Nuclear medicine

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Abstract
Nuclear medicine is one of the most important tools used in medicine right now; as it helps to not generate images of soft tissue organs within the body buy also their biochemical changes and metabolic processes. They filled the gap that radiographic imaging techniques such as x-ray are unable to fill as they pass straight through soft tissues. This article is an introduction to nuclear medicine, its techniques, uses and advancements.

Keywords: Nuclear Medicine, Techniques, Advantages, Disadvantages, Safety Precautions, Applications, Oral and maxillofacial diagnosis, Recent advancements.

Introduction
Nuclear Medicine is a specialization within radiology wherein a small amount of radioactive materials are used to examine the state our body and its organs; and to treat certain diseases. Nuclear medicine imaging can be considered as 'endoradiology' as it involves recording radiation that is emitting from within the body instead of radiation that generates from outside sources, like x-ray, but affect body. Nuclear medicine also differs from radiology as its main emphasis is not scanning anatomy, but the function and such of organs; so it is also called as physiological imaging modality;[1] i.e. it is a scanning modality for finding and measuring any changes in body metabolism, blood flow, regional chemical composition and absorption. It requires usage of tracers or probes, known as radioactive isotopes or radionucleides that emit low level radiation, to reflect their spatial distribution within the body, which in turn reveals physiological activities of tissues or organs. These tracers are analogous to compounds that are common within our body, for ex glucose.[2] not only this, nuclear medicine also plays a part in radiopharmaceuticals (RPh). RPh comprises of a radioisotope produced in medical cyclotron or research reactor, to deliver radiation to targeted areas, along with a carrier molecule for bio-specificity of the organ or lesion or dysfunction.[3]

What are Radiographic tracers and gamma camera?
Radiographic tracers comprise of two components- carrier molecule and radioactive isotopes. The carrier molecule used depends on the organ/tissue being assessed or treated. Tracers use molecules to bind with pre-existing cells or chemical compounds within the body. For most diagnostic studies, radiographic tracers are introduced in the body via an intravenous injection. However, other modes of entry such as inhalation, oral ingestion or direct injection in the organ can also be used. The approved tracers are called radiopharmaceuticals. They must meet FDA's approval for safety standards before being put to use in clinics.[4] gamma cameras are responsible for imaging the radiation emitted by a radiotracer from within the patient's body. They carry out functional scans of brain, thyroid, liver, gall bladder, lungs, kidney and skeleton.[5]

Techniques
2D: Scintigraphy: is a diagnostic nuclear medicine imaging test, in which radioisotope attached to specific drugs travel to the targeted organ to emit gamma radiation which is then captured by external detectors (gamma camera) to form a two dimensional image. Gamma cameras are gamma ray detectors that are coated with materials that scintillate i.e. shine, on being subjected to gamma rays when observed by

optical photon detectors and scintillation counters.[6] For example, HIDA scan, also called cholescintigraphy or hepatobiliary scintigraphy, is an imaging test used to view the liver, gallbladder, bile ducts, and small intestine.[7]

3D: SPECT and PET are the most commonly used nuclear medicine imaging techniques.

1. **SPECT**: Single photon emission computed tomography is used for molecular diagnostics and personalized medicine. It provides a 3 dimensional rendering of our internal organs their working. A conventional gamma camera is used for image detection. It is non-invasive in nature and hence, helps in investigating disease parameters like its onset and the progression, assessing the biological effects of drugs to assess treatment modalities and assists in developing disease biomarkers and monitoring the therapeutic effectiveness of new treatment and/or pharmaceuticals.[8]
2. **PET** i.e. Positron Emission Tomography is more frequently used than any other nuclear imaging technique as it offers a great combination of sensitivity and accuracy. It is a non-invasive 3 dimensional imaging technique that relays information about organs and their functions via application of radiotracers, their movement, distribution and reconstruction. PET scans have become standard for diagnosis and staging in oncology, cardiovascular and neurological disorders due to accurate and easy to understand information like detection, classification, prognosis, staging, treatment planning, and response to therapy, etc.; about tissue and organ function.[9] PET scan uses a special dye that contains radioactive tracers, that are either swallowed, inhaled, or injected into a vein in your arm depending on area of the body is being examined.[10]
3. **Gallium scanning**, also known as liver gallium scan or bony gallium scan is a type of NM in which a gallium radiopharmaceutical isotope is used to obtain images of a healthy or diseased tissue. Radioisotope used can be gallium salts like gallium nitrate and gallium citrate. They are taken up by tumors, inflammation, and both chronic and acute infection. It is also used to identify, Osteomyelitis, particularly of spine, and chronic infections.[11,12]
4. **Indium White Blood Scanning** is done by tagging white blood cells using a special radioactive tracer, which on entering our body, seeks out sources of inflammation and makes them visible to us.[13]
5. **MIBG** scans use iodine-123meta-iodobenzylguanidine, i.e. MIBG tracers, for detection of neuroendocrine tumors, like neuroblastoma and phaeochromocytoma, and carcinoids and medullary carcinoma.[14]
6. **Octreotide scans**, or somatostatin receptor scintigraphy, is a non-invasive test for detection and evaluation of neuroendocrine tumor cells within our body. As neuroendocrine tumors emerge from neuroendocrine cells, they are found throughout the body, like in areas such as brain, thyroid, lungs and GI tract. Somatostatin is a receptor found on these cells, that is targeted during ocreotide scans.[15]

Hybrid scanning techniques refers to the combination of two pre-existing imaging techniques. It is also known as fusion imaging. Combinations are often formed between two different anatomic imaging techniques such as combining ultrasound with CT/MRI or even an anatomic and a molecular imaging technique such as combination of CT/MRI with PET/SPECT scans. For example, real-time virtual sonography, is a combination of Ultrasound B mode image and CT/MRI images in real time.[16]

Advantages and disadvantages of nuclear medicine[17]

Advantages

1. Nuclear medicine provides functional and anatomic information about the soft tissue organs of our body. It is also a useful tool for diagnosis and treatment planning. NM scans can make it possible to determine whether a tumor is benign or malignant. It can also help determine between different treatment modalities such as surgery or other options.

2. Nuclear medicine helps with the staging of cancer, and evaluating the possibility of remission. This eliminates the necessity of exploratory surgery, saving the patient from a painful procedure.
3. It can analyze the function of different organs like spleen, lungs, kidney, gallbladder, etc. to detect any abnormality in blood flow or air passage, or to identify any obstruction or internal hemorrhage.
4. NM scans can provide conclusive aswers for sources of bone pain, to detect bone cancer or osteoporosis, esp. in older patients; when used in conjunction with radiographic imaging techniques.
5. NM is very effective for diagnosis of coronary artery disease, due to accumulation of plaque and cholesterol on the artery walls that blocks supply of blood, nutrients and oxygen to the heart.
6. The amount of radiation received by the patient is same as that of an x-ray, so it is not harmful for internal organs.
7. NM scans provide a more accurate diagnosis, which lessens the need for invasive diagnostic surgical procedures and increases the odds of success for remote or robotic surgeries.
8. It is a painless, safe and cost-effective way of gathering information about internal organs. It is very sensitive to abnormalities in internal organs.
9. It can also be used for radiotherapy procedures for treatment of malignancies.
10. Amount of Radioisotopes given to a patient is carefully calculated on the basis of a patient’s age, weight, metabolism and immune system function; and hence can pass through patient’s body inconsequentially.

Disadvantages

1. Pregnant women and breastfeeding mothers are contraindicated for nuclear medicine procedures.
2. People undergoing NM procedures may experience side-effects such as headaches, dizziness, arrhythmia and temporary hypotension.
3. In some rare cases when a patient is allergic to radiotracers, they may undergo anaphylaxis.
4. Equipment for NM procedures is extremely sensitive, difficult to maintain and expensive, so it is not available in most places, which makes the procedures expensive.
5. While NM provides a very accurate diagnosis, it might not always be 100% accurate, depending on metabolic differences in each person and human error; there may be some cases of misdiagnosis.
6. NM scans require patients to achieve specific body state for it to be accurate and patients might have to make special preparations.
7. Some scanning techniques take a long time to perform and hence, prove to be very time consuming for the patient as well as the doctor.
8. Computers that read information given by gamma cameras require the patient to be absolutely still, which might be difficult to achieve for long time periods.

Safety precautions[18]

Nuclear medicine imaging technique depend on providing limited and controlled dosages of radiation to our body, which are not be harmful under regular conditions, and to maintain this certain guidelines must be maintained:

Diagnostic Tests

1. Diagnostic NM studies should be performed with Tc-99m (technetium-99m), which should not be detectable, even by sensitive radiation monitors, three or four days after a test.
2. Fluorine-18 (F-18), usually attached to glucose (FDG), which is the most common radioisotope used with PET imaging, should be undetectable one day after a test.
3. Technetium-99m (Tc-99m) sestamibi, technetium-99m tetrofosmin, thallium-201 (Tl-201) or a combination of both can be used to do myocardial perfusion (blood flow) imaging.
4. Gallium-68, usually attached to octreotide (DOTATATE), is a PET imaging radioisotope, and should be undetectable one day after a test.

Treatment or therapy

1. Radiodine-131 (sodium I-131), used to treat hyperthyroidism, thyroid cancer and lymphoma, may remain detectable for as long as three months after treatment.

2. Octreotide radiolabelled with Lutetium-177 (177Lu-DOTATATE) is used to treat neuroendocrine tumors, emits low levels of radiation, but may be detectable for few weeks.

Patients planning to travel while undergoing nuclear medicine procedures should carry an approval letter from the doctor, stating their personal information, contact information for the doctor, name of the procedure, date of treatment/test, and information about the radioisotope used.

Applications in body:[19]

Heart

1. To visualize flow of blood and its function (ex. Myocardial Perfusion Scan)
2. Detect presence of coronary artery disease and extent of stenosis
3. Assess damage to cardiac musculature after an event such as myocardial infarction
4. Evaluate treatment modalities like angioplasty and bypass surgery
5. Evaluate results of revasularization procedures
6. Detect possibility of transplant rejection
7. Evaluate heart function during chemotherapy procedures

Lungs

1. Examine lungs for respiratory or blood flow problems
2. Evaluate differential lung function for procedures like lung reduction or transplant surgery
3. Detect signs for lung transplant rejection

Bones

1. Assess bones for fractures, infection or arthritis
2. Assess for bone cancers/metastatic disease
3. Assess painful prosthetic joints
4. Detect sites for biopsy

Brain

1. Examine brain abnormalities in patients with suspected brain disease due to symptoms like seizures, memory loss, aneurysm, etc.
2. Early detection of neurological disorders like Alzheimer's disease
3. Assist in treatment planning via surgery to identify areas of brain that may be causing seizures
4. Assess for chemical abnormalities in brain that may cause controlled movements in patients suspected of Parkinson's disease
5. Assessment for suspected recurrence of brain tumor, surgical or radiation planning or localization for biopsy

Other Systems

1. Detect inflammation or abnormal function of gall bladder
2. Detect bleeding in bowel or gut
3. Evaluate post-op complications after gall bladder surgery
4. Assess lymphedema
5. Assess fever of unknown origin
6. Find the locus of infection
7. Detect the presence of thyroid disease via measuring thyroid function
8. Diagnose blood disorders
9. Diagnose and evaluate hyperthyroidism (overactive thyroid gland)
10. Assess GIT movement and stomach emptying
11. Assess the flow of spinal fluid to find any leaks

Cancer

1. Determine cancer staging via detecting the presence and spread of cancer cell in body
2. In patients with breast cancer or skin and soft tissue tumors, to find sentinel lymph nodes before surgery
3. For treatment planning
4. Assess response to therapy
5. Detect cancer reoccurrence
6. Find rare pancreas or adrenal gland tumors

Renal

1. Assess kidney blood flow and function to find any abnormalities in native or transplant kidney
2. Find urinary tract obstruction
3. Assess for hypertension due to kidney arteries
4. Assess kidneys for infection
5. Find and follow-up urinary reflux

Pediatric applications

1. Assess opening of tear ducts
2. Assess openings of ventricular shunts in brain
3. Evaluate CHD (congenital heart disease) for shunts and pulmonary blood flow
4. Investigate gut abnormalities, like esophageal reflux, motility disorders etc.

Uses in oral and maxillofacial diagnosis[20]

Bone imaging techniques: Jaw lesions are most commonly and easily identified through radiographic imaging techniques but sometimes their early detection is difficult as they don’t develop physical but biochemical changes, like osteoblastic activity, during this time. The resolution for bone scintigraphy is lesser than radiographs, but it can detect change 10% above normal in osteoblastic activity. The more new bone formation there is, the higher morbidity there is. Areas of new bone formation take up more radiotracers and are known as ‘hot spots’. Three types of techniques used are- standard bone scan, three phase bone scan and SPECT. They are used to diagnose:

1. Inflammatory and infectious processes like Osteomyelitis, osteoarthritis, traumatic injuries, periapical and periodontal lesions
2. Mono-osteotic or polyosteotic fibrous dysplasia is seen as a slow and insidious bone enlargement
3. Paget’s disease has abnormal resorption and apposition of bones in one or more areas, initiated by intense osteolytic activity causing resorption of normal bone, followed by vigorous osteoblastic activity forming woven bone. These lesions are clearly demonstrated under scintigraphy. In mandible, bone scan may show increased uptake of radiotracer throughout the bone, from condyle to condyle, called as Lincoln’s Sign.
4. Fractures show increased uptake of radiotracer within hours after trauma. However, in case of older patients, fracture may not be visible on bone scans for a few days. Visibility of fracture on bone scan depends on patient’s age, bone metabolic activity, mineral content, and time elapsed since fracture and imaging technique used.
5. Condylar hyperplasia of mandible results in facial asymmetry, mandibular deviation, malocclusion and articular dysfunction, which can further lead to lateral open bite, prognathism, midline shift, TMJ dysfunction and malocclusion. Bone scintigraphy can be used to detect hyperplasia before morphologic changes have begun.

a. Gallium67-citrate imaging can be used for assessment of abscesses, Osteomyelitis and lymphomas. Gallium scan increases specificity of positive bone scan over triple phase bone scan to monitor treatment response in Osteomyelitis, i.e. reduced gallium accumulation indicates improvement in the condition.

b. Salivary gland scintigraphy can perfectly and quantitatively show parenchymal and excretory function of salivary glands. Detection of gland agenesis/aplasia, obstruction, trauma, fistulas and inflammation can be done through this technique.

c. Lymph node scintigraphy can be used for lymph node mapping to discover the sentinel lymph node that is the first to receive lymph from primary tumor.

d. Radioisotopes are used as oncologic imaging modalities for the detection, staging and determination of prognosis of head and neck cancers. Most common scan is 18F-FDG PET scan, which can even detect distant metastasis. Metastasis possibilities increase in locally advanced diseases (T3-T4), in regional lymph node involvement (N2-N3) with extracapsular involvement and perineural invasion. 18F-FDG PET scan plays an important role in cancer treatment as it is able to assess the treatment response by evaluating the metabolic activity of malignant cells.

e. Brachytherapy is a treatment modality that involves direct injection of radioisotopes to the site of malignant tumor for radiotherapy. These isotopes are covered by a protective capsule to limit its movement to malignant site. These isotopes deliver low doses of ionizing radiation straight to malignant tissue to kill off the cancer cells.

Recent advancements

1. Development of a new PET imaging agent that seeks out a mutation specific to NSCLC (non-small cell lung cancer), which is 80% of all lung cancer, which could potentially reveal weak spots of the cancer for more effective treatment.
2. A PET imaging agent that can detect prostate cancer by targeting Cu accumulation in the tumor.
3. Next-gen SPECT cameras with CZT (cadmium zinc telluride) which can decrease system footprint, shorten exam times and reduce radiation doses.
4. Combination PET-CT and SPECT-CT scanners which overlays both images to better visualize coronary artery and blockages that may be causing perfusion.[21]
5. Development of PET imaging techniques that allows usage of ^{124}I-labelled pharmaceuticals as primary radiotracers for scanning in areas far away from radionuclide production site.
6. Usage of $^{64}CuCl_2$ for linking to antibodies, proteins, peptides and nanoparticles for preclinical and clinical research and imaging of pathological conditions that influence Cu metabolism such as Menkes syndrome, Wilson disease, inflammation, tumor growth, metastasis, angiogenesis, and drug resistance.[22]
7. Development of PET/SPECT scanner using Compton camera[23]
8. Approval for whole body PET-CT scanner by FDA for clinical and research use[24]
9. Development of PET tracers from common biomolecules instead of radioisotopes[25]
10. Usage of targeted radiotherapy combined with chemotherapy kills of 100% of colorectal cancer[26]

Conclusion

Nuclear medicine is an emerging and evolving field of medicine that has numerous applications currently in the field of medicine, but still feels under-utilized when studying the scope of nuclear medicine and the best way to advance it to generate awareness about it, to make its application more generalized than specialized. Its application not just in imaging metabolic processes and body organs, but also in therapeutic procedures for delivering targeted radiotherapy, is both revolutionary and commendable. Nuclear medicine is the future of medicine.

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None.

Conflict of Interest

None.

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