Nuclear medicine is a medical speciality which uses safe, painless and cost effective techniques both to image the body and treat disease. Nuclear medicine imaging is unique in that it documents organ function and structure in contrast to diagnostic radiology which is based upon anatomy. This article provides an overview of some of the common applications of nuclear medicine in clinical practice.

Role of Nuclear Medicine in Brain Imaging
Brain SPECT scan / functional brain imaging is a novel useful technique where CT and MRI scan fail to provide the requisite information. Commonly used brain perfusion imaging agents are Ceretec and Neurolite (Tc99HMPAO and Tc99 ECD) which are lipophilic and are injected by I.V. route and it crosses the blood brain barrier and distributes in the cerebral cells.

Functional Imaging
Functional imaging is simply, the depiction of the physiological or metabolic state of a normal or abnormal structural entity.

The technology of brain SPECT scintigraphy involves injecting minute quantities of the radiotracer Tc99m (Technitium) compound tagged with a chemical i.e. HMPAO or ECD compound which has maximum extraction by the brain tissue and it crosses the intact blood brain barrier. Later on it fixes in the brain cells via conversion to a hydrophilic compound. Twenty to thirty minutes after the injection of the radiotracer a complete controlled rotating Gamma Camera (SPECT) is then used to track the degree of perfusion of the tagged Tc-99m HMPAO/ECD in the cerebral cells. Either 64 or 120 images of the brain of 30 sec/image is taken by this rotating detector. Care should be taken that the patient should be injected with their eyes open and ears-unplugged (blood flow increases by 30% in occipital lobe when eyes are open compared to closed). This should be ideally done in a low light, reduced noise and minimal traffic environment. Caffeine and other vasodilators containing preparations should be stopped 24 hours prior to the scan (Fig. 1).

Transient Ischemic Attacks (TIA)
Tc99m HMPAO/ECD SPECT study may help to identify a subset of patient with TIAs having normal
CT/MRI findings. Persistent focal defects on brain SPECT study at 26-50 hours post event may be an indicator of impending infarction (stroke).

Stroke (Fig. 2)
Brain SPECT study is more sensitive than CT scan in the early (first 24 hours) detection of acute ischaemia (sensitivity 88 - 95% vs 20 - 63% for CT).

The Acetazolamide (Diamox) challenge test may be useful in assessing the vascular reserve following stroke / Transient ischaemic attack. Acetazolamide is a carbonic anhydrase inhibitor that increases the vasodilatation and increases ow in normal cerebral vessels. The areas of perfusion defects in stroke or TIA patient improve with diamox challenge test which suggests that the patient has sufficient reserve thus placing them at a low risk for future stroke. On the other hand, perfusion defects without any improvement with diamox test has higher risk for future brain events and the patient needs carotid artery bypass operation.

Detection of Seizure Focus in Epilepsy

1. Alzheimer’s Dementia
In Alzheimer’s, one classically sees bilateral decreased metabolism (PET imaging) and ow (SPECT imaging) in the temporal and parietal lobes of the brain. The bilaterally symmetrical temporoparietal defects are noted in about 65% of Alzheimer’s patients and are the most consistently recognizable sign of Alzheimer’s. Te99m HMPAO SPECT imaging has a sensitivity between 80-90% and specificity between 65 - 87% for the diagnosis of Alzheimer’s dementia.
2. Multi Infarct Dementia
HMPAO brain SPECT findings that suggest the diagnosis include multiple, bilateral and randomly distributed cortical perfusion defects that follow vascular territories.

3. AIDS Dementia Complex
Multiple areas (small and large) of decreased perfusion are identified. The cortical and subcortical region of the brain often produce a patchy distribution of the tracer. Basal ganglia involvement is also common. The number of defects identified does not necessarily correlate with the severity of patients’ symptoms or clinical findings.

Role of Nuclear Medicine in Cardiac Imaging
Stress SPECT thallium -201 myocardial perfusion imaging or Tc99m Sestamibi Gated SPECT technique is a noninvasive established method for detection as well as assessment of extent and severity in coronary artery disease (CAD). It is definitely superior to other noninvasive tests like routine ECG, stress ECG and 2D-echo cardiography with a sensitivity of 93% and specificity of 95%. Thallium
perfusion imaging or gated sestamibi perfusion study is performed by asking the patient to do a bicycle ergometer stress test to achieve age predicted heart rate maximum or on a treadmill stress test following Bruce protocol. At the peak of the exercise, thallium-201 is injected i.v. route through a prepared medial cubital vein. Patient is asked to continue the exercise for another 1 min. to allow maximum myocardial uptake. Then the patient is positioned on SPECT (rotating) Gamma camera to acquire 32 images of 45 sec/image. The same pattern without exercise is repeated after 4 hours to see the redistribution / reperfusion properties of TI-201 in the myocardium. The stress and rest slices are compared to find out the stress induced perfusion defects with reversible myocardium.

Indication for TI-201/Tc99 gated SPECT Sestamibi myocardial perfusion scan (Fig. 5, 6)
1. High risk patients having strong family history / hyperlipidemia / chronic smokers / uncontrolled diabetes mellitus / essential hypertension.
2. History of intermittent Angina
3. Chronic stable Angina
4. Equivocal or false positive treadmill stress test.
5. Female patients not achieving good effort tolerance in treadmill.
6. Patients having LBBB, cardiomyopathy, LV hypertrophy.
7. Recovering from acute MI to rule out impending ischaemia in other territories for future cardiac events.
8. Pre angioplasty / CABG evaluation to have base line study for the scarred tissue or viable myocardial assessment due to old M.I.
9. Follow up of patient of CABG / post angioplasty evaluation complaining of heaviness in chest / shortness of breath or any other symptoms.
10. To evaluate collateral development in patients having significant coronary artery diseases.
11. Multiple coronary artery disease i.e. Triple vessel disease with poor ejection fraction before subjecting for CABG.

Gated SPECT Perfusion Imaging
Gated single photon emission computed tomography (SPECT) done during myocardial perfusion scintigraphy has been possible with the introduction of Tc99m labelled agents i.e. sestamibi (CARDIOLITE), tetrofosmin (MYOVIEW), Teboroxime (CARDIOTEC) etc. Their uniqueness lie in the high myocardial count density, i.e. higher photon energy resulting in less attenuation and scatter, short half life allowing higher imaging dose, improved spatial resolution and less prominent soft tissue artifacts. Images are therefore easier to interpret. The high photon flux of Tc-99m imaging tracers also allows gated acquisition during multiple intervals of the cardiac cycle, maintaining adequate count density, image contrast and spatial resolution in each image frame. Tc-99m labelled agents i.e. Sestamibi (cardiolite), tetrofosmin (myoview) accumulate in the heart in proportion to regional myocardial blood ow. Once the tracer has entered a myocardial cell it is bound in a relatively stable fashion to mitochondria and remains within the cell. No significant redistribution of the radiopharmaceuticals occur over time.

Half Life and Dosimetry
The physical half life of Tc-99m is 6 h as compared to the 73 h half life of Tl-201. The shorter half life and the biodistribution characteristics of Tc99m labelled agents allow for a total dose up to 30 mCi to be routinely used. The resulting patient radiation exposure is less than or equal to that of Tl-201. Studies of organ dosimetry have shown that a 30 mCi dose of Tc99m labelled agents delivers a lower dose than a 3.5 mCi dose of TI-201.
Differentiation of Attenuation Artifact From Scar

It is well documented that gated SPECT myocardial perfusion scan is useful in improving the specificity of SPECT imaging. The fixed defect on a routine SPECT Thallium-201 myocardial perfusion scan cannot differentiate whether the defect is due to scar formation or attenuation artifact. In these circumstances Tc-99m Sestamibi / Tetrofosmin gated SPECT is useful in recognising possible attenuation artifact from

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<th>T1-201 (3.5 mCi)</th>
<th>Tc99m-sestamibi (30 mCi)</th>
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<td>Total body</td>
<td>0.7</td>
<td>0.5</td>
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<tr>
<td>Testes</td>
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<td>Upper large intestine</td>
<td>0.9</td>
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Fig. 5: Tl-201 tomographic myocardial perfusion imaging showing uniform stress perfusion pattern in all the defined myocardial segments.

Fig. 6: Multiple perfusion defects involving postero-inferior and postero-lateral segments of the myocardium with significant evidence of reversible ischaemia suggesting that patient would benefit from revascularisation procedure.
real perfusion defects.

Diaphragmatic Attenuation
The most common cause of attenuation artifacts is the left hemidiaphragm in men. Thallium-201 myocardial perfusion scan reveals a fixed perfusion defect suggesting a scar in the inferior wall. The same segment on Gated SPECT Tc99m Sestamibi or tetrofosmin perfusion scan demonstrates normal inferior wall motion and thickening, confirming the diaphragmatic attenuation in the slices.

Breast Attenuation
The most common cause of attenuation artifacts is the left breast in women. In the short axis thallium-201 SPECT perfusion images, a moderate decrease in count density throughout the anterior and antero-lateral walls of the left ventricle is seen. Also in the vertical long axis slices, there is a decrease in count density extending from the base of the anterior wall to the apex. In the polar map, a marked abnormality involving the anterior wall and to a lesser degree the antero-septal and antero-lateral walls is present. By quantitative analysis, this defect is identified as a perfusion abnormality involving the anterior, antero-septal and antero-lateral walls. In the gated tomographic slices, wall motion and wall thickening of the anterior wall is normal and just as vigorous as that of the remainder of the left ventricle.

Pharmacological Stress Myocardial Perfusion Imaging
Pharmacological stress perfusion imaging is useful for patients who cannot exercise for various reasons including physical limitations, medications, lung disease, peripheral vascular disease, severe osteoarthritis, elderly aged persons, aortic aneurysms etc.

There are three pharmacologic stress agents used today in cardiovascular nuclear medicine, viz. dipyridamole, adenosine and dobutamine / arbutamine

Sequential Dual Isotope SPECT Imaging with Thallium-201 and Tc99m Sestamibi
Exercise or pharmacologic myocardial perfusion imaging with T1-201 have been widely used methods for the detection of coronary artery disease (CAD). The results with Tc-99m labelled imaging agents have been similar to TI-201. A potential disadvantage of both methods is the length of the protocol used. Thus with TI-201, 4 h delayed images and with Sestamibi, a second set of images are needed 4 h after the initial study or on a separate day. This dual isotope method describes the feasibility and initial results of a shorter protocol using sequential dual isotope imaging with T1-201 and Sestamibi.

Protocol Design
Two different imaging sequences are employed:

1. Rest Thallium / Stress Sestamibi Myocardial Perfusion Studies

2. Stress Thallium /Rest Sestamibi Myocardial - Perfusion Studies

Assessment of Myocardial Viability
Patients with ischaemic heart disease and LV dysfunction may have significant amount of myocardium which is ischaemic but hibernating. It is essential to identify viable myocardium since revascularisation can lead to resumption of normal function in these segments and hence improve the regional and global LV function. However, several studies using stress and 3-4 h delayed T1-201 images have demonstrated that non-reversible perfusion abnormalities frequently exhibit normal perfusion after coronary revascularisation.

Recent publications indicate that conventional T1-201 stress and rest (3-4 hrs) imaging as mentioned above overestimates the extent of infarction thereby underestimating the viable and potentially
jeopardised myocardium i.e. stunned or hibernating myocardium. The current techniques are the following:

- Re-injection of TI-201 imaging
- Re-injection followed by 24 hr delayed imaging.
- 24 hr delayed imaging without re-injection.
- Resting administration of Nitrates or Ribose.
- Gated SPECT Tc-99m Sestamibi / Tetrofosmin imaging
- 18F-FDG metabolic imaging with PET
- Combined use of 1-123 BMIPP and perfusion tracer (Thallium-201/Tc-99m Sestamibi)
- Low dose i. v. dobutamine echocardiography.

18F-FDG Metabolic Imaging with PET

18F-FDG is a glucose analogue which crosses the capillary and sarcolemmal membrane at a rate proportional to that of glucose. Following myocardial uptake, FDG is phosphorylated to FDG phosphate and is then trapped in the myocardium unlike phosphorylated glucose. Regional myocardial uptake of FDG therefore reflects relative distribution of regional rates of exogenous glucose utilisation. In fasting state, fatty acids are the preferred myocardial substrate for ATP production and FDG is taken up very little, if any, by the myocardium. In ischaemic myocardial regions, however, regional substrate utilisation shifts from fatty acid oxidation to glucose utilisation.

Hibernating myocardium therefore would demonstrate increased FDG uptake in the fasting state unlike the surrounding normal myocardium. In the post prandial state, the normal myocardium shifts from fatty acids to glucose as the primary substrate for ATP production. Thus hibernating and normal myocardium both would demonstrate FDG uptake. Therefore preserved or even enhanced FDG uptake in dysfunctional myocardial regions represents presence of myocardial viability.

With the PET perfusion metabolism protocol, when FDG is injected in the post prandial state, three different patterns of myocardial viability may be observed. Regional myocardial perfusion and FDG uptake may be reduced or absent, and is called perfusion metabolism “match” pattern. Based on the severity of perfusion and FDG deficit, the match pattern may be categorised as transmural match, (absent or markedly reduced perfusion and FDG uptake) or non transmural match, (mild to moderately reduced perfusion and FDG uptake). We have used these two terms to indicate that transmural match implies presence of transmural myocardial infarction while non transmural match suggests the presence of mixture of viable and nonviable tissue in a given myocardial region.

When regional myocardial FDG uptake is disproportionately enhanced as compared to regional myocardial blood flow, the pattern is termed perfusion metabolism “mismatch”. This PET pattern is thought to represent hibernating myocardium. Regional dysfunction due to myocardial stunning may be manifested by normal blood flow and normal, enhanced or reduced glucose utilisation.

Myocardial Perfusion Imaging with PET (Fig. 7)

Positron emitting radionuclides are utilized to obtain tomographic images of regional myocardial perfusion, metabolism and receptor density by PET. Four different PET approaches have been utilized for assessment of myocardial viability - perfusion imaging with 13NH3 (ammonia), Rb-82 and 0-15 water, and perfusion metabolism with F-18-FDG.

By far, myocardial viability has been more extensively evaluated with myocardial perfusion F-18-FDG metabolism rather than other PET protocols. With this protocol regional myocardial perfusion is first evaluated with N-13-ammonia, Rb-82 or 0-15 water. Subsequently F-18-FDG is used to assess regional myocardial glucose utilization. Regional myocardial distribution of all the three PET perfusion tracers has been shown to be related to regional myocardial blood flow and extraction fraction of the
myocardium for a given tracer. These tracers have different imaging characteristics, the physical half life of N-13 ammonia is relatively longer (10 min) than those of Rb-82 (75 sec) and 0-15-water (2 min), allowing longer imaging time and higher image count density with N-13 ammonia. Nitrogen-13-ammonia and 0-15-water are cyclotron produced while Rb-82 is produced using a portable generator system.

Role of Nuclear Medicine in Oncology

Radiopharmaceuticals used in oncology for diagnosis and staging of various cancers

- Tc 99 m MDP
- I-131 MIBG
- Tc 99m sestamibi
- Tc 99m antimony sulphur colloid
- F-18 FDG Whole body imaging.

For treatment and monitoring of various cancers

- I-131
- I-131-MIBG
- Sr-89 (Metastron)
- Sm-153 (Samarium) Lexidronam
- Intra-operative probe for mapping the extent of disease involvement.
- Intra-operative tumour targetting with CEA scan.

Tc 99m MDP three phase and static bone scan

- To know the type of disease process
- To know the extent of disease process
- To monitor the treatment out come
  - Cancer breast, Cancer prostate, Cancer lung,
  - Osteogenic sarcoma, Ewing’s sarcoma

Iodine - 131

- To detect the extent and the type of cancer thyroid particularly papillary or follicular or papillofollicular variety.
- I-131 whole body survey scan to detect functioning metastasis any where in the body.
Iodine - MIBG
- To concentrate specifically in to the tissues of phaeochromocytoma.
- Can diagnose primary site and metastatic site.

Gallium-67 whole body tumor scintigraphy used for staging
- Hodgkin’s Lymphoma
- Non Hodgkin’s Lymphoma
- Amyloidosis
- Sarcoidosis
- Infection localisation
- Necrotic hilar lymphadenopathy on CT scan following local RT

Tc 99m sestamibi breast imaging and wash out rate (WOR)
- Diagnosis of Ca breast nodule particularly of indeterminate variety by mammography.
- Before and after chemotheraphy of Ca breast
  - Wash out rate (WOR) normal range = 14-28%
  - Mean 50% ± 18%, WOR cut off is at> 45%
  - Indicate a high risk of chemoresistance
  - WOR <=45% negative, rule out Chemoresistance
  - Sensitivity = 100%, specificity of 80%
- Positive predicative value=83%, Negative predictive value=100%

F-18 FDG Whole Body Imaging
Fluorine -18 deoxy glucose imaging has been available recently has been accepted as gold standard to rule out cancer spread particularly to the soft tissue as compared to CT or MRI imaging. Commonly seen cancers such as cancer breast, cancer bronchus, GI cancers and various type of lymphomas can be better staged with the injection of 10mCi F-18-FDG and whole body PET can be performed showing abnormal areas of FDG accumulation as hot spots. This modality of nuclear medicine investigation would definitely help to detect early cancer spread particularly in the soft tissue, after which various modality of cancer treatment such as surgery, radiotherapy or chemotherapy can be instituted at an early stage with an excellent result.

Renal Imaging
Renal function with imaging is done by injecting Tc99m DTPA under the Gamma Camera. The vascular phase as well as the glomerular and tubular functions can be assessed. The commonest indications are
1. Bilateral or unilateral hydronephrosis.
2. PUJ obstruction.
4. Chronic renal failure.
5. To rule out ATN / rejection in renal transplants.
7. Polycystic kidney.
8. Renal calculi leading to obstructive nephropathy.
9. Ureteric calculi leading to obstructive uropathy.
10. Acute / chronic pyelonephritis leading to scarring (by using DMSA cortical imaging agent).
11. Vesico-ureteric reflux.
GI Bleeding Detection
The radio isotope commonly used is Tc99m SnCl₂ (stannous chloride) usually. Tc99m pertechnetate is injected under the Gamma camera after labelling the RBC’s invivo and delayed pictures are taken 1/2 hr., 1 hr and 1 1/2 hr. These show focal areas of increased tracer uptake in the upper and lower GI tract. It can also detect Meckel’s diverticulum and bleeding from the same structure by injecting Tc pertechnetate. It has sensitivity of 95% and specificity of 96%.

Hepatobiliary Imaging (HIDA scan)
Hepatobiliary imaging (HIDA scan) has been extremely useful particularly in acute calculus / acalculus cholecystitis / chronic cholecystitis / biliary atresia and low CBD obstructions where ultrasound is poor and unable to detect the obstruction. The other important utility of HIDA scan is that it can calculate E.F. (ejection - fraction) of gall bladder in response to fatty meal thus can rule out mild / moderate acalculus cholecystitis.

It can also rule out duodeno-gastric reflux following choleduodenojejunostomy. It can also detect biliary leak. In paediatric patients it can detect biliary atresia which needs early surgery for the survival of the child.

Whole Body Gallium 67 scintigraphy
Gallium 67 scintigraphy is useful in localising the infection in any part of the body or in Hodgkin’s / Non-Hodgkin’s lymphoma. The other indications are sarcoidosis, amyloidosis or normally appearing hilar lymphnodes following chemotherapy in lymphoma on CT scan.

I-131 MIBG Whole Body Scintigraphy
I-131 MIBG (metaiodo benzyl guanidine) localises in medullary CA thyroid or in pheochromocytoma. Patient having suspected pheochromocytoma should receive Lugol’s iodine solution 7-8 days prior to test to block free I-131 to be taken up by the thyroid cells and thus preventing radiation to the thyroid gland.

Parathyroid Scan
Parathyroid scan is being done by injecting dual radiotopes one after another. The commonly used radio isotope are Tc99 pertechnetate and TI-201 tracers. After acquiring these images on the computer, one is subtracted from the other and is visualised only if there is a parathyroid adenoma of superior or inferior or both groups of gland. Normal parathyroid gland is not visualised on the subtracted scan. Recently we have been using Tc99 pertechnetate and Tc99m cardiolite (sestamibi) dual radioisotope to image and locate the parathyroid adenoma.

Lung Perfusion / Ventilation Scan (V/Q)
Lung perfusion imaging is done with Tc99m labelled macro aggregated albumin (MAA) by I.V. route which can also be given in both leg veins to rule out deep vein thrombosis or deep vein obstruction. This is called 2-in -1 study. Lung ventilation study is done with Tc99m. The patient has to inhale and exhale for 5-6 mins in to a closed circuit ventilation system. A normal ventilation scan with an area of perfusion defect otherwise called V/Q mismatch is a classical example of pulmonary embolism which can also be better monitored after starting the thrombolytic therapy.

The other indications are
1. Primary pulmonary arterial hypertension.
2. Chronic obstructive airway disease.
3. Diffuse interstitial lung fibrosis - Wash out curve can be generated and early clearance because of alveolar damage can be studied.
Tc99 HMPAO Labelled Leucocyte Scan
This is a novel technique of labelling WBC (white blood cell) in vitro with Tc99m pertechnetate by the help of HMPAO compound. This leucocyte scan can evaluate any focus of infection / in ammation with sensitivity of 98% and specificity of 99%. The following are the useful indications:

1) Pyrexia of unknown origin (PUO) to detect the focus of infection / in ammation.
2) Chronic inflammatory active bowel disease i.e. ulcerative colitis, Regional ileitis (Crohn’s disease), pelvic abscess.
3) Acute / Chronic osteomyelitis
4) To differentiate prosthetic infection following hip or knee replacement surgery from loosening.

Thyroid scan
The patients who are referred for thyroid scan need to stop eltroxin atleast for a week and to stop all the cough mixtures containing iodine compound. Patient is injected a tracer agent i.e. Tc99 pertechnetate / Thallium-201 / Tc-99 Sestamibi. Half an hour following the intravenous injection, patient is asked to lie down under the Gamma camera to image the thyroid gland. The commonest indications are:

a) Diffuse or nodular enlargement of thyroid lobes.
b) Decompensated / compensated autonomous toxic adenoma
c) Toxic diffuse / nodular goitre
d) Acute / subacute thyroiditis
e) Hypothyroidism
f) Solitary nodular goitre
g) Retrosternal goitre
h) Chronic thyroiditis
i) Thyroid cyst i.e thyroglossal cyst
j) Metastatic thyroid tissue in mediastinum else where
k) To assess the residual thyroid tissue following near total thyroidectomy before administering I-131 therapy.

Conclusion
Nuclear medicine speciality is multifaceted and gives functional and structural information on any organ. It is comparatively cheap and does not have any side effects as compared to radiology or CT scan. It can be repeated frequently as the radio tracer has short half life and quick clearance from the body through urine. I strongly believe that the availability of PET (Positron Emission Tomography) scanning, which is the gold standard in nuclear imaging, has the widest potential in cardiology, neurology and oncology in recent future.