**NUCLEAR MEDICINE**

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1. **Background**

Nuclear medicine is the branch of medicine that deals with the tracer principle of radiopharmaceuticals to assess physiologic, pathologic, metabolic conditions of the body at the molecular level for the diagnostic purposes including therapy and research. It involves the use of radioisotopes labelled with suitable pharmaceuticals to form "radiopharmaceuticals".

Nuclear medicine technique is a medical specialty that relies on imaging technique using radioactive tracers to evaluate cellular function. It may lead to the diagnosis and treatment of disease depending on the patient's condition. Radiopharmaceuticals (Radioisotopes) are applied in this technique due to their penetrating power and ionizing characteristics as a result of emission from decaying atoms [1].

Nuclear medicine imaging involves the uses of radioactive material in small amounts. The technique utilizes a computer and a special camera to create inside images of the body. It helps to provide unique information as compared to other imaging procedures that can lead to diagnose many types of pathological conditions related to heart disease, neurological, endocrine and gastrointestinal disorders, cancers and other health conditions. The technique may lead to detect disease in its earliest stages as nuclear medicine procedures are able to pinpoint molecular activity within the body [2].

The path of these radioactive tracers could be easily tracked by doctors using specially designed cameras. The two most common imaging modalities in nuclear medicine are- Single Photon Emission Computed Tomography (SPECT) and Positron Emission Tomography (PET) scans.

As compare to conventional radiology the diagnostic nuclear medicine is fundamentally a functional imaging process that manifests physiological processes whereas conventional radiology essentially aims at obtaining anatomical images form and structure. The main advantage of function assessment of an organ is that it helps physicians to make a diagnosis and set up treatment plans for the part of the body being evaluated [3].

1. **Radioactive Tracers**

Due to its intricate and essential dependence, the field of nuclear medicine is unique in its own way regarding the use of radiopharmaceuticals for every procedure. Radiopharmaceuticals consist of a radioisotope, produced in a research reactor or particle accelerator like medical cyclotron. The radiation so delivered can be used for targeted therapy and detection-based imaging to render bio-specificity for the organ, lesion or dysfunction being addressed.

Radioactive tracers consist of carrier molecules that are tightly bonded to a radioactive atom. These carrier molecules vary substantially depending on the the scan goals. Some tracers utilizes molecules that may interact with sugar or a specific protein in the body including the patient’s own cells. For example, to know the exact source of intestinal bleeding, sample of red blood cells can be taken from the patient. The sample then be radiolabelled, re-injected in the blood to scan and follow the path of the blood in the patient [4]. Any accumulation of radioactivity in the intestines manifests the region where the problem lies.

1. **Routes of Administration**

In most cases of the diagnostic studies in nuclear medicine, the radioactive tracer is administered to a patient by intravenous injection. A radioactive tracer may also be given to the patient by means of oral ingestion, inhalation or by direct injection into an organ. The administration mode of a tracer depends on the studied disease process.

These tracers are neither dyes nor medicines and have no side effects. In case of a typical nuclear medicine scan, the amount of radiation given to the patient tends to be very low.

After radioactive tracer administration to the patient, one can produce images by detecting radiation from different parts of the body. Nuclear medicine physician then interprets the digitally generated images to make a diagnosis.

  

 **Fig. 1- SPECT and PET scanned images**

1. **Types of Radioactive Tracers**

Radioactive elements have highly energetic unstable nuclides because of excess of energy. These can be stabilize by either the emission of particles, electromagnetic radiation or charged particles during the radioactive decay. There are three types of radiations in this context: alpha, beta minus and gamma. Radiation contains energy with electric and magnetic charges that propagates at a certain speed. It can be generated by natural sources or by artificial devices like cyclotron. Energy emitted by an unstable nucleus result in the generation of ionizing radiation in artificial form or by a cyclotron.

The first radiopharmaceutical was commercialized in 1950.  The first commercially available isotope was 131 Iodine for medical uses.

The main metal complexes used as radiopharmaceuticals are technetium (99mTc), gallium (67Ga, 68Ga), indium (111In), thallium (201Tl), iodine (123I and 131I), sulphur (35S), phosphorus (32P), chromium (51Cr), fluorine as sodium fluorine (Na18F) and fluorodeoxyglucose ( 18F-FDG) which are widely used for diagnosis in nuclear medicine imaging. They have been of significant importance for the early diagnosis in various diseases like cancer [5].

Radiopharmaceuticals are called as approved tracers if they meet the exacting standards of Food and Drug Administration (FDA). It is necessary for the safety and appropriate performance of tracers in clinical use. The tracer will be selected by nuclear medicinephysician for providing the most specific and reliable information about patient's health condition. Whether the patient receives a SPECT or PET scan depends on the use of an appropriate tracer.

### ****Diagnostic Use****

Nuclear medicine is a non-invasive and a painless test that help to diagnose and assess medical conditions. Once a radiotracer is injected in the body, it starts build up in certain areas of the body that needs to be examined, such as a cancerous tumor or inflamed area. They may also bind to some proteins in the body.

The most common radiotracer used is 18F-FDG. Fluorodeoxyglucose is a compound similar to sugar or glucose. Cancer cells needed more energy than normal cells. As a result of which cancerous cells absorb more glucose. Thus, an imaging device creates pictures and shows the location of the radiotracer in the body by detecting the energy given off by FDG [6].

The diseases or pathological conditions primarily diagnosed by nuclear medicine imaging include:

* Cancer
* Heart disease
* Blood disorders
* Bone problems, including infections or breaks
* Thyroid disease, including hypothyroidism
* Gallbladder disease
* Lung problems
* Kidney disease including scars, infections and blockages
1. **Techniques in Nuclear Medicine**

Single photon emission computed tomography (SPECT) and positron emission tomography (PET) are nuclear medicine imaging techniques which provide metabolic and functional information unlike Computed Tomography (CT) and Magnetic resonance imaging (MRI).

**CT:** Computed Tomography (CT) is a computerized X-ray imaging procedure that produces signals which are processed to generate cross-sectional images or “slices” of the body by the machine’s computer. These slices are called tomographic images that contain more detailed information about the internal organs as compare to conventional X-rays.

**MRI:** Magnetic resonance imaging (MRI) is a non-invasive imaging technology used to investigate anatomy and function of the body in both healthy and pathological conditions without the use of damaging ionizing radiation. It is mostly used for detection, diagnosis, and treatment monitoring of a disease. It is based on sophisticated technology that involves excitation followed by the detection of changes in the protons presents in the water that makes up living tissues. Nerves, spinal cord, brain, ligaments, tendons and muscles can be seen with clarity in MRI than with regular X-rays and CT. MRI is often used to create images related to knee and shoulder injuries.

**SPECT:** A single photon emission computed tomography (SPECT) scan is an imaging test that shows how blood flows to tissues and organs using gamma emitting radioisotopes. Gamma rays are a form of light that are different from visible light and moves at a different wavelength. It may be used to diagnose stroke, stress fractures, seizures, infections and tumors in the spine. SPECT imaging instruments generate 3-D tomographic images of the radioactive tracer molecules which get distributed in the patient’s body. A large number of projection images of the body recorded at different angles result in the 3D images that are generated from a computer. SPECT imagers can detect the gamma rayemissions, from the tracers that have been injected into the patient, due to the presence of gamma camera detectors.

**PET:** A positron emission tomography (PET) scan also uses a radioactive tracer in an imaging test that can help to reveal the atypical and typical metabolic activity or biochemical function of tissues and organs. PET scans also create three-dimensional images. PET scans produce small particles called positrons. A positron is a particle with same mass as an electron but oppositely charged. They react with the electrons in the body and when these two particles combine they result in annihilation process that produces a small amount of energy in the form of two photons that shoots off in opposite directions. The PET scanner detectors measure these photons and create images of internal organs. PET's most important clinical role is in oncology, with 18F as the tracer, since it has proven to be the most accurate non-invasive method of detecting and evaluating most cancers. It is also well used in cardiac and brain imaging [7-9].

The prominent difference between SPECT and PET scan depends on the type of radiotracers used. While SPECT scans measure gamma rays, PET scans produce small particles called positrons as a result of the decay of the radiotracers used.

**Table 1- Difference between SPECT and PET techniques**

|  |  |  |
| --- | --- | --- |
| **S.No.** | **SPECT** | **PET** |
| 1. | It is cost effective as compare to PET. |  It is very expensive as compare to SPECT. |
| 2. | It uses gamma emitting radioisotope (tracer). |  It uses positron emitting radioisotope (tracer). |
| 3. |  It gives poorer contrast and spatial resolution as compare to PET. | * It gives better contrast and spatial resolution

as compare to SPECT. |
| 4. | It has usually one large crystal based detector. | It has a ring of multiple detectors. |
| 5. | Examples- * + Technetium (99mTc); iodine (123I and 131I)
 | * + Examples-
	+ [F F- 18 fluorodeoxyglucose (18F-FDG )](https://radiopaedia.org/articles/f-18-fluorodeoxyglucose?lang=us);

F -18 Sodium Fluoride (18F-NaF)  |

Now-a-days, new procedures combine PET with computed X-ray tomography (CT) scans to give co-registration of the two images (**PET-CT**), enabling 30% better diagnosis than with a traditional gamma camera alone. It is a very important tool that provides unique information on various diseases from dementia to cardiovascular disease and cancer.

Combining PET with MRI (**PET-MRI**), enables diffusion-weighted imaging in soft tissue with dynamic contrast and magnetic resonance spectroscopy especially in case of brain imaging.



**Fig. 2*-* Fused CT-PET scans more clearly show tumors and are therefore often used to diagnose and monitor the growth of cancerous tumors.**

The fundamental difference between nuclear medicine imaging and other imaging techniques such as X-rays is the positioning of the radiation source within the body. A view of the position and concentration of the radioisotope within the body can be determined by gamma imaging. Malfunctioning of organs can be indicated if the isotope is either partially taken up in the organ (cold spot) or taken up in excess (hot spot). An unusual pattern or rate of isotope movement could indicate malfunction in the organ if a series of images is taken over a period of time [10-11].

A distinct advantage of nuclear imaging over X-ray techniques is that both soft tissues and bone can be imaged very successfully resulting in its common use in developed countries.

**Clinical Application and Significance**

SPECT scans are primarily used to detect disorders in gall bladder, bone diseases and intestinal bleeding and to diagnose as well as track the progression of various conditions of heart disease, such as blocked coronary arteries. SPECT agents have recently become accessible for aiding in the diagnosis of Parkinson's disease in the brain and thus differentiating this malady from dementias and other anatomically-related movement disorders.

The PET scans are more often used to detect cancer and monitor its progression, response to treatment and to detect metastases condition. Rapidly dividing cancer cells are marked with increased glucose utilization due to intense cellular and tissue activity. As a result, the aggressiveness of most cancer cells is roughly paralleled by their rate of glucose utilization. In last fifteen years, slightly modified radiolabeled glucose molecules (F-18 FDG) have been shown to be the best available tracer for detecting cancer and its metastatic spread in the body.

A combination instrument that produces both PET and CT scans in one examination (PET/CT scanner) has become the primary imaging tool for the staging of most cancers of same body regions [13-14].

To aid in the accurate diagnosis of Alzheimer's disease, a PET probe was approved by the FDA recently, which previously could be accurately diagnosed after a patient's death only. Alzheimer's disease can be difficult to distinguish from vascular dementia or other forms of dementia that affect older people, in the absence of this PET imaging test.

**8. Advantages of Nuclear Medicine**

**1.** Nuclear imaging technique provides functional and anatomical detailed information that is unattainable by means of other procedures.  Extreme sensitivity to abnormalities in an organ's structure or function is one of the unique aspects of a nuclear medicine test.

2. It provides the most useful diagnostic tool or treatment information for various diseases. The nuclear medicine tests have the ability to detect diseases at earliest stages and sometimes even before revealing symptoms.

3. Nuclear medicine technique has digitally and technically enhanced the treatment options for different medical conditions specially in the case of cancer. Cancer treatment involves radiotherapy and chemotherapy. PET scans can ascertain that whether the tumors are malignant or benign. It can prevent a patient from getting a more dangerous or costly surgery.  In severe cases, when patients have lost hope of survival, nuclear medicine has been a blessing to them.

4. Nuclear medicine is an apt technique for detection of highly serious medical conditions. The clarity in the technique is what makes people believe in its power. It has proved to be very beneficial for many physicians and medical professionals to detect difficult possibilities in early stage of treatments.

5. Its accuracy has made many complicated medical procedures simpler as it allows in depth examination and analysis. This is the prime advantage of nuclear medicine technique. Traditionally for detailed diagnosis, patients had to undergo difficult surgeries and procedures. Advancement in nuclear medicine technology with precise procedures has led to investigate a disease in a systemic manner. Nuclear medicine has made it much easier and has become an integral part of modern healthcare medical system.

**9. Limitations of Nuclear Medicine**

**1.** There are many challenges in design and development of more specific, efficacious radiopharmaceuticals to offer effective patient management options in oncology, neurology, cardiology, and other disorders.

**2.** Nuclear medicine technique faces dosimetry issues in transforming the same vector-based radiopharmaceutical product for imaging applications and therapeutic use. The main concern of this technique is the clearance of radiopharmaceuticals from the blood to the excretory organs and to avoid non-target sites accumulation of the radiopharmaceutical product.

**3.** Nuclear medicine technique is expensive as much as it is effective. It requires heavy expenditure in terms of the purchase cost, equipment cost, setting up cost, operations and maintenance. It is one of the biggest limitations of nuclear medicine.

**4.** Unfortunately it results in some serious health issues due to prolonged exposure to nuclear medicine. As these procedures and equipment give away harmful radiations, so it can be fatal especially to pregnant women and elderly patients. There is a threat of severe allergic reactions and also some incurable ill effects with nuclear medicine.

**5.** Nuclear medicine does not give 100% guarantee of cure in spite of the documented benefits and accuracy. There is still room for doubt. Medical science is full of predictions, possibilities and failures too.

**10. Conclusion**

The nuclear medicine has undergone both evolutionary and revolutionary changes over decades. The dynamic and responsive trends in the global development and deployment of radiopharmaceuticals is quite remarkable. The advent of skilled technology imaging systems like single-photon emission computed tomography/computed tomography, PET/CT, PET/magnetic resonance enhances the quantification capability through detecting procedures. Nuclear medicine scans and treatments help to diagnose and determine the severity of a variety of conditions and diseases like heart related diseases, cancers, gastrointestinal, endocrine, and neurological disorders. Nuclear medicine gives more reliable information to physicians and patients to help them understand about the status of disease. The impact of this technology is so positive that in some people it can detect problems even before they start to experience symptoms. Although it may not provide many solutions to treat the problem but the imaging options that are available make it faster to reach a diagnosis compared to conventional methods.

**References**

* + 1. Sureshkumar A, Hansen B, Ersahin D. Role of Nuclear Medicine in Imaging. Semin Ultrasound CT MR. 2020; 41(1):10-19.
		2. Taylor AT. Radionuclides in nephrourology, Part 2: Pitfalls and diagnostic applications. J Nucl Med. 2014; 55(5):786-98.
		3. Hammoud DA. Molecular Imaging of Inflammation: Current Status. J Nucl Med. 2016; 57(8):1161-1165.
		4. Odunsi ST, Camilleri M. Selected interventions in nuclear medicine: gastrointestinal motor functions. Semin Nucl Med. 2009; 39(3):186-94.
		5. Donohoe KJ, Maurer AH, Ziessman HA, Urbain JL, Royal HD, Martin-Comin J., Society for Nuclear Medicine. American Neurogastroenterology and Motility Society. Procedure guideline for adult solid-meal gastric-emptying study 3.0. J Nucl Med Technol. 2009; 37(3):196-200.
		6. Dunphy MP, Freiman A, Larson SM, Strauss HW. Association of vascular 18F-FDG uptake with vascular calcification. J Nucl Med. 2005; 46(8):1278-84.
		7. Mathew P, Kaur J, Rawla P. StatPearls. StatPearls Publishing; Treasure Island (FL): 19, 2023. Hyperthyroidism.
		8. Adams C, Banks KP. StatPearls. StatPearls Publishing; Treasure Island (FL): 8, 2022. Bone Scan.
		9. Slomka P, Xu Y, Berman D, Germano G. Quantitative analysis of perfusion studies: strengths and pitfalls. J Nucl Cardiol. 2012; 19(2):338-46.
		10. Kaller MO, An J. StatPearls. StatPearls Publishing; Treasure Island (FL): 26, 2022. Contrast Agent Toxicity.
		11. Mumtaz M, Lin LS, Hui KC, Mohd Khir AS. Radioiodine I-131 for the therapy of Graves' disease. Malays J Med Sci. 2009; 16(1): 25-33.
		12. Johnson EK, Malhotra NR, Shannon R, Jacobson DL, Green J, Rigsby CK, Holl JL, Cheng EY. Urinary tract infection after voiding cystourethrogram. J Pediatr Urol. 2017; 13(4): 384.e1-384.e7.
		13. Pandit M, Vinjamuri S. Communication of radiation risk in nuclear medicine: Are we saying the right thing? Indian J Nucl Med. 2014; 29(3): 131- 134.
		14. Gopal S, Murphy C. StatPearls. StatPearls Publishing; Treasure Island (FL): 28, 2022. Nuclear Medicine Stress Test.