficacious administration of RPh to the patients, as well as for the overall management of patients, NM premises and the environment, calling for greater care and vigil by all stakeholders.

The multi-disciplinary teams of NM centres have been addressing well, by and large, all the above aspects and



The multi-disciplinary teams of NM centres have been addressing well, by and large, all the above aspects and changing trends over the years. The teaching and training of human resources (HR) have also correspondingly changed, with contemporary topics being periodically brought in to the curriculum in most institutions. The professionals and technologists qualified in NM in the earlier years have also by and large adapted themselves well to the changes, thanks to both formal and informal training and learning exposures available to the ones seeking them. In this context, the role of continuing (medical) education and training of physicians, physicists, radiopharmacists, etc. assume greater significance, as this would be a regular requirement than being an exception. Professional bodies such as ICNM, SNM(I) and its Chapters, ANMPI, NMPAI etc. can, and should, play an effective role towards this purpose. As NM strives to deliver its best for the benefit of patients, surely there will be further emerging trends in NM, and the continuing growth of products and procedures in NM will keep impacting the field and the associated personnel - both technical practices & procedures and patient benefits - more and more in the years to come.

Functionalizing Superparamagnetic Iron Oxide Nano Particles for Non-invasive imaging and Temozolomide Therapy Against Glioblastoma Xenograft

Bola Sadashiva Satish Rao

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Abstract:

Treatment for malignant gliomas are restricted by enormous challenges due to the highly invasive nature of glioma and its complex microenvironment. Further the passage of therapeutic drugs via blood brain barrier / blood brain tumor barrier and complexities in delivery of therapeutic agents specifically to the tumor cells and drug resistance contributes to poor prognosis. Nano-triggers based imaging and therapeutic agents are being functionalized for noninvasive imaging and to deliver versatile payloads capitalizing on the molecular and cellular properties for enhanced specificity, efficacy and safety. Our study formulated a temozolomide based polymeric magnetite nanocomposite with efficacious targeted delivery to the tumor in an orthotopic glioblastoma tumor model in nude mice. Multifunctional polymeric magnetite nanoparticles were engineered with an anticancer drug (Temozolomide) by a ligand transferrin / polysorbate-80 to cross the blood brain barrier along with an additional glioma cell surface targeting by anti-nestin antibody. Upon post determination of their stability, these nanocomposites and pure temozolomide were radio labeled with ^{99m}Tc using stannous chloride as a reducing agent. A comparative evaluation of bio-distribution of these drugs was carried out using SPECT / CT imaging. The results of bio-distribution demonstrated a significantly longer retention of ^{99m}Tc labeled nano-trigger at the site of tumor. Further, tumor response as visualized by CT scan and validated by immunohistochemistry for proliferation markers indicated enhanced regression of intra-cerebral tumor in both the formulations. We conclude that ^{99m}Tc labelled multifunctional temozolomide nanocomposite engineered for specific tumor targeting was useful not only for imaging but also as a platform of efficient drug delivery which may have its direct clinical implications.

Acknowledgements: Dr. K Satyamoorthy, The Director, School of Life Sciences and Manipal University for providing the research facilities is gratefully acknowledged.

"Is Ga 68 a potential "Tc 99m" of PET Radiopharmacy ?"

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Why the Comparison ?

Ga 68, a generator produced positron emitter, attracts the attention of all those PET users, who have to rely on the outsourced supply of Workhorse PET radiopharmaceutical: 18Fluorodeoxyglucose, to run the PET CT section of the Nuclear Medicine Department.



This generator produced Radionuclide, with in house labelling possibilities, at first instance, gives a relief, equivalent to that of ^{99m}Tc for Methoxy Isobutyl isonitrile / Tetrofosmin myocardial agents, which almost washed out the need of cyclotron produced ^{201}Tl thallous chloride.

This comparison of Ga 68 and Tc 99m as Positron emitting and Single photon emitting radionuclides respectively could facilitate our understanding of Ga 68 procedures with respect to the feasibility, radiation safety, user friendliness and finally, applicability in the field of Nuclear Medicine

Ga 68 Vs "Imaging Workhorse": Tc 99m :

Physical Characteristics :

S I No	Characteristic	^{68}Ga	^{99m}Tc
1	Decay mode	89% Positron emission 11% Electron Capture	Isomeric transition
2	Energy emission Bmax Gamma & X Ray	1899(88%), 822 (1%) 511 Kev (178%) 1077 Kev (3%) Others (,1%)	NIL 140 Kev
3	Physical Half life	1.13 hrs	6 hrs
4	Gamma Constant <i>mrem/hr/mCi at 1m</i>	6.7×10^{-1}	1.2×10^{-1}
5	Specific activity Ci/g	4.1×10^7	5.3×10^6
6	Daughter product	Stable ^{68}Zn	^{99}Tc (Beta minus - 2.1×10^5 yrs - $T_{1/2}$) - ^{99}Ru

It can be very well appreciated from the table of Comparison that both ^{68}Ga and ^{99m}Tc are short lived and the daughter radionuclide is actually stable ^{68}Zn as an edge over ^{99m}Tc for its PET counterpart.

Production Mode : Both the radionuclides, ^{68}Ga and ^{99m}Tc are generator produced and hence, can be boasted of for their availability.

SI No	Features	For ^{68}Ga generator ^{68}Ge	For ^{99m}Tc generator ^{99}Mo
1	Parent radionuclide	^{68}Ge	^{99}Mo
2	Physical characteristics of Parent radionuclide Decay mode $T_{1/2}$ Beta/Gamma Kev	Electron capture (100%) 270.95 days -- / KX - 9.36	Beta minus/Gamma 2.7 days 1.214 MeV/740,778 KeV
3	Production of parent	Cyclotron Zn	Reactor/Fission
4	Type of Equilibrium	Secular	Transient
5	Adsorption column *	Inorganic TiO_2 / Organic Silica based as per the supplier	Alumina
6	Eluent **	HCl (0.05 -1N concentration as per the supplier)	Saline
7	Shelf Life	1 yr (Practical : 4 months) *	2 weeks

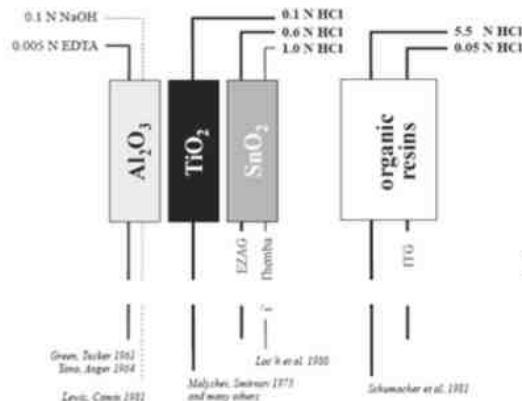
*(For organic column, used in our department. As per the manufacturer's information (iIG) the shelf life is 1 yr or 250 elutions of 4ml eluent each, whichever is reached first)



It can be seen that the long lived parent, ^{68}Ge , along with the features of secular equilibrium with its daughter Gallium, makes the generator more user friendly and longer lived than Mo 99-Tc 99m generator.

However, practically it has been found that Gallium generator deteriorates with respect to efficiency. As for Gallium Generator, after certain elutions, the parent radionuclide gets loosened from the column (mostly organic) and the usable ^{68}Ga yield starts from the mid fraction especially for the inorganic columns (to avoid the metallic impurities, that can adversely affect the radiolabeling) and fractional elution is mandatory as against $^{99\text{m}}\text{Tc}$ which is usable right from the first ml of eluate.

*/** - as shown in the following diagram :



Ref: Roesch, "Current Radiopharmaceuticals" 2012

Sl No	Feature	^{68}Ga	$^{99\text{m}}\text{Tc}$
1	Group	13	7 d block
2	Relative weight	Lightest member of Group 13	Lightest radioisotope
3	Electronic configuration	1s2 2s2 2p6 3s2 3p6 3d10 4s2 4p1	1s2,2s2,2p6 3s2 3p6 3d10 4s2 4d5 5s2
4	Oxidation state	+3	-1 to +7
5	Chemical form	Gallium trichloride GaCl_3 in dimer form that is Ga_2Cl_6	Sodium pertechnetate $\text{Na}^+(\text{TcO}_4^-)$
6	Co-ordination chemistry	Diamagnetic analogue to Fe +3 compounds	Analogues to Iodide ion
7	Shape	Bifurcated	Tetrahedral
8	Reactivity	Lewis acid (electron acceptor)	Reactive in reduced forms lower than +7 oxidation state (+4 /+5 mostly)
9	Ionic form	Cationic Ga^{3+}	Anionic TcO_4^-
10	Solubility	Gallium trichloride dissolves in virtually all solvents, alkanes too (unusual for metal halides)	Pertechnetate dissolves in aqueous form: saline



Radiolabeling :

The quality of ^{68}Ga Radiolabelling is drastically affected by

- pH of the reaction mixture and
- presence of metallic impurities like Fe, Zn

Other factors to be maintained, like $^{99\text{m}}\text{Tc}$ labeling are :

- Reaction temperature and time

The commonly labelled ^{68}Ga were Dotatoc and PSMA 11, ("wet" chemistry) which have been usually successful, till the Generator is around 4 months old. Later on amount of Dotatoc needed per labeling procedure should be increased (doubled) to get an acceptable quality of labelling. (>90% Radiochemical purity with 50% acetonitrile and TLC SG as mobile and static phases respectively)

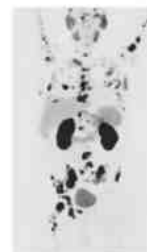
Short half life becomes a very challenging issue, especially to maintain the optimum reaction time and patient scheduling along with the completion of Quality check of the radiopharmaceutical.

The reaction time can be reduced from 10 minutes to 1 minute, if the uniform microwave heating can be standardized in the laboratory.

$^{99\text{m}}\text{Tc}$ labeling depends upon

- The presence of oxygen
- [Reducing agent] (generally SnCl_2)

which is not an issue in ^{68}Ga labeling.



Ga 68 PSMA 11 scan



Ga 68 Dotanoc scan

We have performed 122 scans of Ga 68 Dota rp's and 61 cases of Ga 68 PSMA 11 in the year 2016

Safety Considerations :

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Ref : European Journal Nuclear Med Imaging 2012

Nuclide	Body dose ^a due to point source in air [mSv.m ² /(GBq.h)]	Skin dose ^b due to contact with 5-ml syringe [mSv/(MBq.h)]	Skin dose ^b due to contamination with 50 µl on 1 cm ² [mSv/(kBq.h)]	Lead shielding (mm) To reduce to 1/2	Lead shielding (mm) To reduce to 1/10
$^{99\text{m}}\text{Tc}$	0.02168	0.354	0.00877	0.3	1
^{68}Ga	0.1580	31.4	1.25	6	17



Obviously the positron emitter loses to ^{68}Ga in this context, however, it has to be noted that the doses handled are much lesser than those of the single photon emitter and $t_{1/2}$ is only 68 minutes which shortens its effective time of staying hazardous.

Management of waste generated : especially Generators :

The long shelf life of the long lived ^{68}Ge generator raises concern with respect to waste management.

Volatility of ^{68}Ge should be kept in mind & precautions to prevent the contamination of surrounding must be taken (>100 days $t_{1/2}$ long lived waste).

The waste and storage expenses depend upon the radioactivity amount and container size.

It would take 10 years for the loaded radioactivity of a commonly used 50 mCi Generator to decay to the amount of <1 MBq that would allow the disposal as regular waste.

Hence recycling of this costly ^{68}Ge generator, by the manufacturers could be an answer to the environmental burden, sustainability and economy.

Cost effectivity :

cost of ^{68}Ga labeling procedures is mostly determined by the cost of the:

- Generator
- Usage Synthesis (automation) module to label the pharmaceuticals/manual labeling.
- Cost of the kit/reagents

While ^{99}Tc generator is bought every week, ^{68}Ga generator, with a longer shelf life makes it more cost effective in this aspect.

SI No	Factors	^{68}Ga	^{99}Tc
1	Cost of Generator INR	18-23,00,000	50-55,000
2	Cost of Synthesis module INR	40,00,000	---
3	Cost of Cold kits INR	50,000	4-5000
5	Number of Operators needed	1-2	1-2
6	Time	45 minutes	10-45 minutes

Conclusion :

Finally, the question, "Is ^{68}Ga a ^{99}Tc of PET radiopharmacy?" can be answered affirmatively, as no other generator produced PET radiopharmaceutical has been studied for its utility value and even applied as ^{68}Ga , after ^{18}F .

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Role of $^{188}\text{W}/^{188}\text{Re}$ Generator in Nuclear Medicine

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Introduction:-

Dependable radionuclide supply/availability is a crucial issue for the development radiopharmaceutical either in the case of diagnostic or therapeutic. Radionuclides are directly produced in either accelerators or research reactors.

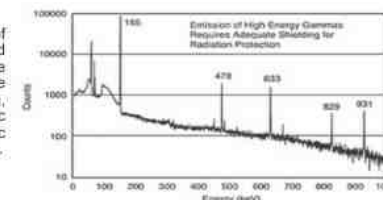
An alternative delivery mechanism is the use of an in-house radioisotope generator system, in which a secondary radioisotope is formed by radioactive decay and is separated from the primary produced radioisotope parent.

The advantages of an in-house radionuclide generator system is that availability of diagnostic and therapeutic radionuclide delivery on demand.

A variety of diagnostic radionuclides are indirectly available from such generator systems, such as ^{99}mTc obtained from the $^{99}\text{Mo}/^{99}\text{mTc}$ generator, ^{68}Ga from $^{68}\text{Ge}/^{68}\text{Ga}$ generator etc.

For therapeutic applications, ^{90}Y is obtained from a $^{90}\text{Sr}/^{90}\text{Y}$ generator and ^{188}Re from an $^{188}\text{W}/^{188}\text{Re}$ generator.

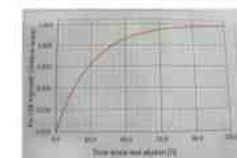
The reasons for a great interest in the clinical use of ^{188}Re is because of its routine no-carrier-added availability from the long shelf-life generator, the emission of the energetic 2.12 MeV beta particle, the emission of a 155 keV (15%) gamma photon for imaging, and the versatile radio-chemistry similar to that of ^{99}mTc for tagging of a variety of targeting therapeutic radiopharmaceuticals using invasive delivery strategies.



Tungsten-188/Rhenium-188 Generator ($^{188}\text{W}/^{188}\text{Re}$)

The $^{188}\text{W}/^{188}\text{Re}$ generator provides a convenient in-house radionuclide production system in which ^{188}Re can be conveniently obtained on demand by elution with 0.9 % m saline solution.

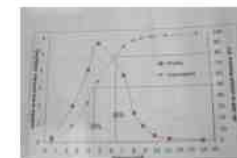
Tungsten-188 ($T_{1/2} = 69$ days) is reactor produced, and following processing, the generator is fabricated by the adsorption of Tungstic acid on acid washed alumina similar to that of ^{99}Mo in the case of $^{99}\text{Mo}/^{99}\text{mTc}$ generator.



Elution of the Generators

The convenient use of the generator system to obtain daily elutions of ^{188}Re is possible. Following removal of the available ^{188}Re , about 62% of the equilibrium levels of ^{188}Re is available after 24 h as shown in the figure.

The greatest benefit of daily elution is to obtain high activity levels of the therapeutic ^{188}Re radionuclide. After 96 h the growth of ^{188}Re almost saturated and maximum growth is expected at 120 h since last elution.



The $^{188}\text{W}/^{188}\text{Re}$ generator is similar to other adsorption type generator system, such as the $^{99}\text{Mo}/^{99}\text{mTc}$ and the daughter are conveniently removed in the radio-pharmacy by simple elution with 0.9% Normal Saline.

For better radionuclide concentration fractional elution may be carried out instead of complete elution.

The above figure demonstrate the elution profile of the $^{188}\text{W}/^{188}\text{Re}$ ITG generator.



The generator has got one inlet of eluent supply (usually physiological saline), and the exit port to collect the carrier free ^{188}Re saline. Yield of the elution is approximately 75 to 85% for ITG generator.

The generator should be operated under dry mode, i.e, saline should be completely removed from the column after each elution. If it is not totally dried up the radio labeling efficiency may come down.

Shelf life of the generator is usually 6 months from the date of manufacture; it may vary for different manufactures.

Rhenium-188 Radiolabeling Chemistry:-

Since ^{188}Re belongs to the same group (7th transition metals) the chemical properties are same as that of ^{99m}Tc . The radiochemical methods to introduce ^{99m}Tc into diagnostic agents can generally be used to as a framework in the preparation of analogs agents radiolabeled with ^{188}Re for therapeutic applications. However the reactivity of ^{188}Re has been found to be lesser than that of ^{99m}Tc , which demands heating.

Radiation Protection:

The generator is self-shielded lead and additional shielding may be required depending up on the strength of the generator. We found that for 1Ci $^{188}\text{W}/^{188}\text{Re}$ generator required additional lead shielding to bring the radiation level to the permissible limit.

Additional Perspex shielding is required to cut down the beta as well the bremsstrahlung radiation from the ^{188}Re , even though the specific gamma ray constant is 3 times lesser that that of ^{99m}Tc . Perspex syringe shields may used whenever feasible

Disposal of the Generator:-

As the half-life of ^{188}W is much higher compared to ^{99}Mo , the generators have to be stored adequate time before disposing. For example a 500mCi $^{188}\text{W}/^{188}\text{Re}$ generator need to be stored for at least 3.5 years before actually disposed.

Ref:

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Current GMP & its Implementation in Hospital Radiopharmacy

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Good Manufacturing Practices (GMP) comprises of everything that has a bearing on quality of the end product. Implementation of GMP ensures the quality and effectiveness of the product. The steps involved in the manufacturing of any product can be essentially classified as follows



Fig. 1 Classification of steps involved in a manufacturing process.

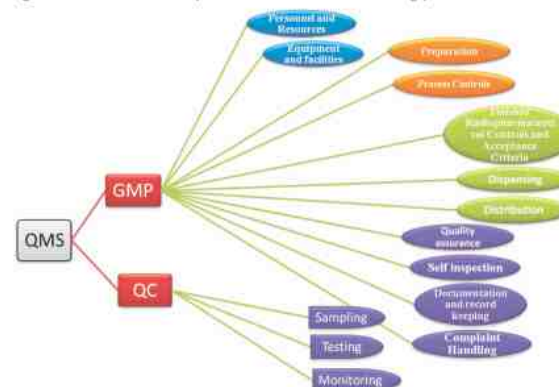


Fig .2 Flowchart showing components that comprise a good quality management system

Good Manufacturing Practices along with Quality Control together constitute the Quality Management system. As shown in Fig. 1, GMP in a radiopharmaceutical production involves

Input

- Personnel and Resources
- Equipment and facilities

Process

- Preparation
- Process Controls

Output

- Finished Radiopharmaceutical Controls and Acceptance Criteria
- Dispensing
- Distribution

Verification

- Quality assurance
- Documentation and Record keeping
- Self inspection
- Complaint Handling

The preparation of radiopharmaceuticals for injection not only involves regulations on radiation protection but also those for working under aseptic conditions. Since a radiopharmaceutical is considered potentially hazardous due to the radioactive tag attached to it, specific radiation safety aspects need to be considered while handling them. At the same time since the preparations in a radiopharmacy will be administered internally to a patient, necessary biological safety aspects in order to ensure a safe product should also be given due consideration. It is therefore essential to have a quality management system that takes a holistic approach while ensuring good practise.

It is important that several parameters be considered, addressed as well as verified, prior to, during and after completion of the process like-

Personnel and Resources: It is important to employ trained and qualified personnel and also ensure continuous updation of their training and knowledge in relevant subjects. It is also necessary to demarcate sufficient space for the facility. Personnel safety (radiation as well as biological) is should be ensured.



Equipment and facilities: It is necessary to have dedicated and self-contained facilities for handling of radiopharmaceuticals. It is recommended by the current good radiopharmacy practise (cGRPP) guidelines to use clean rooms or laminar flow work areas and fume hoods where relevant. It also gives clear recommendations about the air quality within the clean room or laminar flow workbench as per the European Union classification. The aseptic workstation should be cleaned at appropriate intervals and timely microbial monitoring should be carried out.

Preparation and Process Controls: It is recommended to use controlled materials and approved procedures along with qualified equipment. Timely validation of processes and analytical methods by preparing standard operating procedures also ensures end quality. Visual inspection of all materials, their use within declared shelf life, disinfection of vials before use, identification of all containers and radiopharmaceutical preparations including the lead shields with proper labelling is essential.

Finished Radiopharmaceutical Controls and Acceptance Criteria, Dispensing and Distribution: Adherence to QC monographs and its validation before release of each preparation, dispensing of radiopharmaceutical dose with respect to patients age and weight and specified examination should be ensured. For distribution of radiopharmaceuticals proper packaging and transportation regulation specified by the competent authority should be adhered to.

Quality assurance: It is essential to setup a quality assurance unit comprising of atleast two personnel involved in the entire process. This unit should ensure that the RP's are designed and prepared properly. They should ensure that the preparation and control operations are clearly specified and implemented in accordance with the principles of the cGRPP. This unit should also ensure quality control and timely calibration of the instruments and equipments involved in the processes. A system of planned preventive maintenance and calibration should be insitu and proper log and records of the same should be maintained.

Documentation and Record keeping: A complete, relevant, sequential and systematic documentation to ensure traceability of raw material/ resource and each preparation is essential. Written instructions, standard operating procedures and quality control monographs should be maintained after approval and reissued every 2years. Records of purchase and check on arrival of all resources and equipments including RA products should be maintained. Records of all processes carried out during the preparation, quality assurance and audit should be maintained for the legally required period.

Self inspection: Timely internal audits of practices, procedures, personnel, equipment and records should be carried out.

Complaint Handling: Through good documentation and proper traceability of product preparation it will be possible to identify relevant issues or complaints. Any failure of the preparation should be subject to audit and recorded for future reference.

Thus, through a continuous process of teamed effort and following current good radiopharmaceutical practise guidelines, it is possible to ensure good quality product consistently.

Miscellaneous

Journey of Radiation in Healthcare

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Introduction

Ionizing radiation is a very strange physical agent which can both kill and cure. The story of radiation had started more than a century ago in 1895 with the discovery of X-rays. Its journey in healthcare also began thereafter. Discovery of radioactivity and separation of natural radioisotopes such as radium and subsequent production of radioisotopes in reactors gave a different dimension to its use in healthcare. Lot of developments have taken place in this field subsequently and now radiation is inseparable part of various therapeutic, palliative and diagnostic procedures and it is difficult to visualise medical healthcare without it.

Initial Discovery Phase

The journey was begun by German Professor, William Conrad Roentgen who while experimenting with cathode ray tube noticed a faint glow. This glow was not able to be stopped by thick black paper and could affect fluorescent screen



despite objects lying in the way. He could make out that some unknown rays were penetrating the solid objects which he termed as X-rays. A few days later, Roentgen made a photographic image of his wife's hand using the new rays for a permanent record. It was this skeletal hand that captured the imagination of the physicians recognizing that this discovery could change medical practice forever. He published a paper on the subject, "On a new kind of rays" in a local journal in 1895. This was rapidly picked up in scientific circles. A professor at McGill University in Montreal replicated this experiment soon after.

As is recorded, a person had got a bullet shot in his leg during that period. His doctor on learning about the discovery of new kind of rays asked for an image of the patient's leg. After 45 min. exposure, he got an image which was good enough to know the location of the bullet to enable its removal. This prevented possible amputation of the patient's leg. This incident had happened just after 6 weeks of Roentgen's discovery. In 1896, French scientist Henri Becquerel's discovered that that some uranium salts also gave off similar effect on the fluorescent screen. Through further experimentation, he came to recognize that it was the material itself that gave off the rays signalling the birth of radioactivity. Although it was Henri Becquerel who discovered the phenomenon, it was his doctoral student, Marie Curie, who named it: radioactivity afterwards. In 1898, Marie Curie and her husband showed that uranium ore contained at least two substances which were more radioactive than uranium itself, both previously unknown to sciencercadium and polonium.

Little Action Period

Even after recognising its huge potential, the discovery of X-rays and radioactivity did not make much impact on medical practice for almost two decades. One of the reasons was unavailability of high voltage sources for generation of X-rays for good quality images and the other reason was high costs involved in separation of radium. In 1913, Coolidge designed high vacuum X-ray tube that could serve as an intense and reliable source. This enabled introduction of X-ray equipment in military hospitals for location of bullets which were embedded in the soldier bodies during World War-I to help in their removal and for taking chest X-rays for diagnosing tuberculosis etc. More high voltage sources were later developed in 1930s paving way for proliferation of such equipment at other places which made the technique popular.

Ignorance and Misconception Phase

The parallel discoveries of X-rays and radioactivity initiated their use in healthcare. But there was no concern at that time about the hazardous consequences that could occur from the excessive use of these rays. No one knew that these rays could be harmful because of generally slow onset of symptoms. Shoe-fitting fluoroscopes, sold under the names X-ray Shoe Fitter, Pedoscope and Foot-o-scope, were introduced in the United States, Canada, UK, Germany and Switzerland in 1920s to provide best possible fit and for longer-lasting shoes without knowing that this resulted in unnecessary radiation dose which could be harmful. In fact, many people believed that exposure to radioactivity might be beneficial. This misconception in public later resulted in quackery.

Radioactive Quackery

This was a phase when some commercial companies started exploiting the wrong faith in beneficial effects of radioactivity for therapeutic effects. There was no basis of claiming beneficial health effects. Radioactive water suddenly became a rage. It was believed to provide vigour. Radium pendants were used for treating rheumatism. Uranium blankets were used for helping arthritis ridden patients. Thorium based medicines were used for helping in digestion. Many brands of toothpaste were laced with radioactive substances that were claimed to make teeth shine whiter. Such was the belief that one company selling radioactive water even offered prize to anyone who could prove that its water did not contain the amount of radium it was claiming in it. This went on till late 30s before the discovery of nuclear fission and emergence of hazardous effects of extreme doses of radiation received by various persons.

Radiation Hazard Realization

Wilhelm Roentgen, who discovered X-rays, had a hunch that X-rays might be dangerous, though he didn't quite know why. Roentgen had trusted his instincts and lived to a ripe old age. But that was not the case with Marie Curie. The Curies used to handle radiation without any protection. Pierre had died in a road accident at an early age. But Marie had died of aplastic anaemia in 1934 and many of her items left behind were highly radioactive. There was a concern that her skeleton might be radioactive in the grave in which she was buried.

One of the first major events which brought to limelight the dangers of ionizing radiation was the case of the girls who used to paint watch dials with radium. At that time, there was suspicion of the hazardous effects of radiation but the watch company did not take precautions. Girls used to lick the radium laden brushes to properly shape them. This caused radiation sickness resulting in some deaths also. Some of the workers later sued the company which brought the health risks of radiation exposure in to public attention.



Radioactive water and all other such products also had their victims. Radioactive water had claimed life of one of the well-known industrialist Eben Byers of that time who used to drink 3 bottles a day. Byers died in 1932 and inspired Wall Street Journal headline, "The Radium Water worked fine until his jaw came off". This death prompted newly formed US-FDA to crackdown on radioactive health products insisting on proof of their safety and effectiveness. The era of radioactive quackery eventually went to the grave with Eben Byers.

Radiotherapy for Destruction of Cancerous Cells

Radiation in form of Radiotherapy both teletherapy as well as brachytherapy for destruction of cancerous tissues had started early. It started with use of radium. Earliest machine used only 2 gm of radium and was called Radium Howitzer. Then with higher availability of radium, Radium Bomb using 10 gm of radium were introduced. However, difficulties of continuing with radium were realised and it was desired to have an artificial radioisotope to replace radium. Teleradiums were replaced by Telecobalts. Number of developments took place in Telecobalts to avoid irradiation of healthy tissues. Brachytherapy equipment also went through lot of improvements. Use of X-ray for radiotherapy had also begun sometime after introduction of radioisotope based teletherapy.

Turnaround with Manmade Radioisotopes & Radionuclide Imaging.

John H. Lawrence, made the first clinical therapeutic application of an artificial radionuclide when he used ^{32}P to treat leukemia in 1936. Then in 1946, Oak Ridge National Laboratory produced radioisotopes in a reactor for the first time for medical use to facilitate more detailed investigations. Commercial availability of radiopharmaceuticals started in 1950. The US-FDA approved sodium iodide ^{131}I for use with thyroid patients. It was the first FDA-approved radiopharmaceutical.

In 1958, Hal Anger invented the "scintillation camera," an imaging device that made it possible to conduct dynamic studies and with that started Single Photon Computed Tomography (SPECT) technique which went on to revolutionise the medical functional imaging modality. SPECT can be used to complement any gamma imaging study, where a true 3D representation can be helpful, e.g., tumour imaging, infection (leukocyte) imaging, thyroid imaging or bone scintigraphy.

Because SPECT permits accurate localisation in 3D space, it can be used to provide information about localised function in internal organs, such as cardiac or brain.

Radiolabelled biomolecules got introduced which have helped in understanding the phenomena happening and have made a great contribution in drug discovery.

Rosalyn Yalow invented the technique of radioimmunoassay to detect insulin antibodies in human serum. Later kits got developed for so many other biological compounds for their accurate determination and this technique continues to be considered as gold standard.

Further Innovations with X-rays

Radiation in form of Radiotherapy had become inseparable part of procedures for cancer care both in form of teletherapy as well as brachytherapy. More developments took place on radioisotope based external beam radiotherapy. Teleradiums were replaced by Telecobalts. Number of developments took place in Telecobalts to avoid irradiation of healthy tissues which included IMRT and multi-leaf collimator. Brachytherapy equipment also went through lot of improvements. But, it did not stop at this. Developments had taken place in accelerator technology front which brought about introduction of LINACs.

Use of X-ray has grown beyond radiography for anatomical defects. Mammography, Bone Densitometry, Angiography etc. which are based on X-ray have become integral part of various investigative modalities. Mobile C-arm imaging device in which there is an X-ray source on one side and a detector on the other side, also became common. It provides high resolution images in real time thus allowing physician to monitor progress at any time. In X-ray assisted interventional radiology providing minimally invasive image-guided diagnosis and treatment of diseases has also now become common procedure to minimize risk to the patient and improve health outcomes.

Advances in Radiotherapy

Attempts to reduce damage to healthy tissues in radiotherapy has remained an ongoing process from its early days when the panoramic exposures were used. The earlier developments like 2-D conformal to 3-D conformal, IMRT, IGRT, stereotactic equipment and then helical tomotherapy made immense contributions. In the field of brachytherapy also developments took place which were aimed at smaller size of sealed source and increased automation to shrink deep seated tumours.

More recently, proton therapy which utilizes charged particles-protons has come into being. These charged particles damage the DNA of cells, eliminating them or stopping their reproduction. Cancerous cells are vulnerable to attacks on DNA because of their high rate of division and their reduced ability to repair DNA damage. Because of their larger



mass, protons have less side scatter in the tissue and remains focused on the tumour reducing damage to surrounding tissues. All protons of a given energy have a certain range and do not penetrate beyond that avoiding exit dose to healthy tissues unlike X-rays.

Take-off with PET

Another, more recent, development is Positron Emission Tomography (PET) which is a more precise technique employing positron emitting isotopes produced in a cyclotron. A positron-emitting radioisotope is introduced, usually via injection, into the target tissue. As it decays, it emits a positron which combines with a nearby electron to yield two identifiable gamma rays in opposite directions. These are scanned by a PET camera. The introduction of ^{18}F deoxy glucose represents another major step toward practical clinical use of positron-emitting tracers. X-rays can show only the anatomical structures and not the functional details. So far understanding function of brain, heart etc. getting more information becomes very useful. By 1938 Lawrence, Livingston, et al had designed a "medical cyclotron." The subsequent production of ^{11}C , ^{13}N , ^{15}O , and ^{18}F paved way for one of the most useful diagnostic modality for its use in medical and physiological research. It became possible to show how different parts of the brain are activated when performing mental tasks such as hearing, reading, talking, thinking, etc. The first PET scanners had a small number of radiation sensors to build the image, and they could do only a slice at a time. The slices were also very thick. Thus, the images obtained with the PET had a low quality and definition. It was impossible to get the finer details of localization of function making their clinical usefulness limited.

With the developments, which have taken place, one can easily see how the finer details of internal brain structures can be visualized.

A combination of CT and PET is a common technique which is used to obtain CT's high anatomical detail simultaneously with the functional image. MRI also has that attribute though it is not as commonly used in conjunction with PET.

The first safe radiotracer to be used in humans was 2-deoxyglucose. It competitively inhibits a portion of the glycolytic pathway, making it a useful molecule to measure the use of glucose in the brain, which directly translates to brain activity. Now 2-fluoro-2-deoxy-D-glucose (FDG), which is radiolabelled with ^{18}F and is one of the mostly widely used radiotracers today. It was called as "Molecule of the Millennium".

Now PET is being extensively used in the world in the fields of oncology, cardiology and neurological investigations. Large number of PET investigations are being carried and the number is growing very fast highlighting the popularity of this technique and its usefulness.

Efforts are on to improve PET technology further. The search for better detectors and different radiotracers will continue to be explored for enhancing the information which can be obtained from such investigations to make its place stronger in the years to come.

Targeted Radiopharmaceuticals

In recent years, there has been lot of emphasis on the development of targeted radionuclide cancer therapy. It is now possible to use baseline clinical and imaging assessments to determine the most effective therapy and to tailor this therapy during treatment based on tumour response. This has the advantage of maximizing therapeutic effect while limiting toxicity. Developments in radiopharmaceuticals as biomarkers capable of predicting therapeutic response and targeting disease are playing a central role in medical research.

A series of radiolabeled peptides have been designed and optimized for tumour-targeted peptide receptor radionuclide therapy (PRRT). ^{90}Y -DOTA-TOC and ^{177}Lu -DOTA-TATE are two of the most common radiopharmaceuticals with symptomatic improvements. Furthermore, combination treatments, including PRRT combined with surgery, chemotherapeutic agents, or radio sensitizing agents could be applied to increase the effectiveness of PRRT.

Concluding Remarks

Ionizing radiation had an amazing start to its journey for healthcare which had begun more than a century back. It has had an equally fascinating rest of the journey so far with many ups and downs. Now for many therapeutic, palliative and diagnostic procedures it has become indispensable part of medical healthcare. It is providing wonderful service to the society and it can be easily concluded that radiation will continue to serve the society for better health for all the time to come. It is also important to note that radiation can cure but if not handled properly can kill also. Like many other useful facilities science or nature has given us, one must be extremely careful in its safe and secure application to obtain the desired results.



Radiation Resistance: Big Lessons from Small Creatures

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Abstract

The beneficial effects of ionising radiation are accompanied by harmful effects on biological systems. Due to the energy they carry, radiation can induce damage and it is of two broad types - direct, through action on macromolecules including DNA and indirect, through generation of free-radicals. Radiation induced damage elicits apoptosis and can lead to cell-death. Sporadic incidents and side effects have necessitated a search for radiation protection. While radiation protection gears are used, they are of little use in some situations. Added to this the tolerance levels of humans to radiation is relatively very low at 5 Gy.

The favoured approaches for search of radiation protection protocols have been on mammalian models through use of radiation tolerance-enhancing plant extracts and compounds. The success achieved is inadequate. Several studies have used plant extracts. Our initial studies using flavonoids - rutin and quercetin conferred marginal tolerance in mouse model raising tolerance levels to gamma-radiation by a factor of 1.20. The same is true for several compounds. In this background it is interesting to note that there are biological models that are radiation resistant. These include the microbe *Deinococcus radiodurans* (LD₅₀ 5000 Gy), rotifer *Adineta vaga* (LD₅₀ 1200 Gy), tardigrade (*Ramazzottius varieornatus* 3000 Gy) *Chironomus* larvae (LD₅₀ 900 Gy) and the fruit fly *Drosophila* (LD₅₀ 1200 Gy). A search for mechanisms underlying this capacity is on.

Studies in the last decade on *Deinococcus*, *Adineta*, *Ramazzottius*, *Sf 9* cell lines of insects suggest involvement of mechanisms that protect damages from free radicals, protect/repair DNA damage, protein denaturation and subsequent recovery. *Deinococcus*, uses Mn²⁺ based protein-protection mechanisms. *Sf 9* cells invoke antioxidant mechanisms following gamma irradiation. The recent discovery of *Dsup* - a nuclear protein in tardigrade that protects DNA and confers resistance to human cell lines when incorporated in exciting. These mechanisms go parallel with anhydrobiosis tolerance to desiccation. A systematic study on radiation tolerance in *Drosophila melanogaster* through its life cycle has been carried out by us and it differs along the stages of life. The most resistant is the late III instar with a LD₅₀ of 1500 Gy, the early pupal stage being the least resistant. It appears that dividing cells render the early pupal stage more sensitive as other parameters are constant during life cycle. Genes responding to gamma irradiation are being searched for and they may hold key to future approaches to radiation resistance strategies.

Education and Career in Nuclear Medicine for Health Care Professionals

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Nuclear medicine is one of the most dynamic and fast growing branch of medical speciality. The practice of Nuclear medicine has evolved from team efforts of multidisciplinary science of Physics, Chemistry, Engineering, Medicine, and Biology using the radioactive tracers for diagnostic, therapeutic and research applications. The Nuclear Medicine Physician, Nuclear Medicine Technologist, Nuclear Medicine Physicist, Nuclear medicine Pharmacist (Radiopharmacist), Nuclear Medicine Protection (NMP) Specialist- RSO, are the integral part of the Nuclear Medicine Health care professional work force team who all should undergoes standard of education & training to follow professional Standards of practice & professional Ethics with sufficient Knowledge, Attitude and Skill implying Head, Heart and Hand in the domain of human health and Safety.

RMC of BARC, Mumbai (Radiation Medicine Centre of Bhabha Atomic Research Centre, Mumbai), was the Nucleus for the growth of Nuclear Medicine facilities in India since their inception in year 1963 and the only pioneer educational institute for developing the manpower resources for Nuclear medicine before year 2000.

Nuclear Medicine training & education in India begin from RMC by conducting Five (05) weeks short term training (between 1965 to 1976) as "Introductory Course on Medical Uses of Radioisotopes" for both Medical Graduates and Science Graduates to work as NM Physician and as NM Technologist respectively. This was the only training course conducted once in a year for Nuclear Medicine Professionals.



Since 05 weeks short term training course was lacking university awarded academic qualifications and considered inadequate with advent of 99mTc and Gamma Camera for Nuclear Medicine Technologists for career progression so RMC has framed the structure Course curriculum for one Year Full time post Graduate Diploma in Medical Radioisotope Techniques (popularly called as DMRIT) course under Bombay University for Science Graduate degree holders along with the NM Physicians course as PG Diploma in Radiation Medicine (DRM) from year 1973. The, first medical Physics section for Nuclear medicine came into existence in 1975 at Radiation Medicine Centre (BARC).

With the time Manipal University being first Private deemed university started Four Years BSc NMT with Diploma in Nuclear Medicine Technology dual degree program from Year 2004. All India Institute of Medical Sciences, New Delhi (AIIMS) a premier medical institute in India has started 02 years M.Sc. Nuclear Medicine Technology from the Year 2003 with intake of 6 students. Currently about 07 educational Institutes are running 3 yrs. BSc NMT with One Year Internship, 02 institutes are running Post Graduate Diploma as DMRIT/ DFIT, 07 institutes are running 2 Yrs. M.Sc. Nuclear Medicine Technology. Only 02 institutes are having structured PhD program in Nuclear Medicine. Two more Non- University Certificate Training Programs in India are running First one is the IAEA sponsored Distance Assisted Training (DAT) Programme for Nuclear Medicine Technologists and another One is running by the Leading Professional Body Association of Nuclear Medicine Physicians of India (ANMPI) as 2 yrs. Nuclear Medicine Technicians Training Program with In-field training. Both certificates courses are Strengthening Manpower requirements as Supporting Technical staffs for nuclear medicine facilities. Nuclear medicine technology programs are currently offered in a wide variety of nonstandard formats.

Didactic teaching and clinical educational tools that responds to changing trends in routine and advanced technology practice may need careful review by the professional bodies that guide and oversee NMT training. Quickly evolving practice needs necessitate creative strategies to optimize academic and continuing education opportunities, Continuous Professional Development (CPD), Training of Trainers (TOT), Faculty Development Program (FDP) to assure meaningful learning of NM Science, knowledge, and skills.

The Technology, procedures and practice of Nuclear medicine are changing from Manual to automatization, by entering from Analog to digital computer data processing, Obsolete of few radiotracers and addition of new generation radiopharmaceuticals, by entering of Gamma Camera to SPECT to PET Camera, to SPECT-CT to PET-CT (Fusion Imaging modality), to medical Cyclotron type of high end nuclear medicine equipment's, & generator PET Radiopharmaceuticals towards personalized medicine and targeted therapy. Like United Kingdom, in India also there is the need to modernising the non-medical health care Science Work force. The drivers for this changes would be Impact on the outcome of "Patient care with Public Safety", "Proper Work Force Planning & Career Pathway", and "Education Standard and Curricula development" compatible to Technological advances & level of Clinical organisational settings.

In India, Nuclear Medicine Practice for radiation Professionals are regulated & Controlled by Atomic Energy Regulatory Board (AERB) as per the Safety Code for Nuclear Medicine Facilities (published in 2011), in Which responsibilities of the Nuclear Medicine Technologist as well as for RSO-II are admxid for UG and PG level educational qualifications. There is no clear demarcated job description between Bachelor's degree and PG diploma / degree holders in Nuclear Medicine Technology. As the Technological advancements in all the aspects are quite fast and to compete with other clinical speciality there is the gap between Nuclear Medicine Physician and Nuclear Medicine Technologists job responsibility. In order to maintain the safety and the Quality assured patient care delivery and research outcome there is the need of the qualified, Skill-Mix, competent and responsible "Nuclear Medicine Physicist" and "Nuclear Medicine Pharmacist" to be bridged in between them by assigning their role and responsibility as per the organisational level and clinical settings which will help to open career pathways justifiably. Nuclear Medicine Physicist (NMP) can serve in the health care service, academic teaching institutions and in the research centres. NMP can play a role as Clinical Physical Scientist, as a Health Care Practitioner (Specialist), as an Nuclear Medicine Educator and as a Clinical Researcher.

The ambit of Professional Body like Nuclear Medicine Physicists Association of India (NMPAI) can play a greater role to help regulatory bodies (AERB) and regulatory Councils (Allied Health Science Central Council India) to "cadre reform" of Nuclear Medicine Health Care Professionals, to regulate standards of education & Practice, to ensure Registration, Verification, Accreditation and Licensing of NM Health Professionals as Nuclear Medicine Technologist, Nuclear Medicine Physicist, Nuclear Medicine Pharmacist and Radiation Protection Specialist (RSO) based on the level of education and credentials to practice.



Radium to Radium: A hundred years cycle

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Soon after the discovery of radium by Madam Curie, its life saving property was recognized followed by its life threatening property. Since then varieties of radionuclides are used for human welfare, especially in the field of nuclear medicine. The short-lived reactor produced radionuclides, ^{99m}Tc , acted as a magical radionuclide and huge quantity of this radionuclide is daily demand worldwide. Accelerator produced radionuclides like ^{18}F , ^{67}Ga , ^{201}Tl , ^{211}At , completed the reactor-produced radionuclides portfolio from late nineties. Astatine and technetium are two elements in the spotlight of nuclear medicine. ^{211}At is used for targeted therapy due to its suitable half-life and high energy α -particles.

After the Fukushima-Daichi incident, world voice is against setting up new reactor facilities for isotope production. Upcoming large-scale facilities like neutron spallation sources are now in the focus as alternative sources of clinically important radionuclides. Recently CERN has launched the CERN-MEDICIS project as a unique facility for the production of large quantities of radionuclides dedicated to biomedical research. I will discuss the evolution of clinically important radionuclides.

Molecular and Cellular Profiling for Radiosensitivity Analysis and its Clinical Significance.

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Abstract

The accidental or intentional exposure of the public to radiation has greater than before with the extensive increase in the use of nuclear technology. With the absence of physical dosimetry, precise measurement on the radiation exposure levels during mass exposure is of utmost importance. Similarly prior understanding on the radiosensitivity of normal / tumor cells for cancer patients undergoing radiotherapy is also of key importance. This presentation will give translational significance of radiation induced DNA damage, its repair based cellular /molecular biomarkers and their possible clinical implications.

We assessed the variation in radioresponse using gamma H2AX foci in healthy individuals ($n=100$) and the contribution of genetic polymorphisms to the observed variation for its implications in radiation biodosimetry. Further, radiotherapy (RT) induced normal tissue toxicity is one of the major limitations for achieving the desired therapeutic effect and has an adverse impact on quality of life. Therefore, predicting the risk of developing acute reactions before the initiation of RT using cellular and molecular based assays may serve as a potential biomarker. Hence, this investigation also envisaged the predictive potential of gamma H2AX foci analysis for assessing the risk of acute normal tissue adverse reactions in breast ($n=132$) and head & neck ($n=183$) cancer patients undergoing curative RT. Our results suggest that XRCC6 rs2267437 ($P = 0.0340$) and LIG4 rs1805388 ($P = 0.0250$) influenced the DSB repair in healthy individuals. Further, the gamma-H2AX assay and genetic variant in NBN rs1805794 may have its potential to be developed into a clinically useful predictive biomarker. The insight gained from this extensive investigation may be helpful for the detection of radiosensitive individuals in a healthy population and may have its clinical implications in the prediction of the risk of developing adverse skin reactions in those patients undergoing radiotherapy.

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Texture Analysis in Nuclear Medicine

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This article includes the glimpses of content intended to be delivered during my presentation.

The field of Medical Imaging has undergone a paradigm shift in its role in the past few decades. Now, the medical images are being used to understand and predict the behavior of cancers and other diseases. This new field in medical science is referred to as Radiomics. Radiomics refers to a branch of science that deals with utilization of information available from Medical Images to characterize



and quantify the tumor phenotypes and thus identify new quantifiable feature of clinical significance. The hypothesis involved in Radiomics is that advanced imaging analysis methods when applied to conventional and novel medical imaging technologies could capture additional and valuable information.

Texture Analysis

As the field of Radiomics continues to evolve, it has been recognized that medical images contain more information than is utilized by clinicians and researchers in a routine clinical setting. This has given rise to new possibilities in identifying factors that can predict, prognosticate and help in planning the treatment of the diseases they are applied to in medical images. Texture analysis is being increasingly identified to play these roles with a good reliability in comparison with conventional tools for medical imaging.

Texture: Definition

There is no generally agreed upon the definition of texture. It has been formulated by different people depending upon the particular application. Image texture, defined as "*a function of the spatial variation in pixel intensities (gray values)*", is useful in a variety of applications and has been a subject of intense study by many researchers. Texture analysis is a major step in texture classification, image segmentation and image shape identification tasks.

The term 'Texture Analysis' in essence refers to a class of mathematical procedures and models that can be used to characterize the spatial variations within an image for the purpose of extracting any surplus information the image can offer.

Approaches to Texture Analysis

The mathematical procedures that are used for texture analysis broadly fall into the following groups:

- (a) Structural
- (b) Statistical
- (c) Model-based
- (d) Transform

Structural methods represent texture of an image by a set of well-defined primitives (which represent 'microtexture') and a hierarchy of spatial arrangements of these primitives (which represent the 'macrotexture' of the image). In order to describe the texture by these methods, one has to define the primitives and rules of placement for these primitives. This can be advantageous as it offers flexibility in assessing the texture of an image as the user has the liberty to define the components. However, in the context of analysis of medical images, it is expected that any algorithm applied to obtain relevant information can be standardized and is uniform wherever it shall be applied. Hence the flexibility that these methods offer can itself be a detriment as standardization becomes an issue.

Statistical methods, more popular owing to their simplicity of application are used to analyze the spatial distribution of the gray values in an image. They are employed to compute local texture features at each point in an image and thus derive a set of statistics that define the distribution of these local features.

Depending on the number of pixels that define the texture features, these statistical methods are divided into first order (defined on individual pixels), second order (defined on pair of pixels) and higher order statistical methods. Of these, the second order statistical methods based on the gray level co-occurrence matrices (GLCM) are most often used and are most validated in the available literature.

Model-based methods are based on fractal and stochastic models and interpret an image texture by use of, respectively, generative image model and stochastic models. The parameters of the model are estimated and then used for image analysis. Though model-based approach has been used and validated in bio-medical imaging, in practice, the computational complexity arising in the estimation of stochastic model parameters is the primary problem.

Transform methods of texture analysis, such as Fourier, Gabor and wavelet transforms represent an image in a space whose co-ordinate system has an interpretation that is closely related to the characteristics of a texture (such as frequency or size). Methods based on the Fourier transform perform poorly in practice, due to its lack of spatial localization. The usefulness of Gabor filters is limited in practice because there is usually no single filter resolution at which one can localize a spatial structure in natural textures. The problem with wavelet transform is that it is not translation invariant.



Gray-Level Co-occurrence Matrix:

Gray level Co-occurrence Matrices (GLCM) employ statistical methods to define the texture features of an image. It is also known as a Gray level Dependency Matrix and is defined as "A two dimensional histogram of gray levels for a pair of pixels, which are separated by a fixed spatial relationship".

Consider a 4 x 4 matrix transform of an image represented in Figure 1a (labeled as Test Image) with four gray-tone value from 0 through 3. A generalized GLCM for that image is shown in figure 1b where $\#(i,j)$ stands for number of times gray tones i and j have been neighbors satisfying the condition stated by a displacement vector d (which is in turn defined by a radius δ and orientation θ). The general form to the Test image is represented in Figure 1b as below:

0	0	1	1
0	0	1	1
0	2	2	2
2	2	3	3

Figure 1a. Test image

Gray tone	0	1	2	3
0	$\#(0,0)$	$\#(0,1)$	$\#(0,2)$	$\#(0,3)$
1	$\#(1,0)$	$\#(1,1)$	$\#(1,2)$	$\#(1,3)$
2	$\#(2,0)$	$\#(2,1)$	$\#(2,2)$	$\#(2,3)$
3	$\#(3,0)$	$\#(3,1)$	$\#(3,2)$	$\#(3,3)$

Figure 1b. General form of GLCM

If for the above matrix, the displacement vector d is assigned with value of δ as 1 and θ as 0° , 45° , 90° and 135° , the respective GLCMs rendered as a result are shown in Figures 2a-d.

4	2	1	0
2	4	0	0
1	0	6	1
0	0	1	2

Figure 2a. GLCM for $\delta=1$ and $\theta=0^\circ$

6	0	2	0
0	4	2	0
2	2	2	2
0	0	2	0

Figure 2c. GLCM for $\delta=1$ and $\theta=90^\circ$

4	1	0	0
1	2	2	0
0	2	4	1
0	0	1	0

Figure 2b. GLCM for $\delta=1$ and $\theta=45^\circ$

2	1	3	0
1	2	1	0
3	1	0	2
0	0	2	0

Figure 2d. GLCM for $\delta=1$ and $\theta=135^\circ$



Figure 2: Various GLCM matrices rendered for the test matrix in Figure 1 at (a) 0° (b) 45° (c) 90° and (d) 135°

Most commonly employed GLCM-based texture parameters and their interpretations have been described below:

Texture Parameter	Mathematical Formula	Significance
ASM	$\sum_{i,j} p(i,j)^2$	Maximum value of 1. More homogeneous the image, closer is the ASM to 1
IDM	$\sum_{i,j} \frac{p(i,j)}{1+(i-j)^2}$	Low value for inhomogeneous images and higher value for homogeneous images
Contrast	$\sum_{i,j} p(i,j)(i-j)^2$	Measures local variations in an image. Measures contribution of a pixel away from the diagonal
Entropy	$-\sum_{i,j} p(i,j) \ln p(i,j)$	Measure of disorder/complexity of an image; inversely correlated with ASM
Correlation	$\sum_{i,j} p(i,j) \frac{(i-\mu_i)(j-\mu_j)}{\sigma_i \sigma_j}$	Measure of gray-level dependencies between pixels in relation to each other

Table 5: Shows commonly used GLCM-based texture parameters, their mathematical representation and their significance in image analysis

The result of experimental study conducted using GLCM matrices will be discussed during the presentation.

ORAL PRESENTATIONS

OR 01: Title: Liver segmentation of PET/CT images using fuzzy C-means clustering

Authors: Deepak Aheer, Anil Kumar Pandey, Jay Prakash Kumar, Anshul Sharma, CD Patel, CS Bal and Rakesh Kumar

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Objective: The aim of this study was to perform segmentation and extraction of liver from PET/CT fused images of suspected HCC patients, using Fuzzy C-means clustering.

Method: Fifty PET/CT liver images of patients with suspected hepatocellular carcinoma were used. The methodology involved following operations applied in sequence: 1. removing bones from CT images using thresholding technique, 2. segmentation of liver based on fuzzy C-means clustering, 3. mathematical morphological operation to extract liver. MeVisLab 2.7 was used for fuzzy C-means clustering and remaining operations were implemented using MATLAB R2013b. The result of segmentation method was validated with ground truth and also by the visual interpretation made of two experienced Nuclear Medicine Physicians.

Results: The bones were removed from CT images at the threshold gray level between 75 and 190. Segmentation of liver on CT images was achieved with input parameters of Fuzzy C-means algorithm as follows: the number of classes as 5, fuzziness as 1.5 and epsilon as 0.9. Figure-1 shows an input image, extracted liver and the ground truth PET/CT image respectively. The Sensitivity, specificity and accuracy of the proposed method used in this study were found to be 96.11%, 99.40% and 98.97% respectively. Forty-three out of fifty (86%) segmented liver images were rated as good when independently evaluated by two experienced nuclear medicine physicians.



OR 02: Title: "Estimation of Radiation Dose to Caregiver of Patient Treated with High Dose Iodine-131"

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Objective: The aim of this study was to determine dose received by the caregivers from the thyroid carcinoma patients treated with radioactive iodine 131I after the discharge from the hospital living in different condition and using different mode of travel is within the tolerance limit or not.

Methods: The administered activity ranged from 50 mCi to 250 mCi. One or two designated caregivers received specific radiation safety instructions prior to treatment. Twenty patients with differentiated/papillary thyroid carcinoma, referred to the department were treated with high dose radioiodine I-131. All patients were discharged on reaching AERB prescribed dose limit (5mR/h). Following discharge, caregivers were provided with a TLD crystal in the form of a locket to be worn on the neck. Cumulative radiation dose over a period of seven days after the discharge of patients were measured. The TLD crystal was analyzed in TLD reader. The common supporting and caring activities done by the care-givers after discharge of the patients includes travelling together in the common vehicle providing food and medications. All patients recruited in the present study had Karnofsky performance score > 60 i.e. they did not need any assistance in their daily activities.

Result: Cumulative exposure to the care-givers were from 6mGy-12mGy (7.94(Mean) $\pm$ 1.97(SD)).
Conclusions: The radiation dose to caregiver in seven days after discharge (7.94(Mean) $\pm$ 1.97(SD)) is above the presently prescribed dose limit for general public as per ICRP guidelines of 5mSv/yr. As this is ongoing work still it emphasizes the need for detailed radiation safety instruction to the caregiver and cumulation of more data before reacting on a firm conclusion.

OR 03: Studies on life-cycle stages of Drosophila melanogaster suggest proliferative stage to be radio-sensitive.

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Introduction: Harmful effects associated with radiation have always prejudiced the minds of public and policymakers about benefits of radiation. Humans are among most radio-sensitive organisms. Discovery of radiation tolerance in some organisms have raised questions as to how tolerance is achieved. The *Drosophila melanogaster* is one such animal and adults of which are post-mitotic and less susceptible to radiation. The *Drosophila melanogaster* is emerging as a suitable model for radiation research. The advantage of this model are: 1. It exhibits relatively high levels of tolerance. 2. Provides genetic approaches to address physiological questions. 3. It has different life stages in its life cycle that keeps some parameters constant, while others vary. These aspects render it an attractive model to address mechanisms of radiation tolerance.

Purpose: Discovery of radiation tolerance in some organisms have raised questions as to how tolerance is achieved. To answer this question we performed experiments which will help to understand radiation tolerance and mechanism underneath.

Method: To understand levels of radiation tolerance analysis of LD50, 1 hour post-irradiation in all life stages of fly was studied. Total antioxidant capacity (TAC) by phosphomolybdenum method and protein carbonylation (PC) by DNPH assay, were performed for all the life stages.

Result: The sensitivity decreases as the fly develops from egg to third instar larva (LD50 of 452 Gy to 1590 Gy). However, the early pupa stage exhibited an interesting incidence of relatively high radiation-sensitivity (LD50 of 50 Gy). The adults recovered from this episode of sensitivity and regained tolerance (LD50 found 1228 Gy for males and 1250 Gy for females).

Conclusion: We postulate that early pupal stage has a high rate of cell proliferation that renders the organism radiation-sensitive at this stage. Analyses of TAC showed highest levels of antioxidants during early-pupal stage. PC increased along life stages and it is highest during early-pupal stage and the levels of catalase marginally decreased during this stage. Taken together, the observations suggest that high cell proliferation increases metabolism, DNA and protein synthesis, which makes it sensitive to carbonylation. The organism therefore exhibit highest sensitivity at this stage of life cycle.

Abbreviations: LD50- Lethal dose to kill 50% population, Gy- Gray.



OR 04: Synthesis and Evaluation of New Radiolabeled Bombesin Analogs as Receptor Targeted Tumor Imaging Agent

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Introduction: Bombesin(BN) is a tetradecapeptide that binds specifically to gastrin-releasing-peptide(GRP) receptors which overexpressed on several cancers, including prostate, breast, and colon. Radiolabeled bombesin analogs with high affinity for GRP receptors might therefore be used for scintigraphic imaging of these types of tumors.

Purpose: The goal of this study was to synthesis 99mTc labelled new BN analogs (BN1, BN2 and BN3) with favorable pharmacokinetic properties in order to improve the breast tumor imaging properties as new diagnostic radiotracers in comparison with truncated BN peptide BN(7-14)NH2.

Methods: Solid-phase-peptide synthesis method was used for the synthesis of truncated BN analogs conjugated with bi-functional chelating ligand HYNIC. Radiolabeling with 99mTc was performed using EDDA/tricine as co-ligands and analysed by TLC/RHPLC methods. Its lipophilicity and stability were also investigated. The IC50 and internalization properties were determined using the GRPR expressing breast cancer cell line MDA-MB-231. In addition biodistribution and imaging experiments were performed in tumor bearing rat.

Results: Labeling yield of peptide conjugates >94% was obtained with good stability in presence of serum. Radiopeptides have showed significant internalization (30-47%) into MDA-MB-231 cells with high receptor-binding affinity (nanomolar range) for cells. In biodistribution studies, a receptor-specific uptake was observed in GRP-positive organs and tumor. Biodistribution and clearance kinetics in rat revealed an efficient clearance from the blood and excretion mainly through the renal-urinary pathway. In addition, tumor uptake was higher than non-specific organs, such as spleen, liver and muscles. Tumor-to-muscle and tumor-to-blood ratios for radiopeptides have showed high values at 1 h post-injection. Furthermore, blocked studies using cold bombesin peptide were performed, which demonstrated an important decrease in tumor uptake, indicating a tumor specificity for 99mTc-BN analogs. SPECT imaging studies also resulted in clear delineation of the tumor. Among the three analogs 99mTc-BN1 displayed more significant radiochemical characteristics, and adequate affinity to breast tumor cells.

Conclusion: Therefore observed results suggest that among three new 99mTc-BN analogs, 99mTc-BN1 possess most favorable properties, thus rendering it as potential candidates for non-invasive receptor targeted imaging of tumor and which are encouraging enough to carry out further experiments.

OR 05: Radiolabelling of Tamoxifen as a potential imaging agent for Estrogen Receptor positive Breast Cancers.

Authors-Anupriya, Jaya Shukla, Priya Bhusari, Rakhee Vatsa, Kanchan, BR Mittal **Introduction/Purpose:-** Tamoxifen is a FDA approved a selective estrogen receptor modulator (SERM). It is used as an adjuvant therapy for estrogen receptor positive breast cancers. This study aimed to radiolabel tamoxifen with Tc-99m via tricarbonyl complex as a diagnostic imaging agent for ER positive breast cancers.

Methods- Sodium boranocarbonate, a carbon monoxide producing source, was dissolved in 0.1M PBS (pH=7.5) and 30mCi of Tc-99m was added. The reaction mixture was incubated at 80 °C in water bath. Reaction mixture was cooled followed by quality control using saline, acetone and methanol:HCl (99:1) as mobile phase. Tamoxifen was added to the carbonyl solution and incubated at 100 °C at various pH (3.5, 6, 7.5). Quality control was done with ITLC using methanol:HCl (99:1) as mobile phase. Further, to rule out the presence of free technetium-99m, 0.1ml Tc-99m tricarbonyl mixture was incubated with 0.05M EDTA without adding tamoxifen. For characterisation of the radiolabelled complex MALDI-TOF was performed.

Results- Tc-99m carbonyl complex and Tc-99m-tricarbonyl-tamoxifen complex were prepared and the Rf on ITLC were 0.3 and 0.4, respectively in methanol:HCl (99:1). In saline, the peak of Tc-99m-tricarbonyl-tamoxifen complex was observed at the base (due to hydrophobic nature of tamoxifen). The peak of EDTA containing Tc-99m tricarbonyl was observed at the solvent front with acetone and saline thus confirmed the formation of tricarbonyl core and absence of free technetium-99m. The radiolabelling efficiency was found to be >90% at all pH (3.5, 6, 7.5). In MALDI-TOF a peak was observed at the molecular weight corresponding to of Tc-99m-tricarbonyl-complex (568Da).

Conclusion- Tc-99m-tricarbonyl can be used to label tamoxifen that can be used for imaging ER positive breast



OR 06: Effect of energy window width and peak shift on SPECT images

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Introduction: The different factors that affect the gamma camera uniformity of Single Photon Emission Computed Tomography (SPECT) technique have been analyzed including peak shift (%) and window width of energy. The effect of peak shift and window width on SPECT image uniformity has been investigated using a point source (Tc-99m) to perform intrinsic flood images.

Methods : After performance of intrinsic flood images by using a point source (Tc-99m) made visual analysis of acquired images. The relation between calculated integral & differential Centre Field of View (CFOV) and Useful Field of View (UFOV) uniformity values were plotted with peak shift and window width change. The effects of window width of energy 5%, 10%, 15%, 20%, 25%, 30% on SPECT images were investigated using the point source (Tc-99m) radioisotope with energy of 140 KeV.

Results: Although 0% shift is the optimum peak shift, but in the current study we have found that the data in the range of 0% to 3% peak shift provides result with satisfactory image quality. Integral Uniformity (IU %) and Differential Uniformity (DU %) values of CFOV and UFOV were noticeably changed with the change of energy window width. In this study, the optimum energy window width of the images of different flood phantom has been found to be in the range from 15% to 20%.

Conclusion: Finally, 0% to 3% peak shift at 15% energy window width applied on head and body phantoms provide suitable images leading to proper diagnosis which conform our findings.

Key words: Single Photon Emission Computed Tomography (SPECT); Center field of view (CFOV); Useful field of view (UFOV); Integral uniformity (IU); Differential uniformity (DU).

OR 07: Radio -labeling of DOTA-NOC with 68Ga eluted from itG Ge-68/Ga-68 Generator

Mehjabeen P, Priya M, Rutuja P, Beena Shetye, Rangarajan V

Aim : To Calculate radiolabeling yield of Ge-Ga Generator for a period of one year.

Introduction: 68Ge/68Ga generators provide cyclotron independent access to PET radiopharmaceuticals. 68Ga is a short lived positron emitter (half-life 67.6 min) and is eluted from 68Ge (half-life of 270.8 days). The 270 days half-life of the parent allows the use of the generator potentially up to 1 year. Ideally a 30 mCi Ge-Ga generator should give 30 mCi 68GaCl3 and it is expected to get 30 mCi labeled product i.e. 68 Ga DOTA-NOC. In reality 68Ga recovery from chromatographic column is less than expected value.

Material and Method : itG 68Ga-68Ge generator, Dose calibrator, itG IQS 68Ga Fluidic Labeling Module. Labeling was performed using the ITG's IQS 68Ga Fluidic Labeling Module and the ITG 68Ga Peptide. For 68Ga - DOTANOC indigenously prepared chemicals were used for labeling (25 µg) of DOTANOC (GMP grade) in 900UL of Na acetate buffer. Radiolabeling involved heating at 105° C for 10 minutes. The labeled molecule was purified in-line with the labeling module using a reverse phase C-8 Sep - Pak Light (Waters, USA) and filtered through a Sartorius 0.2µm filter for sterilization.

We calculated uncorrected Radiochemical yield (RCY) using formula: %RCY = Labeled Activity of product/Activity obtained at elution X100.

RESULTS: Radiochemical yield are typically reported as either decay corrected or uncorrected yield. The %radiochemical yield was found constant over the period of 1 year.

68Ga - DOTA-NOC labeled peptide gave the consistent RCP >95%.

Conclusion : An itG 68Ga-Ge generator with itG-IQS 68Ga Fluidic Labeling Module is suitable for the use of 68Ga Radiopharmaceutical as it gives consistent RCY and RCP.

OR 08: Comparison of fusion of PET and CT images using techniques of Alpha-blending and Principal Component Analysis.

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Objective: To compare usefulness of PET and CT images fused using alpha-blending or principal component analysis



Methods: 1294 sets of registered PET and CT images in dicom format were processed using Matlab R2013b. For alpha blending method, alpha value for each pixel was calculated using Porter and Duff Equations [1]. The PET image was used to compute alpha values. The PET/CT fused image If was obtained using the following relation $If = I1 * \alpha + I2 * (1 - \alpha)$ Where I1, and I2 are CT and PET images respectively. For Principal Component Analysis (PCA) based image fusion, PCA of CT and PET images were determined and PET/CT fused image was obtained using the following relation: $If = I1pca * I1 + I2pca * I2$ Where I1 and I2 are CT and PET image respectively and where I1pca and I2pca are PCA of CT and PET image respectively. The resultant fused images from two methods above were compared for their fusion index using Feature Mutual Information metric (FMI) [2]. Student's-t test was used for significance of difference of their means. The null hypothesis was that the two techniques (PCA and alpha blending) produce similar fused

images at significance level $\alpha = 0.05$.

Results: Based on fusion index using FMI, the difference between PCA and alpha-blending algorithm used for PET/CT image fusion was statistically significant at $p = 1.5833e-099$ (with $\alpha = 0.05$). The FMI (mean, variance) for PCA and alpha-blending algorithm were (0.91461, 0.003841) and (0.95625, 0.00050472) respectively.

Conclusion: Fusion of PET and CT images using Alpha-blending of gives better results as compared to their fusion by PCA.

OR 09: Role of various semiquantitative parameters of F18-FDG PET/CT studies obtained from primary tumor for interim treatment response evaluation in non-small cell lung cancer (NSCLC).

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Introduction: Early treatment response evaluation is important in NSCLC patients so that treatment course can be changed in patients with progressive disease and toxic effects of chemotherapy can be avoided. A wide array of semi-quantitative metabolic parameters obtained from F18-FDG PET/CT is currently being employed for assessment of response to therapy and prognostication.

Objective: To prospectively evaluate the role of three semiquantitative parameters of primary tumor (TBR, SUVmax, SUVavg) obtained from F18-FDG PET/CT and to determine best one for response assessment to chemotherapy in biopsy-proven NSCLC cases.

Method: 32 patients (M/F=25/7) with mean age 54.71 ± 12.65 yrs with biopsy proven NSCLC (21 adenocarcinoma, 11 SCC) were enrolled in study. Each patient underwent baseline and post 4 cycle chemotherapy whole body F18-FDG PET/CT scan after injecting 0.14-0.21mCi/Kg of F18-FDG i.v. Images were analysed by two experienced nuclear medicine physicians and three PET/CT parameters of primary tumor were evaluated (TBR, SUVmax, SUVmean) for both scan along with their % changes (). Patients were divided into two response groups as per RECIST 1.1 criteria: responders (complete and partial response) and non-responders (stable and progressive disease). All parameters were compared among two response groups by using appropriate statistical methods, $p < 0.05$ was considered significant.

Results: Of 32 patients, 5 had stage III and 27 had stage IV disease at baseline evaluation. Sixteen patients were responders and 16 were non-responders. All parameters evaluated in post-chemotherapy scans were significantly higher in non-responders as compared to that of responders ($p < 0.05$). Among the % changes of three parameters, SUVmax was significant ($p = 0.02$), TBR was marginally significant ($p = 0.048$) and SUVavg was non-significant ($p < 0.05$) in prediction of response. In ROC analysis, post-TBR came out to be most accurate with AUC 0.83 followed by post-SUVmax (AUC 0.80), post-SUVavg (AUC 0.75) and SUVmax (AUC 0.70).

Conclusion: Among all the parameters obtained from post-chemotherapy scans, post-TBR and among the %



OR 10: Re-188 Patch Radionuclide Therapy for Keloids : A 3 year follow up study

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Background : Keloids are irregularly shaped scars composed of mainly either type III (early) or type I (late) collagen which tend to enlarge progressively. No treatment is 100% effective and invasive methods like surgery lead to recurrence & increase in size.

Purpose: The aim of the study was to determine the efficacy of Re-188 radioactive skin patches for treatment of keloids and to determine the long term effects of the patch radionuclide therapy.

Methods : Nine patients (2 males and 7 females) aged between 22-59 years with 29 lesions were included in the study. All patients had clinically diagnosed keloids. Eleven lesions were on chest, 6 on arms, 4 on shoulder, 3 on pubis, 2 each on earlobes and abdomen and one lesion was on neck. All the patients complained of pruritus and pain over the lesions. None had infection or exudations from the lesion. Sealed patches incorporating Re-188 were custom made according to size and shape of the lesions and applied locally on the lesion site. The patches were reapplied on alternate days so as to deliver approximately 50 Gy of radiation dose superficially in total 3 fractions. Patients were followed up initially at 2 weeks, 4 weeks, 8 weeks and 12 weeks. Post 3 month follow up, patients were followed up 6 monthly to determine any recurrence or any long term effects.

Results : Excellent response with almost complete disappearance of lesion was seen in 12 (41%) lesions. Six lesions (21%) showed good response and the remaining 11 lesions (38%) demonstrated partial response respectively. There was a greater than 50% decrease in lesion size in 18 (62%) lesions. Spectrum of radiation dermatitis ranging from pain, itching, erythema, crusting and desquamation was observed as side effects in all lesions post therapy which gradually healed by 8 weeks. Routine haematological and biochemical examinations at the follow ups did not reveal any toxicity. None of the lesions had any recurrence upto 3 years post therapy.

Conclusion: Re-188 Patch Radionuclide Therapy is an effective and safe therapeutic option for treatment of keloids

OR 11: Renal and haematological toxicity in patients undergoing Lu-177-DOTATATE Capecitabine therapy for neuroendocrine tumors

Ajay Mohan, Ashwani Sood, Priya Bhusari, Jaya Shukla, Bhagwant Rai Mittal

Introduction: Neuroendocrine tumors (NETs) have neuro-endocrinal origin. There are many types of NET's and most of them express the somatostatin receptors 2 and 5. Positron emission tomography (PET) imaging using Ga-68-somatostatin analogues is routinely used to assess the distribution, spread of disease, prognostication and indicating the patient's suitability for Peptide Receptor Radionuclide Therapy (PRRT). PRRT is used in patients with metastatic/inoperable disease using Lu-177 labeled somatostatin analogues and capecitabine. The risk of toxicity associated with this treatment is there. The kidneys are the critical organ in Lu-177-DOTATATE therapy because the uptake is mediated by the endocytic receptor megalin in the proximal tubuli of the nephron followed by haematological toxicity. The aim of this study is to assess the toxicity of Lu-177 DOTATATE in patients undergoing PRRT.

Purpose: To assess the renal and haematological toxicity in patients undergoing Lu177-DOTATATE treatment. **Methods:** Twenty consecutive patients underwent NETs therapy (4 cycles) with Lu177-DOTATATE (200mCi per cycle) after fulfilling the eligibility criteria. Amino acid infusion was done along with administration of Lu-177-Dotatate for nephro-protection. A post therapy scan was performed 24 hr post administration of therapy dose. The patients were followed-up with determination of renal function including GFR evaluation, liver function and complete haemogram on 3rd, 6th and 9th week after each cycle of Lu-177-Dotatate therapy.

Results: Evaluation of renal function at 3, 6 and 9th week intervals did not show significant reduction in renal parameters. Also the blood profiles at these time intervals did not show significant reduction in cell counts and haemoglobin content. In few patients, a significant increase in the serum creatinine level and mild drop in the platelet count was observed during the therapy.

Conclusion: PRRT with Lu177-DOTATATE in neuro-endocrine tumors with amino acid infusion is an effective and safe treatment with transient toxicity in few of patients of the study group.



OR 12: 99mTc-HYNIC-RGD as a neo-angiogenesis imaging agent in locally advanced breast cancer (LABC) patients.

INTRODUCTION: RGD (Arg-Gly-Asp) is a peptide targeting $\alpha_v \beta_3$ integrin receptors which are over-expressed during neo-angiogenesis in both endothelial and tumor cells. Labeling the peptide with 99mTc can help us in early diagnosis of growing tumor.

PURPOSE: To establish cost effective and efficient angiogenesis imaging agent with reduced radiation burden using low energy 99mTc.

MATERIALS AND METHODS: The lyophilized kit for HYNIC-RGD was incubated with 70 mCi 99mTcO₄⁻ in water bath at 100 ° C for 20 minutes. The preparation was allowed to cool at room temperature for 10 minutes. Paper chromatography was performed with Whatman strips using saline and acetone as mobile phase. The strips were scanned using radioTLC Scanner, also the counts were taken in well counter. 20 mCi dose of 99mTc-HYNIC-RGD was administered to each patient (n=9) through i.v injection. Planar whole body scan was acquired after 2 hours of dose administration.

RESULT: Paper chromatography using saline as mobile phase showed peak at solvent front and with acetone peak was obtained near the origin front. Rf calculated was 0.9 and 0.2 with saline and acetone respectively. From the counts obtained in well counter radiolabeling efficiency was found to be $\geq 95\%$. Physiological uptake was seen in nasopharynx, salivary glands and gastric mucosa. In some patients mild uptake was observed in thyroid. Tracer showed renal excretion. Intense uptake was observed in breast lesions in all LABC patients. In two patients axillary lymph nodes were also visualized. 99mTc-HYNIC-RGD reduces the radiation burden to the patient. 99mTc-HYNIC-RGD is cost effective as compared to already existing 68Ga-RGD.

CONCLUSION: 99mTc HYNIC-RGD can be labeled with high radiolabeling efficiency and may be used as a promising SPECT radiopharmaceutical for imaging neo-angiogenesis in LABC patients

POSTER PRESENTATION

PT-01: Is maximum safe dose calculation based on EANM Dosimetry committee recommendation reliable in Radioiodine therapy of differentiated thyroid cancer?

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Introduction

The empiric fixed dose approach is practised world-wide for the radioiodine treatment of differentiated thyroid cancer patients including children and adolescents. Many investigators have performed internal dosimetry in adult patients undergoing RIT, however, few have done dosimetry in children and adolescents, and none have applied bone marrow (blood) approach in paediatric patients

Objectives

It was planned to dosimetrically determine the maximum safe dose (MSD) for therapy using bone marrow (blood) approach presented by EANM dosimetry committee in 2009 (modified Benua approach) that provides blood dose estimates from a single external measurement of the whole body retention 1 or 2 days after radioiodine administration and enables blood dose-based therapy for routine ablation as well as treatment of metastatic disease with minimum effort. Here the therapy dose was determined targeting 0.3 Gy blood absorbed dose which is considered to be safe.

Materials and Methods

Ninety seven patients with age ≤ 21 years with proven DTC were given 2 mCi (74MBq) diagnostic dose of ¹³¹I. The whole body scan (WBS) was done on a dual head gamma camera at 2 and 24 hours. The percentage retention of radioiodine at 24 hour was determined from the geometric mean of anterior and posterior whole body counts using the 2 hour pre-void image as baseline. Blood volume was estimated for each patient and the dose rate (mGy/MBq) was calculated by putting these parameters in the below mentioned equation to calculate the MSD. Of the total 97 patients, 25 patients had no evidence of disease (NED) on scan and 72 patients had lesions on scan at the time of inclusion in



the study. Moreover, in 64/72 patients repeat dosimetry was done on six month follow-up. Out of which 45/64 patients had NED and remaining 19/64 patients had lesions on scan. Of a total of 161 dosimetry, 70/161 had NED (Group A) and 91/161 had lesions on scan (Group B). Of these 91 studies available 10 had a lobe only, 23 had remnant only, 34 had either only nodes or nodes with remnant and 24 had either only lung metastases or lung metastases with nodes/remnant.

Results and Discussion

There was no significant difference in the MSD in both the groups. In Group A the mean values of whole body retention, absorbed dose rate and MSD was found to be $26.46 \pm 6.95\%$, 0.108 ± 0.02 mGy/MBq and 79.41 ± 18.36 mCi respectively whereas in group B patients it was 29.91 ± 9.60 , 0.1239 ± 0.04 mGy/MBq and 71.04 ± 20.74 mCi respectively. Moreover, no difference in the therapy dose was found depending on the extent of disease in remnant, nodal and lung metastasis. The mean values of therapy dose in patients with only lobe, only remnant, with only nodes or , nodes with remnant and lung metastases only or lung metastases with nodes/remnant was found to be 59.09 ± 6.82 mCi, 70.96 ± 16.61 mCi, 71.64 ± 19.41 and 75.41 ± 28.07 mCi respectively.

Conclusion

EANM dosimetry committee recommendation was not found to be useful in calculation of MSD as there was no difference in patients with or without disease or depending on the extent of disease.

PT-02: Fast OSEM3D SPECT Reconstruction with GPU

Shashi Duraiswami, Segami USA

OSEM3D is generally admitted as an efficient reconstruction method for SPECT Imaging, but may be time consuming when calculations are performed on central processor unit (CPU). To speed up reconstruction we have implemented an OSEM3D application in Oasis, namely IRIS3D using the graphic processing unit (GPU). The parallel nature of the graphics pipeline is particularly adapted to the reconstruction problem.

Background:

OSEM3D is generally admitted as an efficient reconstruction method for SPECT Imaging, but may be time consuming when calculations are performed on central processor unit (CPU). To speed up reconstruction we have implemented an OSEM3D application in Oasis, namely IRIS3D using the graphic processing unit (GPU). The parallel nature of the graphics pipeline is particularly adapted to the reconstruction problem.

Purpose:

The aims of this paper is to demonstrate that use of GPU decreases reconstruction time. Materials and methods

Segami's IRIS3D, an OSEM3D reconstruction implementation is programmed on GPU. The projection and backprojection operators of OSEM3D include collimator with detector varying response model. Optionally, tissue attenuation is considered during the iterative process (OSEM3D+AC). Images are loaded on graphic cards as texture with the OpenGL library and computations are carried out using arithmetic operations of fragment shaders. Two internal data representations were tested: 16 bit and 32 bit floating point data. No pre-computed matrix coefficients are needed for GPU method.

Reconstruction times were measured on a standard PC (Dell XPS, GPU: GeForce 7950GX2, CPU: Intel Core 2 Duo E6700 2.66GHz) for 128x128 120 projections brain images.

Results:

The use of 16 bits precision instead of 32 bits has a negligible effect on image quality, and is ten times faster. So it is clearly not indicated to go until the highest precision. In 16-bit programming, we performed 8 iterations with 5 subsets of OSEM3D in 30 seconds and OSEM3D+AC in 107 seconds on GPU instead of about 1 hour and 10 hours, on CPU respectively. With continued advances in GPU libraries and improved video cards, the reconstruction time continues to decrease.

Conclusion:

Segami's IRIS3D, an OSEM3D with GPU implementation, provides a real gain of time and allows the use of this algorithm in a clinical context and on a standard PC.



PT-03 :Normal Limits for Left Ventricular Ejection Fraction and Volumes Determined by Gated SPECT: Comparison Between Cedars-Sinai Medical Center's QGS and Segami's CardioGam

Shashi Duraiswami, Segami USA

Background:

Several gated SPECT processing software are available in the market however, due to the difference in the left ventricular modelling and methods of myocardial definition, the results are substantially different. Therefore it is necessary to define normal limits specific to each software and understand the reason for their differences to adequately interpret individual cases.

Purpose:

The aims of this study were to define normal limits of ventricular volumes and ejection fraction for Cedars-Sinai's QGS and Segami's CardioGam software and to evaluate the relationships between the results. Materials/Methods

QGS, developed at Cedars Sinai Medical Center, is an automatic gated SPECT processing software operating in 3-dimensional space, based on asymmetric Gaussian fitting of count profiles across the myocardium and identification of endo and epicardial surfaces.

In CardioGam, by Segami in collaboration with Stanford University, the location of the myocardial wall is defined by statistical parameters and not by edge detection. The algorithm operates in a 3-dimensional space and determines the center of myocardial wall, which location is defined as the center of gravity of each activity profile plotted from the center of left ventricular cavity outward.

Results:

The mean ejection fraction was similar between the methods but the volumes and cardiac output were significantly lower for QGS than CardioGam. QGS lower limit for LVEF was 43% for men and 51% for women compared to 49% and 53% respectively for CardioGam.

Conclusion:

QGS has been reported to underestimate ventricular volumes and consequently overestimate LVEF. This explains the low cardiac output values observed with this method and the trend in ejection fraction differences. CardioGam gave higher volume values (diastolic and systolic) and consequently higher stroke volumes and cardiac output results. Given the differences between the techniques, it is necessary to apply different normal limits for each software and consider these factors when interpreting individual cases

PT-04: A comparison study of filtered and unfiltered radio labeled colloid for detection of sentinel node

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Objective: The purpose of the study is to compare the detection efficiency of sentinel node for filtered and unfiltered radio labeled colloids.

Material and methods: A study of 30 patients, 15 patients on each category for filtered and unfiltered radio colloid, has been done. [99m] Tc Sulfur Colloid, 14-22MBq, used for injections. Scintigraphic study done by SPECT system (Siemens healthcare) and Gamma probe (Crystal photonics, Germany) used for the detection of sentinel node.

Results: The study results that filtered colloids/tracer (size 50-220 nm with mean of 100 nm) moves faster and show early peak uptake compare to unfiltered (size 50-5000nm, mean 450 nm) colloid into sentinel node. The unfiltered radio colloid has wide range of particle size and show slow and delayed peak uptake so it can be used for delayed or next day procedures.

Conclusion: Filtered radio colloid is suitable for early procedures and also requires lesser dose of radio colloid as compare to unfiltered radio colloid.

Keywords: radio colloid, [99m] Tc sulfur colloid, gamma probe



PT-05: Preliminary experience with Tc-99m Trodat in Uttarakhand Understanding the myths.

Vandana Kumar Dhingra*, Nisha Bhatia, Ashutosh Panday***

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Background : Tc-99m TRODAT imaging provides indispensable functional information of the basal ganglia but is performed in very selected centres in our country and none exist in the state of Uttarakhand.

Purpose: Assumed to be logistically difficult we evaluated the technical aspects in the initial series of Tc-99m TRODAT Scans. Methods: We examined the technical steps of performing a Tc-99m TRODAT Scan in the initial series of patients. These were divided into procurement and isotope logistics, procedure timing and qualitative labelling quality. We also looked for requirement of repeat study.

Results: We included the first 6 procedures of Tc-99m TRODAT (three batches of two subjects each) which were performed in our department and studied the aforementioned parameters in all. We procured an indigenous TRODAT kit in a cold box (with dry ice). It was stored in a deep freezer till use. All the instructions for labelling of the Tc-99m TRODAT cold kit were followed strictly especially the volume of Tc-99m (less than 1ml) and radioactivity of 60mCi. The isotope in the first or second day of the new Mo-Tc-99m generator was concentrated enough to comply with these instructions. Patients were injected within 15 minutes of preparation. One patient and one voluntary control were injected with each batch of Tc-99m TRODAT. Imaging was started after 240 minutes of injection and took around 120 minutes. Bio-distribution of Tc-99m TRODAT in the brain was checked qualitatively and bilateral stria were well visualised in control cases images of all three batches of Tc-99m TRODAT prepared. None required repeat study.

Conclusion(s): This study helped us in alleviating the negative myths associated with Tc-99m TRODAT imaging. Though time consuming and technically demanding, if performed in a planned and meticulous way, clinically useful images can be achieved within routine working hours.

Key words: Tc-99m TRODAT, Uttarakhand

PT-06: Evaluating the impact of fluidics usage of an IQS Ga68 Fluidic Labeling module on the production yield of Ga-68 PSMA.

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BACKGROUND: The IQS Ga68 Fluidic Labeling module by ITG is a manual, self-shielded system including an organic based Ga68-Ga68 generator with a fixed tubing system (FLUIDICS). The company recommended frequency to change the tubing system is after every 10 elutions. The effect of not changing the fluidics after 10 elutions on the yield of Ga-68 PSMA was observed.

AIM: To determine if the product yield of Ga-68 PSMA is affected if the fluidics in the IQS Ga68 Fluidic Labeling module are used for more than the recommended 10 elutions.

METHOD: Fresh fluidics were prepared after every 10 elutions of the Ga-68 PSMA productions. For some of the Ga-68 PSMA productions, the fluidics were used for more than 10 elutions. The success of the elution was determined by calculating the percentage of waste activity to the product activity. Yield = (Waste activity * 100) / Product activity. This percentage was compared for the 1st and 2nd time fluidics were used and the fluidics used greater than 10 times.

RESULTS: For fluidics number 1 & 2 the percentage range was from 0.76 to 2.56 with an average of 1.415. For fluidics used greater than 10 times the percentage range was from 0.65 to 4.02 with an average of 1.27.

CONCLUSION: The use of fluidics greater than the recommended 10 elutions in a IQS Ga68 Fluidic Labeling module does not have much impact on the production yield of Ga68 PSMA. Thus the fluidics can be used for more than 10 elutions in unavoidable circumstances



PT-07: CT Dose Management in Nuclear Medicine: A Sketch

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Background: Medical radiation is the commonest cause of exposure to ionizing radiation to general population and health professionals. Hybrid imaging techniques like SPECT/CT and PET/CT account for a majority of radiation dose burden currently.

Purpose: The aim of this article is to provide CT dose management as level of appropriateness in Nuclear Medicine.

Description: The significance increase in the use of CT, alone or in combination with SPECT or PET (Hybrid Imaging) has raised concern about patient radiation exposure and associated risk of cancer. This becomes more concerning point in case of pediatrics and radiosensitive organs. Appropriate dose management and safety is need of an hour in Nuclear Medicine. We divided dose reduction methodologies into following four categories.

1. Human Based- Radiologist and technologist i.e. Justification of procedure, awareness of technical methods)
2. Machine Based i.e. Appropriate settings of Tube Current, Automatic exposure control, Tube potential, Beam collimation, Pitch, Speed, CT dose metrics)
3. Software based 3D Reconstruction Algorithm (Iterative reconstruction)
4. Protocol Based i.e. Appropriate organ based protocols.

Conclusion: Clinical application of CT has been revolutionized in medical imaging and plays an enormous role in routine Nuclear Medicine with hybrid imaging techniques. CT dose management should be prime concern in accordance with radiation protection to patients and health professionals. We should maintain just practices and continuing education for awareness, develop protocols and skills of CT dose management in routine practice. We propose four broad categories for understanding and developing methods of optimizing dose reduction. For this Nuclear Medicine Physicists and Technologist can contribute in a significant way.

PT-08: To Compare the reliability and accuracy of Glomerular Filtration Rate (GFR) calculated by the DTPA technique versus the ethylene dicysteine (EC) technique.

Rahul Kumar Tripathi, Satyawati Deswal, Dhananjay Kumar Singh, Shashwat Verma, Devesh Chandra Bhatt, Sandeep Kumar, Navratna Kumar Singh, Dr. Ram Manohar Lohia
Institute of Medical Sciences, Lucknow

Introduction: Radionuclide evaluation of genitourinary system includes estimates of renal perfusion and function. Tc-99m diethylenetriaminepentaacetic acid (DTPA) is excreted almost exclusively through glomerular filtration and hence used for the evaluation of glomerular filtration rate. About 20% of Tc-99m-DTPA is extracted from the blood with each pass through the kidney. Less than 10% of injected DTPA is bound to plasma proteins, hence Tc-99m DTPA tends to underestimate Glomerular Filtration Rate (GFR). The images acquired at high creatinine level are of poor quality leading to fallacious results in patients with impaired renal function. Tc-99m labelled agent mercaptoacetyl triglycine (MAG3) is protein bound and is cleared predominantly by the proximal tubules (95%) with minimal filtration (less than 5%) and it behaves much as radiiodinated orthoiodohippurate (OIH) does. Tc-99m MAG3 produces much better images than DTPA with an extraction fraction of 40% to 50% (more than twice that of DTPA). Tc-99m ethylene dicysteine (EC)6, a metabolite of ethylene cysteine dimer (ECD), is a new technetium-labelled renal tubular function tracer introduced as an alternative to orthoiodohippurate (OIH) and with imaging qualities similar to 99mTc-mercaptoacetyl triglycine (MAG3). Within 1 h 70% of 99mTc-EC is excreted in the urine. It is used to measure effective renal plasma flow (ERPF). GFR is 20% of ERPF. 99mTc-EC is produced by BRIT and it is available at a much lower cost compared to 99mTc MAG3. It is available in lyophilised kit form which can be easily prepared at room temperature, and the compound remains stable for at least 8 h. Both in normal individuals and in patients, plasma clearance of 99mTc-EC has been reported to be around 0.75 of OIH clearance.



AIM: To compare the reliability and accuracy of Glomerular Filtration Rate (GFR) calculated by the DTPA technique versus the ethylene diethylene (EC) technique.

METHODS: The GFR obtained by the EC technique is compared with the GFR obtained by the DTPA technique, and both is compared with the "gold standard" technique of 24-hour urine Creatinine clearance. Categorical variables shall be compared using Mann-Whitney U-test, chi square test or Fisher's exact test. Continuous variables shall be compared using t-tests or ANOVA. Regression analyses, receiver operating characteristic (ROC) curves, as well as uni- and multi-variate analyses will also be employed, as necessary.

RESULTS: The GFR estimated with 99mTc-EC correlated better with GFR measured by 24-hour urine Creatinine clearance. The GFR measured with 99mTc-DTPA was statistically different from that measured with 24-hour urine Creatinine clearance but in some cases both (EC and DTPA) gave nearly same results. **CONCLUSION:** The GFR estimated with 99mTc-EC is comparable with that measured with 24-hour urine Creatinine clearance, while the GFR values measured with 99mTc-DTPA presents a significant statistical difference from that measured with 24-hour urine Creatinine clearance.

PT-09: When to add SPECT/CT to a Routine Whole Body Bone Scan in Cancer Patients.

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Introduction: In nuclear medicine department bone scintigraphy is performed frequently to identify skeletal metastatic lesion. Maximum patient with skeletal pain shows abnormal uptake in bone scintigraphy. In whole body scintigraphy we acquired an anterior and posterior projection.

Purpose: The objective of present study was to assess the value of additional regional SPECT/CT for corroboration of lesion detected on whole body scintigraphy and to train/educate technologist to determine the need of additional SPECT/CT after routine whole body scan.

Material and Methods: This study group comprised of 134 patients, out of which 47 were male and 87 females (Age range 13-85 yrs). Between February 2016 to April 2016 98 bone scan were performed. Out of 134 scan 51 patients were with normal scan and 83 patients were Benign, Equivocal or Mets.

Result: Out of 134 scan 51 patients were with normal scan and 83 patients were Benign, Equivocal or Mets. The results of this study show that nuclear medicine technologists, after a period of formal training, are able to decide when an additional SPECT/CT examination is necessary after a whole-body bone scan.

Conclusion: With the help of training/educate nuclear medicine technologist are able to determine the need of additional SPECT/CT after routine whole body scan.

PT-10: AUTOMATIC DOSE DISPENSER: INITIAL EXPERIENCE

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INTRODUCTION: Recently many centers around the world have started using Autodispenser system to reduce the radiation exposure of person working in nuclear medicine. Also it is important to maintain the standard for hot lab procedures to optimize the patient care and minimize radiation exposure to all nuclear medicine personnel, patients and public. Autodispenser is used to dispense and dilute the radiopharmaceutical automatically leading to a high dispensing accuracy and with optimum radiation protection.

AIM: The aim of this study was to know the effectiveness in reducing the overall radiation exposure. **MATERIALS & METHODS:** In this study four persons were involved and using the same radiopharmaceutical (99mTc-



MDP) & they injected the same no. of patients (10/person) with the same injected dose (20mCi per patient). The data before using Autodispenser were placed in group 1 while data after using Autodispenser were placed in group 2. The actual injected radioisotope dose of each patient was measured and the dispensing deviation was calculated.

RESULT: Positive result found, it is very much useful in significant dose reduction with high dispensing accuracy in minimum time duration.

CONCLUSION: Efficient for the use in Hot Lab to dispense and dilute the radiopharmaceutical automatically leading

PT-11: Optimization of dose of lithium to be used as an adjunct to radioiodine therapy

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Introduction: Radioiodine therapy is a nuclear medicine treatment for an overactive thyroid; a condition called hyperthyroidism, and also may be used to treat thyroid cancer. When a small dose of radioactive iodine I-131 (an isotope of iodine that emits radiation) is swallowed, it is absorbed into the bloodstream and concentrated by the thyroid gland, where it begins destroying the gland's cells. Another hand Lithium, which has been experimented for its adjunctive role to radioiodine therapy, shows both positive and negative findings in clinical trials to maintain euthyroid state. Therefore, in the aim present study we optimized the dose of lithium in experimental rat per Kg body weight so as to be effectively used as an adjunct to I-131 therapy.

Purpose: To assess the 4 hrs and 24 hrs %age uptake of I-131 in thyroid of rats treated with different dose of lithium.

Methods: Female wister rats weighing 180g were procured from Punjab university, Chandigarh. All procedures done under ethical guidelines. Animals were segregated into four groups. Groups-I were feed standard water ad libitum while group II, III, IV were fed lithium at a dose of 10mg/kg body weight, 20mg/kg body weight, 30mg/kg body weight respectively. Dose lithium was started one week prior to radioiodine therapy and continued another 8 days.

Results: Study observed a highly significant increase in the % age uptake of I-131 at both the time intervals of 4hrs and 24 hrs in the thyroid of lithium treated rats when compared to the % age uptake in normal control animals.

Conclusions: The analysis concludes that the lowest dose of lithium (10mg/Kg body weight) has been shown to be effective in causing the preferred effect of increased retention of I-131 in thyroid but did not result in perfecting the levels of thyroid hormones. Since, the higher doses of lithium (20mg/Kg body weight and 30mg/Kg body weight) did not show significant difference in the uptake and retention of I-131 when compared to low dose group and also resulted in hypothyroid conditions as speculated from the thyroid hormone levels. The study proposes the low dose of lithium viz 10mg/Kg body weight to be an effective and safe dose to be used as an adjunct to I-131 therapy.

PT-12: Comparative evaluation of 24-Hour I-131 thyroid uptake by Gamma Camera using High Energy Collimator with standard Probe based method

Devesh Chandra Bhatt, Satyawati Deswal, Dhananjay Kumar Singh, Shashwat Verma, Rahul Kumar, Navaratna Kumar, Sandeep Kumar, Dr. Ram Manohar Lohia
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Introduction: Thyroid uptake determination is the measurement of the fraction of an administered amount of radioactive iodine that accumulates in the thyroid at selected times following ingestion.

Purpose: To make a quantitative comparison between 24-hr thyroid uptake calculated by thyroid uptake probe and under Gamma camera and after administration of a diagnostic I-131 dose in patients with benign thyroid disorders.

Methods: Informed consent was taken from all the patients. This study group comprised of 30 patients, out of which 9 were male and 21 females (Age range 25-50 yrs). These patients had benign thyroid disorders and were referred for thyroid evaluation to our department. A liquid form of I-131 (50µCi [1.85MBq]) was administered to patients with adequate flushing of vial to ensure maximum oral administration of dose. The dose was prepared with the help of pipetting technique and pre administration counts were taken with activity places inside Lucite neck phantom. A 24-



hour 131I uptake was measured with the help of thyroid probe and also under gamma camera with patient lying supine and detector at a distance of 25 cm from the neck anteriorly. Pre and post 131-I administration counts were taken under gamma camera.

Result and Discussion: In 25 patients out of 30 patients, the radioiodine uptake value measured by gamma camera was around fifty percent of that measured by thyroid uptake probe. Therefore by applying a correction factor we can equate the uptake value of probe method and gamma camera method.

Conclusion: On the basis of precision in counting by thyroid uptake probe it takes the edge over gamma camera method. Therefore gamma camera method can never be an ideal substitute. Hence thyroid uptake probe method cannot be replaced by gamma camera method.

PT-13: NUCLEAR MEDICINE ON WHEELS

Mitali kale, SOAHS, Manipal

INTRODUCTION-

Nuclear medicine is a branch of molecular imaging that uses small amounts of radioactive material to diagnose and cure various diseases via therapy.

PURPOSE-

This imaging modality is available only in a few selected cities of India.

The aim of this poster presentation is to put Nuclear Medicine on wheels:

1. Establishing NM department in remote areas has many limitations.
2. Inconvenience of patients having to travel long distances to get diagnostic imaging from other health facilities will be eliminated.
3. Advantage to bed ridden /severely ill patients .
4. RIA and In-vitro techniques like radioactive iodine uptake tests can be performed.
5. We can not only diagnose the diseases but also provide treatment such as I131 for Thyrotoxicosis.

METHOD-

Many small portable or hand held gamma cameras are commercially available which perform general nuclear medicine routine scans like Thyroid , Renal, Liver scan etc.

The vehicle should belong to a base hospital which can be government or private. It should shock resistant. It should have small dispensing room and washroom with decay tank.

This vehicle can be used to supply radionuclides to the cities in which transport by road is more feasible and time saving. Permission for transport of radiation should be sought.

Permission can be sought from competent authority for visiting hospitals where patients require NM scan.

As per AERB regulations, a technologist, RSO and NM physician should be licensed also the driver should be trained for carrying radioactivity.

Documentations requirement should be taken care of by the RSO and technologist. AERB compliances should be satisfied and wise radiation safety measures.

CONCLUSION/RESULTS -

1. Treatment for the poor and needful i.e I131 therapy for Thyrotoxicosis.
2. Cost effectiveness.
3. More treatments leading healthier environment.
4. Boost to Nuclear Medicine in Indian Scenario.

PT-14: Quantification Radiochemical purity (RCP) of a radio-pharmaceutical by Gamma camera system."

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Background/Introduction:

Radiochemical purity (RCP): of a radio-pharmaceutical is defined as "the percentage of the total radioactivity present in the desired chemical form in a radioactive pharmaceutical". Without acceptable RCP in a diagnostic radio-pharmaceutical, image interpretation can be compromised which can result in a delay of an accurate diagnosis and unnecessary radiation exposure since the nuclear medicine study must be repeated. With a therapeutic radio-pharmaceutical, an unacceptable RCP can lead to the radiopharmaceutical localizing in an unintended target, which may result in organ damage.

Chromatography: is a procedure for separating the components of a mixture or solution, thus allowing the quantification of the desired compound and the impurities. The components of the mixture traveling the farthest are those that are most soluble in the solvent and least attracted to the stationary medium. In traditional nuclear pharmacy, the most frequently encountered procedures involve solid phase extraction or instant thin-layer and paper chromatography.

Purpose: Analysis of Radiochemical purity Quantification of Radiopharmaceutical by using Gamma Camera in absence other recommended counting system.

Methods: Radiochemical purity (RCP) quantification of 99mTc-DTPA, 99mTc-MDP and 99mTc-ECD (as per procedure mentioned in BRIT QC manual) done by the Gamma Camera (Hawkeye 4 hybrid) and Well counter (Capintec-CRC 25W) and the Values were analysed.

Results: The quantification is as follows:

- 1) RCP 99mTc- DTPA: 97% using Gamma Camera & 98.5% using well counter.
- 2) RCP 99mTc- MDP: 97 % using Gamma Camera & 99.8% using well counter
- 3) RCP 99mTc-ECD- 97.20% using Gamma camera & 99.30% using well counter
- 4) RCP 99mTc-MDP: 29.4% using Gamma camera & 32% using well counter (after 8-9 hrs. of preparation just to see the result)

Conclusion(s): We conclude that in the absence of recommended counting system the Radiochemical Purity quantification can be done by using the Gamma Camera and results were found satisfactory.

PT-15: Significance of reviewing a Sinogram data in Multiheaded Cardiac Spect Analysis.

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Introduction : The daily quality control test of gamma camera includes evaluation of pulse height spectrum and uniformity tests. When these two are performed the physicist is generally assured of the quality of the results obtained. Similarly, when a SPECT study is performed the sinogram is usually used as a quality control parameter to check and correct for patient motion. We share our recent observations of altered sensitivity of detector responses brought out upon careful evaluation of sinogram during routine analysis of cardiac SPECT study.

Methods : The daily quality control of a SPECT gamma camera is performed by a photopeak check and uniformity evaluation of each detector head, with flood filled phantom containing 141 Ce. Patients were injected ~10mCi of 99mTc-MIBI and asked to take fatty meal after 30 minutes. A gated cardiac study was acquired 60 mins later, on a SIEMENS Symbia camera, in 64 X 64 matrix, for 34 projections from RAO to LPO for 40 secs/view. The sinogram generated during processing was evaluated for correction of motion and quality of data. The photopeak and uniformity test for both detectors was repeated. The photomultiplier tubes were tuned using PMT TUNING protocol by placing a 30uCi 99mTc point source at the center of the detector after removing the collimator. The photopeak and uniformity correction were reanalysed and the patient's cardiac study re-acquired as described above.

Results : The baseline daily quality control tests of gamma camera were found to be within normal limits. The sinogram data revealed a difference in intensity of the projections acquired for Head-1 and Head-2. A repeat PHA thereafter with standard 141Ce source revealed shift in photopeaks outside the given acceptable range limits and difference in the sensitivities of the GC. After the tuning procedure the photopeaks reverted to normal window range centered at 140 keV. The quality of sinogram improved post PMT tuning.

Conclusion: Photopeak in the photomultiplier tubes can drift due to various reasons like temperature changes, voltage instability, humidity, angular motion, magnetic disturbances etc. leading to abnormal scan findings. Alertness while evaluating sinogram as shown above can reduce the aberrations in scan findings.



PT-16: What is a difference when you have pet-ct in your facility.

S V RAMANA MURTHY

Several studies have shown an increase in radiation exposure among professionals in Nuclear Medicine since introduction of PET-CT scanner.-

Purpose: operating systems to minimize radiation professionals exposure .

METHODS: what are the factors influence the site evaluation for pet-ct shielding.

- 1) How to calculate shielding thickness of different materials for scan room.
- 2) How to calculate shielding thickness of different materials for UPTAKE ROOM.

CONCLUSION: Technologists receives dose can be minimized by proper operating system and well layout site plan.

PT-17: Radiation Safety consideration in Nuclear Medicine

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Introduction: Radiation exposure of worker, patient and general public cannot be avoided in nuclear medicine practice, where open sources of radiation are handled and radioisotope is administered in the form of radiopharmaceutical resulting in the patient them self becoming a source of radiation.

Aim and objectives: To make a balance between health care ethics and radiation safety of radiation worker, general public and environment to achieve ALARA.

Methods: In nuclear medicine the choice of radiopharmaceutical is very important to determine important parameters for protection, monitoring procedure, reducing absorbed dose to patient. Personal monitoring :TLD is used for personal monitoring, all staff, students should wear two sets of personalized TLDs, as per the AERB guidelines (20 mSv/year) .

Lay out and shielding : Layout of department should be designed as approved by the competent authority, radioactive sources should be properly shielded and all equipment should be calibrated by certified agencies. All facilities should be separate comprising of independent radio pharmacy and post-injection waiting areas.

Radiation handling: Precautions are taken during handling of radioisotope and injected patients to avoid any mishaps, which could lead to unnecessary radiation exposure.

Radiation survey, radioactive waste management and disposal: Radiation survey is an integral part of radiation safety to maintain the quality of work. Lead lined dust bins are used to discard radioactive wastes to maintain proper segregation and allowed to decay in the radioactive waste storage room for 10 half-lives or below the prescribed limit.

Result: There is no lower limit for radiation exposure that can be considered safe for humans. It may bring deterministic or stochastic effects. It is considered prudent for public safety to assume that every exposure to ionizing radiation, carries small risk.

Conclusion: The benefits of nuclear medicine procedures are immense and certainly exceed the risks and studies are optimized to obtain the best image quality with the lowest radiation dose. In the coming years, numerous efforts will have to be made in these areas to justify and optimise medical procedures using radiation.

PT-18: Radiation Hormesis: Evidences and Current Status

JAHANGIR HUSSAIN SHEIKH, SOAHS, MANIPAL

INTRODUCTION: Radiation hormesis is the hypothesis that low doses of ionizing radiation are beneficial, stimulating the activation of repair mechanisms that protect against disease, that are not activated in absence of ionizing radiation.

PURPOSE: The major scientists working on radiation during the 1800s and early 1900s had already shown that low level radioactivity was beneficial for living things. Plants and animals grew bigger, reproduced better, had fewer cancers and infectious diseases and had a longer lifespan.



RESULT: Several recent studies suggest that radiation exposure, under some circumstances, can be beneficial. Epidemiological and experimental evidence support the radiation hormesis paradigm.

CONCLUSION: Living organisms, which have established efficient defense mechanisms against radiation through 3.8 billion years of evolutionary history, can tolerate radiation at low dose rates. In fact, people have lived for generations without adverse health effects in high background.

PT-19: Operational and Radiation Safety Aspects in a Newly Installed 18MeV Medical Cyclotron

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Introduction: We have 18 MeV (HM-18 Sumitomo Heavy Ind. Ltd) vault-shielded medical cyclotron in the basement of our PET facility. HM-18 Cyclotron is a fixed-energy isochronous cyclotron which accelerates negatively charged hydrogen ions as proton (H-) to 18 MeV and deuteron (D-) to 10MeV. The cyclotron has two ports with eight target, each side has four target to produce various radio isotopes such as 18F, 11C, 13N, 15O, 18F2 gas, 64Cu, 123I, and 124I. The radiation exposures were measured in the facility at various designated locations before, during and after irradiation of cyclotron to assess the radiation safety status in the facility.

Purpose: To present the radiation safety status before, during and after irradiation of cyclotron for the production of 18F-FDG.

Methods: Presently we produce 18F- for the synthesis of 18F-FDG by following a set of protocol, current 40 μ A for 40 min to bombard the target. The 18F- ions are produced by the 18O (p, n)18F nuclear reaction in a niobium target assembly filled with 2.5 ml of enriched 18O water. During production the various operational parameters, (beam current, target pressure, He pressure, chiller temp etc.) which influence the yield of 18F- production were also monitored and maintain a record of any unusual events that may be occurred during the operation. The radiation exposure levels at various designated locations within the facility were monitored and recorded by using installed real-time on-line fully automated monitoring system (ROTEMS Medismart) as well as by portable radiation survey meter and neutron monitor.

Result: The radiation survey was successfully performed around the newly installed cyclotron and radiochemistry laboratory area before, during and after irradiation. The radiation exposure before, during and after irradiation was as follows 0.1 to 0.7 μ Sv/h, 0.3 to 1.8 μ Sv/h, and 0.1 to 0.8 μ Sv/h.

Conclusion: The radiation survey was successfully performed around the newly installed cyclotron and radiochemistry lab. All the values are below recommended levels of exposure.

PT- 20: Oasis Multi-Modality Applications [MI Register/SISCOM]

Shashi Duraiswami, Segami USA

Different imaging modalities such as CT, MRI, PET and SPECT are based on different physical principles and capture different but often complementary information. Any clinical practice would benefit from an integrated visualization and combined analysis of multimodality images. The abstract aims to demonstrate use of Mutual Information based Registration algorithm and a SPECT-MRI multimodality application in patients with epilepsy.

Background:

MRI is the investigation modality of choice in patient with epilepsy as T1, T2 and flair images are crucial in increasing the conspicuity of otherwise undetectable lesions. SPECT, a nuclear medicine imaging technique based on the knowledge of seizures causing increased ictal region cerebral perfusion and decreased interictal perfusion. A side-by-side visual analysis of ictal and interictal SPECT images has limitations (doesn't account for differences in injected dose, tracer decay) and is subjective (user-dependent).

Purpose:

The aims of this paper is to demonstrate use of multi-modality applications to find precise seizure focus in the brain of epileptic patients with the help of SPECT and MRI images acquired on separate equipment. Materials and methods

Oasis-MIRegister to automatically register medical data volumes from the same or different modalities, based on a normalized mutual information algorithm.



Oasis-SISCOM (SPECT-MR) application to provide a snapshot of the cerebral blood flow patterns during seizure and show areas of hypoperfusion in the region of seizure focus in between seizures (rest).

Results

The MIRRegister user interface allows for the control of parameters, such as thresholds for cortical activity, FOV necessary to accomplish the registration. SISCOM application creates a fused representations of regions of focal activation with the structural information of the MRI.

Conclusion/Discussion

MIRRegister algorithm is pixel intensity based (no need for anatomical landmarks) and therefore can be used for any combination of modalities (SPECT, PET, CT, MRI) and is applicable to all body parts (e.g., Lung, Abdomen, Head/Neck). Expensive hybrid scanners, with long acquisition times are in the nascent stage. A more effective and low-cost multi-modality software solution might be the practical solution proving boon to both patients and clinicians. Oasis PET-CT for lung tumor detection, PET-CT-MR for localizing brain lesions, PET-MR fusions for prostate cancer are just a few other applications in Oasis.

PT - 21: Study of genotoxicity factors associated with F-18 mediated diagnosis, an *in-vitro* approach

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There is rising interest in studying of radiopharmaceuticals drug in humans for potential diagnosis and therapy of cancer and other disease. F-18 is a radioisotope used in the medical imaging modality positron emission tomography (PET). In the routine practice, it is synthesized into 2-deoxy-2-(18F) fluoro-D-glucose, a glucose analog, with the positron-emitting radionuclide fluorine-18 substituted for the normal hydroxyl group at the C-2 position in the glucose molecule. The present study was undertaken to evaluate the genotoxicity effects of F-18 in isolated peripheral blood lymphocytes of human at different dose and incubation time period. DNA damage study was evaluated by comet assay and karyotyping method. The comet study shows a percentage of tail length of about 11.85 ± 3.24 and by the karyotype analysis, four type of chromosomal aberration was identified in the control and experimental groups. Dicentric chromosomes are more abundantly found from the other type of abnormalities.

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