A Doctor's Guide to Nuclear Medicine

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Definitions:

Nuclear Medicine is a medical speciality that uses the nuclear properties of radioactive elements in diagnosis or therapy of diseases. The most visible component of this is in the use of gamma-ray emitting radioisotopes to produce images (scans). There is also extensive use of in-vitro diagnostic tests (e.g. Cr 51-EDTA), and use of elements decaying with gamma and beta radiation producing higher radiation doses as therapeutic agents.

Because many of these radionuclides are delivered to their intended site by linking them to complex organic or biological molecules, and because of the change in the emotion generated by the word “Nuclear” in the 60 years of the speciality’s existence, the term “Molecular Imaging” is becoming more widespread in journals and special society titles.

Background

Nuclear Medicine relies on the “tracer” principle, where the distribution of a substance depends on physical or chemical processes. The tracer material is itself, or is labelled with, a radioactive material. The combination is usually referred to as a radiopharmaceutical. The most commonly used radioactive material used in conventional nuclear medicine is technetium 99m ($^{99m}\text{Tc}$), the chemistry of which allows its attachment to many molecules, allowing, in turn, concentration in multiple organs or processes (e.g. bone, heart, liver, kidney, lung etc.). It has an ideal γ-ray energy for imaging, a half life long enough to allow preparations to last a working day, but short enough to minimise patient radiation exposure (typically similar to an X-ray of the corresponding region) by decaying to negligible amounts shortly after the end of the diagnostic process. For diagnostic (not therapeutic) doses of radiopharmaceuticals in the patient, there is no need for the surgeon to delay operating, as the radiation dose arising from the patient will be negligible.

Radioactivity is a property of the nucleus of the element in which the ratio of protons and neutrons in the element is such that an adjustment has to be made for the nucleus to be at the lowest energy state. This can be done by the release of an alpha particle (2 protons and 2 neutrons), a heavy, charged particle, which gives a large radiation dose, and travels less than a millimetre within soft tissue, and cannot be detected from outside
the intact body. Alpha (α) emitters are therefore of potential use in therapy, but are of little use in diagnostic applications. Many heavy or natural radioisotopes (Uranium, Radium) are alpha emitters. Beta (β) emission occurs from many of the frequently used radionuclides, and accompanies the transmutation of a neutron to a proton (β⁻) from radioactive isotopes produced in a nuclear reactor, or positrons (β⁺) from isotopes produced in cyclotrons. These latter tracers are more usually used in positron emission tomography (PET). β⁻ travel several mm in tissue, again causing a radiation dose to tissue, but not readily detected at the surface.

The radiotherapeutic effects of many radionuclides (eg ¹³¹Iodine) are caused by their β emissions.

Gamma (γ) rays are electromagnetic waves physically undisguisable from X-rays and pass relatively freely through tissue, and causing least radiation effect of these radiations. As they will exit the body and are relatively easily detected, they are of most use in non-invasive imaging using gamma cameras.

The time-activity relationship of uptake or transit of tracer in or through an organ may be determined with dynamic studies (eg gastric emptying). Nuclear medicine particularly lends itself to quantitative studies. Frequently, the distribution of tracer in the process of interest at one time point “static image” is all that is required (eg presence or absence of a tumour). Computed Tomography is very commonly performed in nuclear medicine. This is commonly performed with conventional tracers SPECT, Single Photon Emission Computed Tomography, or PET, Positron Emission (computed) Tomography. When looking at nuclear images, it should be remembered that they are not “shadows” but images of radioactive organs. The display, therefore is as if the observer were “viewing” “luminous” organs, and therefore in an anterior image, the patient’s left is on the observer’s right, but from posterior right is on right.

Diagnostic nuclear medicine interacts with many medical specialities.

Most frequently, the radiopharmaceutical will either localise in the organ of interest, and so diagnosis is based on disturbance in the anatomy or dynamics of the organ, or it will localise in the pathological process of interest (eg cancer, infection).

The following topics are arranged in organ systems preceded by the relevant radiopharmaceutical

**Bone**

**Radiopharmaceutical:** Tc⁹⁹m bisphosphonate (adsorbed to actively mineralising bone)

**Uptake:** local blood flow, mass of bone, and metabolic activity
INDICATIONS:

1. Screen for bone metastases in patients with known or suspected cancer.
2. Infection (Osteomyelitis vs. cellulitis).
3. Evaluation of suspected fracture, including stress fractures.
4. To help determine age and metabolic activity in areas of aseptic necrosis and trauma.
5. Evaluate response to therapy, chemotherapy or radiation treatment for cancer.
6. Evaluation of prosthesis for loosening or infection.
7. Location of biopsy site.
11. Metabolic bone disease.
12. Confirm the diagnosis of RSD.

**Infection**

Flow/metabolism increased within hours (before x-ray changes). Other imaging may show soft-tissue changes of oedema early. Each of 3 phase study (dynamic blood flow: 0-1min, blood pool showing tissue hyperaemia; 1-2min, and delayed images; 2-3hr after injection) showing increased activity in the bone (not adjacent soft tissue). In acute oedema and tamponade, perfusion may be compromised (cold scan)- indication for urgent decompression. Bone may remodel and show increased uptake for an extended period after any insult, therefore less valuable for the follow-up of osteomyelitis or diagnosis after trauma (surgery). Other tracers, which localise in inflammatory tissue (67Gallium or labelled leucocytes), are likely to be more specific.

**Fracture**

On occasion, the fracture line is not easily seen on X-ray in association with undisplaced bone (including athletic stress fractures or osteoporotic insufficiency fractures). Three phase techniques will see local metabolic response in a matter of hours in the young, or 2-3 days in the elderly. The bone scan will show soft tissue involvement in conditions such as tendonitis.
Avascularity

Avascularity - either post trauma (femoral neck) or spontaneous (Legg-Perthe’s disease). Is seen early as absent uptake, but later as increased uptake as revascularisation and remodelling occurs. (MRI marrow signal is often abnormal early) Post traumatic heterotopic calcification may be seen before significant x-ray abnormalities, and its progress monitored.

Tumours

Primary or metastatic malignancies usually have bony remodelling at periphery - increased uptake. MRI shows soft-tissue component, particularly in primary. Some benign lesions show increased uptake on the bone scan, (eg the classically painful and difficult to diagnose osteoid osteoma is very “hot” on the bone scan).

Malignant lesions are seldom “cold”, and bone scanning is performed very frequently to diagnose or monitor metastatic disease. Both lytic and sclerotic metastases are “hot” on the bone scan except multiple myeloma, which may have normal bone scan appearances.

The whole body bone scan is sensitive in screening the whole skeleton for metastases (although the yield may be low in early stage of most malignancies and not routinely indicated). Other commonly occurring pathologies (eg vertebral crush fractures, arthritis) will also give an abnormal scan, but accuracy of the reporter is often enhanced by experience and pattern recognition. Directed Plain X-ray, CT and MRI add specificity. The whole body scan is useful in following progression or therapy of established metastatic disease. Awareness of the “flare” phenomenon (increased visualisation of previously invisible, but successfully treated healing metastases) is needed.

Paraneoplastic phenomena, such as hypertrophic pulmonary osteoarthropathy, or the results of malignant hypercalcemia (lung, stomach and increased bone uptake), may also manifest on the bone scan.

Urinary Tract

Radiopharmaceuticals:

- $^{99m}$Tc-DTPA - cleared by glomerular filtration
- $^{99m}$Tc-MAG3 - cleared by glomerular filtration and tubular excretion - more useful if renal function is impaired or in children
**99mTc-DMSA** - accumulates in renal tubules, gives map of functioning renal tissue, useful in cortical masses or scarring

**INDICATIONS:**

1. Evaluation of renal perfusion and function.
2. Evaluation of renal trauma.
3. Diagnosis of renovascular hypertension.
5. Diagnosis of acute tubular necrosis.
6. Renal evaluation in those with allergy to radiographic contrast.
7. Evaluation of renal transplant patients.

**Function**

Relative renal function dictates the uptake or clearance of radiopharmaceuticals in the kidney in proportion to local renal function, and therefore their relative contribution to renal function may be derived from the scan. Global GFR (total renal function) can calibrate this by measuring plasma clearance of activity. Follow up and surgical decisions may then be made on quantitative data.

**Renal artery stenosis**

May be recognised by its effect on the inflow into and subsequent reduced function of the affected kidney. This is enhanced by prior administration of Angiotensin Converting Enzyme inhibitor. The technique is useful for screening, but also monitoring the effect of revascularisation surgery. Functional results of renal artery stenosis are shown by changes in size or function, rather than the anatomical lesions shown by conventional imaging, which may not be associated with significant functional change.

**Infection**

Particularly in paediatric patients, localised functional disturbance in renal parenchyma with prognostic
significance (often a prelude to scarring in children with reflux) may be demonstrated with $^{99m}$Tc-DMSA scanning and prompt decisions regarding intervention. Reflux in children may be assessed by direct (activity introduced into the bladder via catheter) or indirect ($^{99m}$Tc MAG$_3$ excreted by kidney) cystography. This has a radiation dose advantage on the x-ray techniques.

**Obstruction**

Dilated renal collecting systems may not be “obstructed” (normal function, good prognosis) Interventional decisions may be assisted by the diuretic renogram which uses a rapidly cleared radiopharmaceutical to fill, then “stress” the dilated system with diuretic. The dilated, but not obstructed system, clears promptly (typically half-clearance time < 13min. The differential renal function is also important to confirm loss if present.

**Transplant**
In the early post-operative period, perfusion to the transplant may be determined. Acute tubular necrosis is usual and rapid fading of filtered tracer will occur without excretion. Urinary leaks or obstruction may also be diagnosed and differentiated from lymphocele. Later, serial studies may be used to monitor rejection.

**GI imaging**

**Radiopharmaceuticals:**
- $^{99m}$Tc colloid (reticulo-endothelial function)
- $^{99m}$Tc red cells (acute GI bleeding, hepatic haemangiomata)
- $^{99m}$Tc heat-damaged red cells (splenunculi)
- $^{99m}$Tc-IDA derivative (excreted in bile)
- Na$^{99m}$TcO$_4$ (Meckel’s Diverticulum)
- $^{111}$In labelled leucocytes (inflammatory bowel disease)

**GI Motility**

**Radiopharmaceuticals:**
labelled foodstuffs, (liquid, or semisolid) usually labelled with $^{99m}$Technetium

**Liver masses**

The traditional colloid liver scan (depending on phagocytosis of particles in liver Kupffer cells and splenic sinusoids) is obsolete other than for confirming focal nodular hyperplasia.

**Biliary function:**

**INDICATIONS:**

1. Diagnosis of acute cholecystitis.
2. Evaluation of patency of hepatobiliary system.
4. Detection of biliary reflux.
5. Diagnosis of biliary atresia and other congenital anomalies of the biliary tract.

$^{99m}$Tc IDA – derivatives are useful in assessing biliary tract disease. Visualisation of the gall bladder an hour after injection (enhanced by 2mg iv morphine to cause sphincter of Oddi contraction if indicated) virtually excludes acute cholecystitis. Quantitative studies may be useful in patients in
whom biliary dyskinesia is a problem (gall-bladder ejection fraction following fatty meal or iv cholecystokinin is normally >40%). Post-traumatic and post surgical biliary leaks are readily assessed. Scanning after administration of a $^{99m}$Tc IDA derivative can demonstrate adequacy of perfusion, uptake by liver parenchyma, excretory function and patency of biliary channels. Serial imaging is particularly useful.

**Spleen**

Autologous red cells labelled with $^{99m}$Tc and damaged by heating to 49°C for 20 minutes are taken up very avidly by splenic tissue. Following relapse of conditions treated by splenectomy, (spherocytosis, ITP), regenerating splenic rests or splenunculi are often to blame. This is the procedure of choice to localise these splenic rests.

Apart from the exclusion of splenic infarction (wedge–shaped defects often in an enlarged spleen), most indications for splenic colloid imaging are obsolete. It has no part to play in trauma.

**Gastric Emptying:**

**INDICATIONS:** Diagnosis of functional gastric obstruction/dysmotility

Radionuclide *gastric emptying* is the “gold standard” in gastric emptying assessment. It is often useful simultaneously follow the emptying of both solid and liquid components of a meal. Indications include the assessment of possible gastroparesis, unexplained nausea and vomiting, reflux and after surgery.

**Haemorrhage:**

**INDICATIONS:**

1. Detection of active gastrointestinal and non-gastrointestinal bleeding sites. Localization provides *approximate* location only. Although detection of gastric bleeding has been reported, this study is mainly limited to bleeding beyond the ligament of Treitz and is most sensitive for lower GI bleeding.
2. Detection and localization of a Meckels diverticulum containing functioning (bleeding) gastric mucosa.
3. Detection of Barrett’s esophagus

If the bleeding is acute and rapid, then localisation of the bleeding site is
feasible. Autologous erythrocytes are labelled with $^{99m}$Tc and reinjected. Bleeding rates of 0.5-1 ml/min should be identifiable in the GI tract. It is important that images are taken serially (at short intervals of no more than a few minutes to localise the bleeding. If the patient is imaged only several hours after beginning, then the extravasated activity will have moved distally, and redundantly confirm that the patient was bleeding. In the paediatric or young adult population, if Meckel’s diverticulum is considered then $\text{Na}^{99m}\text{TcO}_4$ may be used. It is taken up by excretory epithelium, (particularly gastric mucosa) and will localise within a few minutes in native and ectopic gastric mucosa, adjacent to which is the ulcer causing bleeding.

Inflammatory bowel disease

May be difficult to assess in activity or extent by conventional techniques. Leucocytes (mixed or granulocytes) localise at sites of active bowel inflammation and are shed into the lumen. Imaging can localise and score disease activity.

Inflammation and infection

**Radiopharmaceuticals:**

- $^{67}$Gallium citrate (non-specific)
- $^{99m}$Tc-colloid
- $^{99m}$Tc-Exametazime - HMPAO
- $^{111}$In labelled leucocytes
- $^{99m}$Tc-antileucocyte antibodies - Leukoscan

**INDICATIONS:**

1. Evaluation of inflammatory bowel disease.
2. Detection of abscess or acute (<4-6 weeks) infection.
3. Fever of unknown origin.
4. Acute osteomyelitis (particularly useful in diabetics).
5. Prosthesis infection, graft infections.
acute leucocytic infiltration. Chronic inflammation (infection) is less likely to have leucocytic infiltration, and therefore labelled leucocytes may not reveal these. Particular use has been made in determining infection in bone, and inflammatory bowel disease, but the technique is useful in localising acute inflammation anywhere. Abscesses are readily seen, and acute appendicitis is readily visualised, although anatomical imaging is usually used first. Pyrexia of unknown origin without suspected focal sepsis has a poor yield with these investigations.

Endocrinology.

Radiopharmaceuticals:

\[ ^{99m}\text{Tc}\]Sestamibi (MIBI) (parathyroid)
\[ ^{111}\text{In}\]Octreotide (nuroendocrine tumours)

Thyroid

INDICATIONS:

1. Determination of thyroid size, function, and position.
2. Evaluation of functional status of thyroid nodules.
3. Evaluation of thyroid and neck masses.
4. Evaluation of patients with history of head and neck irradiation.
5. Quantitative thyroid uptake (I-131 uptake).
6. Detection of ectopic thyroid tissues such as substernal or sublingual locations of thyroid tissue (I-123).
7. Treatment for hyperthyroidism, neoplasm (I-131).

Nuclear techniques remain relevant in the assessment of thyroid structure and function. Although ultrasound and fine needle aspiration are most frequently used to determine the nature of palpable nodules, assessment of global thyroid uptake (most conveniently with Na\[^{99m}\text{Tc}\]O\(_4\)) may give useful information about the function of nodules. Malignancy is less common in functioning than “cold” nodules, and prior to surgery for hyperthyroidism, the exclusion of an autonomously functioning “hot” thyroid nodule, or the lack of uptake in viral or drug induced thyroiditis may be worthwhile. Whole body
iodine scanning (most usually $^{131}$I) is indicated in the follow up of follicular and papillary thyroid cancer after radionuclide ablative treatment. Medullary thyroid cancer arises from a different cell line and is not iodine avid. Despite these thyroid cancers having less uptake than normal thyroid, they have far more uptake than other tissues, and will concentrate radioiodine for diagnostic or therapeutic purposes. Use in recurrence of thyroid cancer tends to be complementary to thyroglobulin assay.

**Parathyroid:**

**INDICATIONS:**

Detect and localise hyperfunctioning parathyroid adenomas prior to surgery or re-exploration.

Although open surgery is very effective in locating and treating hyperparathyroidism, it may fail in 5-10% of operations. Minimally invasive parathyroid surgery is also becoming more common. Both of these are indications for pr-operative parathyroid imaging. The sensitivity of CT, MR, ultrasound and MIBI scanning is similar (70%-90%) The nuclear scan is particularly useful in demonstrating mediastinal lesions and in the post – surgical situation, where conventional imaging is difficult because of scarring. Both the thyroid and parathyroid will take up the current agent of choice, MIBI but the parathyroid lacks the P-Glycoprotein mechanism which clears sestamibi from the thyroid, hence parathyroid tissue retains activity for several hours. Some thyroid nodules also lose this mechanism, and therefore they may be a differential diagnosis for focal uptake in the neck.

**Adrenal cortex**

$^{131}$I or $^{75}$Se cholesterol is incorporated into the biochemical pathway manufacturing steroids in the adrenal cortex. In selected cases these tracers will confirm the function of a known mass, or localise a functioning lesion suspected biochemically. Availability of these tracers is limited.

**Neuroendocrine tumours**
MIBG SCAN:

INDICATIONS:

Identification and localisation of tumours of neuroectodermal tissues:

1. Benign and malignant pheochromocytomas.
2. Neuroblastomas.
3. Carcinoid tumors.
4. Medullary thyroid tumors.
5. Paragangliomas.
6. Chemodectomas.

MIBG-usually labelled with $^{123}$I is a catecholamine precursor, which is taken up in phaeochromocytoma (faintly in normal adrenal medulla and adrenergic nerve endings), and some other malignancies (eg carcinoid, neuroblastoma). It may be used in the confirmation of the nature of incidentally found lesions, as well as detecting those in hypertensive patients with appropriately abnormal biochemistry. Functioning metastases are also localisable.

OCTREOTIDE SCAN

INDICATION:

Functional imaging, detection, follow-up and monitoring tumours that contain somatostatin receptors such as carcinoids, islet cell tumors, small cell lung tumours, CNS (neuroendocrine tumors) and some thyroid carcinomas.

Octreotide (a somatostatin analogue usually labelled with $^{111}$In) is frequently taken up in primary and metastatic carcinoid tumours and other neuroendocrine tumours such as gastrinomas and pituitary neoplasms.

Other tumour localising agents
## Radiopharmaceuticals:

<table>
<thead>
<tr>
<th>Radioisotope</th>
<th>Name</th>
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<tbody>
<tr>
<td>$^{99m}$Tc</td>
<td>Tc-MIBI</td>
</tr>
<tr>
<td>$^{201}$TI</td>
<td></td>
</tr>
<tr>
<td>$^{67}$Ga</td>
<td></td>
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<tr>
<td>$^{99m}$Tc</td>
<td>TcDMSA(V)</td>
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Many radiopharmaceuticals will localise within tumours as a result of their intrinsic biodistribution. $^{99m}$Tc-MIBI is initially distributed by blood flow and metabolic activity. It has been shown to be useful in the diagnosis of primary and recurrent breast cancer, particularly in mammographically dense breasts. The technique is not sensitive enough for local staging. Uptake has also been shown in sarcomata and lung cancers. $^{99m}$TcDMSA(V) is also a non-specific tumour scanning agent, shown to be useful in medullary thyroid cancer, and may detect recurrences indicated by calcitonin increases. $^{201}$Thallium whole body scans may detect iodine non-avid metastatic thyroid malignancy, sarcomas and brain tumours.

## Lymphoscintigraphy

### Radiopharmaceuticals:

<table>
<thead>
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<th>Radioisotope</th>
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<tr>
<td>$^{99m}$Tc</td>
<td>antimony colloid</td>
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<tr>
<td>$^{99m}$Tc</td>
<td>sulphur colloid</td>
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<tr>
<td>$^{99m}$Tc</td>
<td>nanocolloid</td>
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### INDICATIONS:

2. Investigation of the cause of lymphoedeoma of the lower or upper limb.

Soluble or fine colloidal materials injected interstitially will be taken up into lymphatic vessels and subsequently particulate material will be taken up into draining lymph nodes, mimicking the presumed behaviour of micrometastases.

Sentinel lymph nodes are nodes receiving direct drainage from the tumour, and are regarded as those most likely to be involved with (micro) metastases and predictive of the status of the entire nodal basin. The technique has found most use in cutaneous melanoma and breast tumour. When staging the axilla in breast cancer, many studies have shown concordance between the sentinel node and axillary status of better than 95%. Localisation of lymph nodes is
best performed with a combination of radioactive tracers and blue dyes.

Lymphedema results from the progressive accumulation of protein rich fluid in the interstitial spaces secondary to an anatomic or functional obstruction of the lymphatic system. Patients with lymphedema experience extremity swelling, decreased mobility, and secondary infections. There is both a superficial and deep lymphatic system which drain at very different rates. The superficial system is the primary route for lymphatic drainage. Deep lymphatic transport is less than 10% of the superficial transport system.

### Pulmonary embolism

**Radiopharmaceuticals:**
- $^{99m}$Tc-MAA
- $^{99m}$Tc-aerosol

**INDICATIONS:**

1. Diagnosis of pulmonary embolism.
2. Evaluation of regional pulmonary perfusion and ventilation in acquired pulmonary disease (COPD, asthma, carcinoma, etc.).
3. Evaluation of pulmonary perfusion and ventilation after treatment with anticoagulants.
4. Pre-op evaluation of lung function for thoracotomy. In this case, the study should be ordered as *quantitative*.
5. Assessment of congenital pulmonary abnormalities and cardiac shunts.

Pulmonary embolism is a frequent post operative complication, and confirmation has important therapeutic implications. The ventilation-perfusion (V/Q) scan has been a mainstay of diagnosis for many years, and continues to have a very high predictive value with normal or scans with mismatch. Its specificity is reduced if there are chest-x-ray abnormalities, and in this situation, CT pulmonary angiography will likely give more information, but has a number of contra-indications.

### Therapy
Differentiated thyroid malignancy was the original condition treated by radioisotopes, which remain a mainstay of treatment. Metastatic disease is treated by at least two doses of radioiodine ($^{131}$I). The first dose is needed to ablate the remaining normal thyroid tissue post-surgery, which remain no matter how extensive the surgery. The metastases are usually less avid than normal thyroid tissue. Scanning should be performed after therapeutic doses, as sensitivity for thyroid metastases is greater. The patient should have an elevated TSH at the time of iodine administration (cease thyroid hormone therapy or administer synthetic TSH- rTSH).

For hyperthyroidism as an alternative to medical or surgical therapy, the larger the dose of radioiodine administered, the more rapidly control is reached. Ultimately most patients will become hypothyroid. Debate continues regarding the role of radioiodine in the therapy of non-toxic multinodular goitre.

$^{32}$P is used in the treatment of polycythaemia.

Painful bony metastases will localise other bone-seeking radiopharmaceuticals using the same mechanism as bone-scanning agents. $^{153}$Sm EDTMP and $^{89}$Sr have been shown to be useful in palliation. Labelled monoclonal antibodies are effective in treating certain lymphomas and specific antibodies are being developed for other indications.

Nuclear cardiology is one of the main indications for nuclear medicine studies. The major areas of study include assessment of blood flow to the heart muscle itself (perfusion scanning), the contractile function of the heart muscle, and occasionally the determination of whether a myocardial infarct has occurred recently.
If a patient has typical symptoms of angina, and intervention to improve blood-flow to the heart is planned, then generally a coronary angiogram will be performed. This is an invasive test which usually involves the passage of a catheter.

**Nuclear Cardiology Perfusion Scanning**

In some general departments, this may account for half the workload. Although different techniques may be used, the general principle involves the comparison of the myocardial distribution of a tracer under conditions of stress (hyperaemia) with the distribution at rest. The differences in these images might suggest:

- Normal (expected distribution, unchanged between stress and rest)
- Myocardial scar (defect in distribution, unchanged between stress and rest)
- Ischaemia (relative defect after stress which reduces in extent and/or degree when imaged at rest).

The stressors used are pharmacological intervention:

- **Vasodilator.** Most usually Dipyridamole (which prevents the breakdown of intrinsic Adenosine) or the short-acting Adenosine itself. These agents act directly on coronary and other vessels, and in normals may increase coronary flow by a factor of 4. There agents by their physiology may cause hypotension and flushing, headache and dipyridamole causes headache frequently. Their effect is blocked by Xanthine agents. Hence Caffeine containing foods and beverages (tea, coffee, chocolate, energy drinks) should be ceased 24 hr before a study. IV aminophylline reverses the side effects if they are uncomfortable. The flow tracer, should, of course be injected first. Vasodilators are indicated particularly in Left Bundle Branch Block, where the increase in heart rate from exercise or sympathomimetics may cause a false-positive defect due to the dyskinesia of the septum. They may exacerbate bronchospasm and are contraindicated if there is a clear history of asthma.

- **β-agonists.** Dobutamine infusion increases myocardial flow and oxygen needs by combined isotropic and chronotropic drive. It may be given to asthmatics.

Each of these stressors is associated with a small risk, and patient informed consent is important.

**Radiopharmaceuticals:**

- $^{210}$TI chloride has been in use for 30 years. It is a potassium analogue, and is transported to the myocardium by blood-flow, and actively
transported across the cell-membrane by an energy-using process. Its distribution therefore reflects both flow and local metabolic rate. It leaks out of the cell, and will be taken up again, “redistribution”, therefore images should be taken immediately after stress. Images obtained 3-4 hrs later may reflect flow and metabolism at rest.

- $^{99m}$Tc-Sestamibi have similar properties. They are distributed to the myocardium by perfusion, diffuse into the cell and are trapped. They therefore represent the flow at the time of injection. They do not reperfuse. Two injections are needed for a stress/rest series of scans.

**Indications:**

Myocardial perfusion scanning is used usually to:

- Diagnose coronary artery disease in typical or atypical chest-pain syndromes.
- Localise or characterise the severity and reversibility of defects in patients with known coronary disease
- Assess prognosis
- Detect viability
- Assess local and global myocardial contractility by “gating” studies.

The images obtained are usually tomographic (slices) displayed in a standardised orientation (not anatomical) related to the long axis of the left ventricle which is >80% of myocardial bulk. These may also be related to typical distribution of coronary artery territory, but anomalous vessels cannot be recognised on these studies. Displays may be enhanced by “bullseye” images, which display the entire myocardium in one picture of concentric slices, apex to the centre.

**Gated Blood Pool Scanning. (gated heart pool scanning)**

**INDICATIONS:**

1. Assessment of cardiac function:
   - Left Ventricular ejection fraction (LVEF).
   - Right Ventricular ejection fraction (RVEF).
   - Chamber size.
   - Sequence of chamber contraction.
   - Chamber wall motion, including detection of akinetic and dyskinetic segments.
2. Detection of ventricular aneurysm.

3. Prospective evaluation prior to cardiac medications or drugs known to affect myocardial function (i.e. Adriamycin). Follow-up post-treatment.

4. Quantification of left-to-right intracardiac shunt (only with first pass technique).

5. Measurement of diastolic dysfunction.

6. Evaluation of valvular disease

By acquiring images synchronised with the heart beat (ECG), sufficient radioactive counts may be collected to produce an image of a typical cardiac cycle. This principle was seen above in the myocardial perfusion scanning section, where the movement of the myocardium itself was monitored. Although those images may be used to estimate an ejection fraction, this depends on a number of geometric assumptions, which may be incorrect, particularly in disease, and therefore the precision of ejection fractions obtained from perfusion scans is not high, particularly if they are to be used to monitor the progress of a patient.

If the blood (usually the red-cell component) rather than the myocardium is labelled, then the ejection fraction may be estimated from the counts ejected per cardiac cycle, rather than the geometry. This is more accurate and reproducible for the left ventricle. Focal and general movement abnormalities may also be seen.

The major indication is in the assessment of cardiac function in oncology, when cardiotoxic anthracycline chemotherapy is administered to the tolerance of the patient. Cardiac function needs to be monitored. The technique is also used in the workup before cardiac transplantation. Typical precision of LV ejection fraction (Normal 50%-80%) is 5%. Computer processing of the dynamic data is often used to produce “functional” images. Additional analysis of the volume time curve can also provide additional information such as peak filling rate, time to peak filling and peak ejection rate. This technique is most useful to determine LV function. For RV function, a “first pass” study allows the estimation in a beat-by-beat technique which removes the interference of overlying cardiac chambers.

Cardiac shunt studies
Confirmation of shunting from the left to the right side of the circulation (e.g. atrial septal defect), and quantification of this may be simply done in a study taking a few minutes. Rapid frames are taken following IV injection of tracer. Early recirculation to the lungs implies shunting of blood. The ratio of blood flow through the systemic to pulmonary circulation (QP/QS) may be calculated.

If the shunt is in the opposite direction (venous to arterial side, reversal in VSD, AV shunting in the lungs), then $^{99m}$Tc MAA, used in lung scanning, will bypass the pulmonary circulation, and lodge in the next capillary bed (brain and kidneys in particular at rest). The proportion shunted may be easily calculated.

### Neurology

#### Radiopharmaceuticals:

- **Tc-99m-hexamethylpropyleneamineoxime (Tc-99m-HMPAO)** - SPECT
  - $^{123}$I-ioflupane (Dopamine transporter, DaTSCAN)

**99mTc-HMPAO**

This is a non specific radiopharmaceutical which is able to cross the blood-brain barrier because of its lipophilic property. It is extracted from the bloodstream into the cerebral parenchyma and is dependent on the cerebral blood flow. This has a role in the imaging of neurodegenerative conditions with characteristic findings in Alzheimer’s disease and frontotemporal dementia as well as other neurological conditions.

It has also been used in epilepsy and shows increased uptake in focal seizures when injected during the seizure (ictal imaging). Hypoperfusion may be demonstrated on interictal imaging.

**123i-ioflupane – DaTSCAN**

This is a specific radiopharmaceutical which is taken up by dopamine specific transporters found in the presynaptic nerve terminal. These transporters are found most abundance in the basal ganglia. In Parkinson’s disease, parkinsonian syndromes (multiple system atrophy, progressive supranuclear palsy & corticobasal degeneration) and Lewy body dementia, the uptake is reduced significantly in the basal ganglion. In drug-induced Parkinson’s disease or essential tremor, uptake is not affected.