Guidelines for Nuclear Medicine Investigations

Edition II

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Paediatric section
Dr Russell Troedson
## Clinical Problems

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<td>Bilhary \ Biliary obstruction \ Gall Bladder disease \ Liver \ Cirrhosis</td>
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Foreword

This booklet has been written to explain the various nuclear medicine techniques and their application in assisting diagnosis in general practice. The first edition was printed in 1997 and in the last eight years there have been several exciting developments that have warranted a second edition.

There is a completely new section devoted to paediatric applications (our thanks go to this sections’ contributor, Dr Russell Troedson) as well as brief overviews of therapeutic nuclear medicine and positron emission tomography (PET scanning). The latter became available in Western Australia in 2002 and is now becoming part of mainstream imaging in Oncology.

Nuclear medicine procedures can be tailored to address your particular diagnostic problem. It is therefore often helpful to discuss the clinical problem with the Nuclear Physician performing the examination.

Nuclear medicine sites are located at
- Bentley, 9458 1373
- Joondalup, Nuclear Medicine WA, 9400 9830
- Midland, 9250 2829
- Rockingham, 9592 1222
- Subiaco, Magnetic Resonance Centre, 9380 4888
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Introduction

Diagnostic nuclear medicine is predominantly concerned with physiological and pathological alterations in cellular function and, often, is a more sensitive indicator of cellular abnormality than other imaging techniques. Short-lived radio-isotopes used in trace amounts are administered usually by intravenous injection, the purpose being to provide early evidence of pathological change before structural changes occur.

Techniques are available for imaging almost every organ in the body. The majority of studies are performed using Technetium as the radioactive source. It has the advantages of a short half-life (6 hours) which limits the dose received by the patient and its physical properties are optimal for detection by a gamma camera. Its functionality is achieved by its ability to be chemically bound to a wide range of substances.

Scintigraphic images are functional representations created from the concentration and distribution of the radioactive tracer within the target organ. Tomographic images (SPECT) can assist localisation of activity within an organ. The distribution of the activity imaged sequentially within an organ over time can be analysed mathematically and estimations of normal and abnormal cellular function can be performed.

Although some patterns of tracer distribution are characteristic for certain disease processes, not all studies are of high specificity and there may be a requirement for other anatomical imaging techniques for complete evaluation.
At a glance

1. Bone
   - skeletal metastases or malignancy
   - suspected fracture & overuse syndromes eg shin splints/stress fractures
   - chronic pain syndromes eg back pain associated with degenerative facet joint disease
   - ongoing pain following joint replacement and spinal surgery

2. Heart
   - evaluation of known or suspected coronary artery disease
   - gated heart scanning allows measurement of left ventricular function

3. Lung
   - suspected pulmonary emboli
   - pre-op lung reduction surgery
   - R to L shunts

4. Renal
   - renal scarring following urinary tract infection in children
   - suspected obstruction eg PUJ obstruction
   - follow up of urinary reflux
   - assessment of hypertension where renal artery stenosis is suspected

5. Thyroid
   - hyperthyroidism; allows differentiation of Grave’s disease from thyroiditis
   - evaluation of thyroid nodules

6. Brain
   - differentiation of depression and dementia
   - localise seizure foci where surgery is considered
   - assess cerebral vascular reserve (eg pre carotid endarterectomy)
   - CSF studies: VP shunts, leaks and flow in hydrocephalus
   - tumour recurrence post surgery and radiotherapy
   - brain death

7. Gastrointestinal
   - Oesophageal, gastric and colonic transit
   - inflammatory bowel disease
   - GI bleeding

8. Hepatobiliary
   - diagnosis of acute and chronic cholecystitis
   - focal hepatic lesions
   - biliary leak (eg post cholecystectomy, trauma)
Procedural Techniques

1. Bone
   - Initial injection and dynamic images - 15 minutes.
   - Delay of 2 to 4 hours depending on type of scan with imaging for 30-80 minutes.
   - Patient is instructed to drink extra fluids and to empty their bladder regularly.

2. Cardiac
   - Fast for 6 hours prior to study and NO caffeine-products for 24 hours prior to the study.
   - No episodes of angina for 48 hours prior to the study.
   - Rest injection and rest imaging (1 hour).
   - Stress procedure 1 to 3 hours later with either exercise (treadmill, bike) or dipyridamole, then imaging (1 hour).

3. Lung
   - A current chest x-ray is required for interpretation of the lung scan.
   - Initial ventilation study followed by perfusion study.
   - Duration of study 1 hour.

4. Renal
   - DTPA or MAG3 - Bolus injection followed by 20 minutes of imaging.
     Furosemide may be administered to assess clearance.
   - Captopril study - Tracer is injected 1 hour after oral Captopril and imaging is performed for 30 minutes.
   - DMSA - Imaging for 40 minutes after a 3 hour delay.
   - Isotope cystogram - Tracer is administered via a catheter until the patient micturates.

5. Thyroid
   - No iodine for 6 weeks prior to the study. (Includes radiographic contrast and amiodarone).
   - Preferably cease carbimazole and PTU 2 days prior to the study.
   - Initial injection followed by imaging 20 minutes later. Imaging lasts 30 minutes.

6. Brain
   - Baseline Study - IV line is inserted and patient lies with eyes open in quiet darkened room for 20 minutes prior to injection.
   - Diamox study - Acetazolamide administered over 3 minutes, blood pressure measured 5 minutey for 20 minutes prior to tracer injection.
   - Imaging commences 30-45 mins following injection and will take approx. 45 minutes.
7. **Gastrointestinal**
- Gastric emptying - Fast for 6 hours prior to ingestion of tracer. Images taken over 2 hours.

8. **Hepatobiliary**
- Fasting for 4 hours prior to the study.
- Initial injection followed by imaging for 1 hour
- Imaging may continue for a further 30 minutes following IV morphine if the gallbladder is not visualised initially or if cholecystokinin is administered to assess gall bladder emptying.
## Bone

- skeletal metastases or malignancy
- suspected fracture & overuse syndromes eg shin splints/stress fractures
- chronic pain syndromes eg back pain associated with degenerative facet joint disease
- ongoing pain following joint replacement and spinal surgery

The skeleton is imaged using *Technetium-labelled diphosphonates*. The diphosphonate is adsorbed onto the surface of bone especially at sites of new bone formation. Uptake will depend on local vascularity and the degree of osteoblastic activity.

The tracer is injected into the venous system and after a first pass through the circulation it rapidly enters the extracellular space (*blood-pool or tissue phase* of the study). Imaging this component will assess the *degree of vascularity* associated with the disease. This is helpful in suspected bone injury and infection.

The diphosphonate then slowly adsorbs onto the bone matrix which takes approximately 2-3 hours. *Regional or whole body* images are then acquired.

Although bone scans are very sensitive they are often non-specific. Any cause of increased metabolic activity whether due to metastatic disease, primary bone tumour, inflammation or trauma can cause increased tracer uptake. It is recommended that both the bone scan and current radiographs are analysed at the same time leading to a single conclusion, thereby avoiding conflicting reports.

Non-skeletal sites of uptake may also be demonstrated eg effusions and some soft-tissue tumours. Excess tracer is excreted via the kidneys and patients are encouraged to drink during the study and empty their bladder frequently to assist elimination of the activity.

### Indications:

1. **Metastatic bone disease**

   Scintigraphy is used in the initial staging and follow-up of malignancy that has a predilection to metastasise to bone (particularly breast and prostate).

   *Skeletal scintigraphy remains the most effective means of screening the skeleton for metastatic involvement.*

   Approximately 30-50% of patients with positive bone scans will have negative radiographic findings. Bone scanning has a false positive rate of approximately 2%.

   Photopenic (cold) lesions may result either from compromise of the bone blood supply, replacement of marrow or bone by tumour, or due to a purely lytic (osteoclastic) process. Carcinomas of the lung, breast, kidney, and thyroid are common primary sources for such lesions. Multiple myeloma is a frequent cause of a false negative bone scan and in this group.
Bone screening should still be in conjunction with a full radiographic skeletal survey.

Follow-up studies may show an apparent deterioration in appearances (manifested by increasing intensity of lesions or new lesions) despite improvement in the patients’ clinical condition. This may indicate a “flare response”. It generally occurs in the first three to six months after treatment. The cause is thought to be due to osteoblastic remodelling/healing at sites of tumour resolution.

It has been described in patients with breast carcinoma, prostatic carcinoma, small cell carcinoma of the lung, and lymphoma, and in response to chemotherapy, radiotherapy, and hormonal manipulation. A repeat bone scan will show marked improvement after 4-6 months if the treatment has been successful.

![Fig 1. 68yr male with Prostate Carcinoma and rising PSA](image)

2. Evaluation of malignant and benign primary bone lesions

Plain radiographs remain the essential tool for diagnosis and characterisation of malignant and benign primary bone lesions.

M.R.I. and C.T. will also be used to assess the characteristics of the lesion and the tumour’s relationship to adjacent tissues.

Scintigraphy readily determines whether a lesion is solitary or multiple

The degree of vascularity and uptake by a lesion has been shown to correlate with its malignant potential. Some slow growing low grade malignant lesions however, may show little uptake while some benign metabolically active bone lesions may show avid uptake. Tumours such as osteoid osteoma will often show a typical pattern of uptake that allows confident diagnosis.
3. Bone, joint and soft tissue injury

*Evaluation of suspected fracture when plain films are normal*

Particularly the:

- Wrist and hand: Scaphoid fracture detectable after 24 hours
- Foot and ankle: Impingement syndromes, talar dome injuries, stress fractures
- Hip: Non displaced hip fractures detectable at 48hrs.

![Fig 2. # L distal radius shown on bone scan (b) with initial normal x-ray (a). Repeat x-ray (c) following bone scan shows sclerotic area in distal radius.](image)

**Stress fractures:** Very sensitive. Can differentiate stress fracture from overuse syndromes such as shin splints.

**Other - enthesitis & tendinitis:** Changes at ligamentous attachments (enthesitis) eg plantar fasciitis or tendinopathies eg Achilles, de Quervain’s tenosynovitis.

**Non accidental injury:** Detects shaft and metaphyseal fractures and remains positive up to 3 months. May miss some metaphyseal fractures due to normal intense uptake in adjacent growth plate. Not appropriate for skull fractures.
4. Evaluation of chronic pain syndromes

Nuclear Medicine may be helpful in localising appropriate joints for steroid injection. Persistent back pain - active facet joint arthropathy can be differentiated from inactive disease (Pars interarticularis defects,) and other conditions such as infection and tumour eg osteoid osteoma and metastases but is less sensitive for the diagnosis of myeloma.

Joint pain in association with degenerative or inflammatory arthropathies eg identify the most active joints as well as associated impingement syndromes, and arthritis/sacro-iliitis distribution and activity,

Avascular necrosis eg Perthes, Keinboch’s or post traumatic such as head of femur following fracture. Initially cold while avascular then increased uptake as remodelling occurs (less sensitive than MRI).

Crush fractures - increased vascularity may persist for 6-8 weeks following injury
- delayed uptake may be increased for up to 2 years

Joint prostheses - the bone scan may suggest loosening, fracture, or infection. A radionuclide arthrogram is a sensitive method for the assessment of femoral stem loosening in the workup of a painful prosthesis.

Complex Regional Pain Syndromes (RSD) - characteristic pattern of increased blood flow and periarticular bone phase uptake.
Fig 6. Pars defect L5

Fig 7. Lumbar facet arthropathy - left L4/L5, right L3/L4
Bone

5. Evaluation of suspected bone or joint infection

The bone scan is usually abnormal 2-3 days following the onset of symptoms. Interpretation can be difficult when there has been recent surgery or a fracture as normal healing is associated with increased uptake.

In children a triple phase bone scan without resort to gallium will usually be sufficient.

In adults a bone scan followed by a gallium or labelled white cell scan may be optimal. This is particularly so for the evaluation of joint prostheses or the diabetic foot to differentiate infection from neuropathic arthropathy.

Fig 8. Osteomyelitis R greater toe in a patient with IDDM and non-healing wound

Fig 9. Infected left hip replacement
Bone

6. Evaluation of other bone diseases

Paget’s disease – monostotic vs. polyostotic, disease activity, malignant transformation

Fibrous dysplasia

Metabolic bone disease eg osteomalacia, hyperparathyroidism

Fig 10. Polyostotic Paget’s Disease
Cardiac evaluation of known or suspected coronary artery disease

assessment of left ventricular function - ejection fraction, wall motion & thickening

Cardiac imaging provides a non-invasive technique for the assessment of coronary artery blood flow and myocardial perfusion. This test is used to assess myocardial perfusion in a number of clinical situations:

The patient with chest pain of uncertain cause: Where ischaemic heart disease is suspected because of either chest pain or a positive ECG stress test a normal myocardial perfusion imaging study (MPI) will exclude significant coronary artery disease. The overall sensitivity and specificity for the detection of coronary artery disease is approximately 91% and 73%.

The patient with known coronary artery disease: MPI will determine the location and extent of suboptimal myocardial perfusion. This will help in determining the likely benefit to be obtained from coronary artery revascularisation. If a significant reversible perfusion abnormality is seen then further investigation with coronary catheterisation may be indicated.

1. Myocardial perfusion imaging

Regional perfusion can be assessed using Technetium labelled sestamibi and tetrofosmin, or Thallium. Tc-Sestamibi becomes intracellularly bound to mitochondria and undergoes minimal redistribution. Thallium is a potassium analogue that is transported into the cell by the Na/K ATPase pump and washes out over time.

The scan is performed in two stages. A stress study is undertaken using either exercise (treadmill or bicycle) or a pharmacological agent (dipyridamole). This is preceded or followed by a resting study. The radiopharmaceutical localises in the myocardium proportional to blood flow. The test is more sensitive and specific than an exercise ECG stress test and should be used where left bundle branch block precludes an exercise ECG for the assessment. A myocardial perfusion study using dipyridamole stress is an accurate means of assessing the presence and extent of significant coronary artery disease.

Where the clinical question is viability and a fixed perfusion abnormality is present, 24 hour Thallium redistribution imaging can be performed. The delay between injection and imaging allows time for the tracer to be taken up by viable but ischemic myocardium.

The study is displayed as a series of tomographic images in 3 orientations and with a polar map (“Bull's eye”) that compares the patients’ stress and rest images with a standardised database.
Cardiac

Three patterns are seen:

Normal stress and rest images – excellent prognostic indicator

Fixed perfusion abnormality on both stress and rest images: This can be seen following infarction without significant peri-infarct ischaemia and also with soft tissue attenuation. Characteristic patterns of soft tissue attenuation are seen in both males and females. Septal hypoperfusion can be seen as an artefact in left bundle branch block. Breast tissue may attenuate anteriorly and laterally, and sub-diaphragmatic structures inferiorly. Normal wall motion excludes transmural infarction as a cause of a fixed perfusion abnormality.

Abnormal perfusion on the stress images which reverses on the rest study. This is the characteristic pattern of myocardial ischaemia. The size and position of the abnormality gives a guide to the principle vessel or vessels involved.

*Fig 11. Large area of significant reversible anteroseptal ischemia in female with atypical chest pain.*
MPI with cardiac gating

Various software analysis packages are now available that allow assessment of regional wall thickening, wall motion and ejection fraction in addition to the perfusion data. During imaging (usually in the post stress phase), the R-R interval from the ECG is divided into separate time bins or gates (usually 8) and the counts collected through each cardiac cycle are allocated a time bin. This data is summed from the entire acquisition period and using a cine format can display an image of the beating heart. This technique has been validated against gated blood pool imaging, left ventriculograms and cardiac MR and been shown to be an accurate and reproducible technique.

2. Gated blood pool scanning

This uses Technetium labelled autologous red blood cells. Both left and right ventricular ejection fractions can be measured. This gives an accurate assessment of cardiac function and is indicated where serial measurements of LVEF are required eg patients on cardiotoxic chemotherapeutic agents. It is also useful for assessing systolic function in ischemic heart disease, cardiomyopathy, and cor pulmonale. Regional wall motion can be evaluated eg post infarct, ventricular aneurysms can be detected but echocardiography is superior.

3. Infarct avid tracers

Tc-Pyrophosphate can assess whether a recent myocardial infarct has occurred by localising in damaged muscle (2-8 days post event). This is useful in assessing non-cardiac causes of increased cardiac enzymes eg following trauma or surgery but is now rarely performed.
Lung

- suspected pulmonary emboli
- pre-op assessment for lung reduction surgery

The lung is most commonly assessed by combining studies of ventilation and perfusion.

Ventilation studies are usually performed with aerosolized liquid but radio-active gases or aerosolized particles can be used.

The perfusion study is performed after injecting macro-aggregated albumin which causes micro-embolisation of approximately 0.2% of the lungs capillaries before being degraded by macrophages.

**Indications:**

1. **Suspected pulmonary embolism**

   *A current chest x-ray is required in the interpretation of the lung scan.*

   The scan interpretation is usually made with reference to the PIOPED investigation which is the largest prospective trial of the investigation of patients with suspected pulmonary embolism to date. In this trial patients with suspected pulmonary embolism had both lung scans and pulmonary angiography. Detailed analysis of the findings has allowed the accurate assignment of the risk of pulmonary embolism according to the pattern of changes noted on the lung scan. The characteristic findings in patients with pulmonary embolism are segmental perfusion abnormalities, which are mismatched on the ventilation study. Interpretation will be assisted if previous lung scans are available for comparison.

   **The study is graded according to the number of mismatched defects into**

   - high probability
   - intermediate probability
   - low probability
   - normal

   Patients with a high probability scan can be assumed to have had pulmonary embolism and be commenced on anticoagulation.

   A normal lung scan excludes recent pulmonary embolism.

   A low probability lung scan confers an overall probability of 16% for PE, however, these will generally be small and not clinically significant.
Lung

Patients with an intermediate probability lung scan (20-79% risk or 30% overall risk) can be further categorised by reference to the clinical probability of PE.

Extensive matched defects which are commonly seen in long-term smokers are usually due to COAD. Further investigation with doppler venous ultrasound can be useful in this sub-group of patients. If lower limb DVT is confirmed then anticoagulation should be commenced without the need for further investigation.

The role of CT angiography for assessing PE is currently being evaluated. It appears to be most promising when there are abnormalities present on the CXR that would lead to difficulties interpreting the VQ scan or result in an intermediate lung scan interpretation.

2. Assessment of lung function prior to lobectomy or pneumonectomy

Regional and residual lung function can be accurately predicted using a perfusion lung scan combined with pulmonary function tests. A residual forced vital capacity of greater than 1 L will be required to allow survival without the need for supplemental oxygen.

3. Epithelial permeability (interstitial lung disease)

A Tc-DTPA ventilation study is used to assess absorption rates across the interstitial and alveolar membranes. The half clearance time will increase with inflammation and the result can be used to monitor treatment response in inflammatory lung disease.
4. Assessment of right to left shunts

A perfusion study is performed and the ratio of activity within the lungs against the rest of the body is calculated. Normally less than 5% of the tracer is shunted through the lungs into the systemic circulation.

5. Gallium

This can be used to assess parenchymal inflammation eg sarcoidosis, scleroderma, pulmonary fibrosis and the response to steroid therapy.
Urinary Tract

- assessment of hypertension where renal artery stenosis is suspected
- renal scarring following urinary tract infection in children
- follow up of urinary reflux
- suspected obstruction eg PUJ obstruction

**Indications:**

1. Renal function
   Can assess divided and regional function and calculate glomerular filtration rate
   - Preservation of poorly functioning kidneys considered for nephrectomy (10-15% residual function used as a cut-off)
   - Residual function following possible donation or resection
   - Response to revascularisation procedures
   - Assessment of equivocal obstruction after IVU or U/S

2. Assessment of obstruction vs. dilatation
   Obstruction is often first considered after finding dilatation on a prior imaging investigation. Nuclear medicine contributes little to determining the cause of the obstruction but provides functional information to assist management.
   
   Diuresis renography can provide information about renal function in obstruction and differentiate dilated non-obstructed systems from obstruction. If there is obstruction then flow will be impaired at high and low flow rates, if slow elimination is due to urinary stasis then the increased flow-rate produced by the diuretic will lead to washout of tracer.
   
   A time activity curve following the administration of furosemide is obtained. A half clearance time of less than ten minutes is normal and a time greater than 20 minutes is evidence of obstruction. A half clearance time between 10 and 20 minutes is regarded as equivocal and these patients will require follow up.

3. Assessment of renovascular hypertension secondary to renal artery stenosis
   Most hypertension is essential hypertension with a small number (0.5% to 5%) having secondary causes. Renovascular hypertension accounts for the majority of these causes. Renovascular hypertension, however, is a retrospective diagnosis established after demonstrating cure or improvement of hypertension following surgery or angioplasty for a stenosis.
   
   Doppler renal ultrasound and captopril enhanced renography are commonly used techniques for the assessment of suspected renal artery stenosis. Both have insufficient specificity (approximately 85%) to be used as general screening procedures.
ACE inhibitors accentuate physiological differences between the normal and dysfunctional kidney. Captopril reverses the angiotensin induced vasoconstriction and dilates the efferent arterioles reducing the intraglomerular pressure and therefore the GFR in the affected kidney. This exaggerates the asymmetric function between the ischaemic and contralateral kidney. A positive study is a good predictor of response to intervention. Difficulties may occur when there is bilateral disease and if the renal impairment is longstanding. The sensitivity is 83-94% and the specificity 85-100%.

4. Acute renal failure and transplant follow-up

DTPA or MAG3 renogram studies are routinely performed in the post renal transplant patient. Perfusion, function and drainage are evaluated. Alterations can be seen with acute or chronic rejection, cyclosporine toxicity, perinephric collections eg haematomas, lymphoceles, urinomas, abscess arterial, venous or ureteric obstruction.

Deteriorating renal function will often require a renal biopsy to make a definitive diagnosis.
Thyroid

- hyperthyroidism - Graves vs. thyroiditis
- thyroid nodules
- goitre
- thyroid cancer management and follow-up

Introduction:
Sodium pertechnetate is injected 20 minutes prior to imaging and an estimate of the amount of tracer uptake by the thyroid is made (normal 0.6-2.7%). Images of the distribution within the gland are then acquired.

Precautions: Interference with tracer uptake can occur following recently administered X-ray contrast media (up to 4-6 weeks), food high in iodine content (eg kelp and some vitamin preparations) and some drugs such as amiodarone.

Technetium is transported into the thyroid by the same mechanism as iodine but is not organified, therefore, agents that block organification such as propylthiouracil and carbimazole will not interfere with pertechnetate uptake.

Indications:
1. Hyperthyroidism
Allows differentiation of Graves disease from thyroiditis and an autonomous functioning nodule (Plummer’s disease).

2. Solitary/dominant nodule
For a patient presenting with a palpable thyroid nodule F.N.A. as the initial investigation is the most cost-effective means of assessment.

Ultrasound will detect nodules several millimetres in size in many glands that are not clinically significant and are below the imaging resolution of scintigraphy.

Scintigraphic detection of nodules

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<th>Percentage</th>
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<tr>
<td>&lt;5mm</td>
<td>unlikely</td>
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<tr>
<td>0.6-1cm</td>
<td>56%</td>
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<tr>
<td>1-2cm</td>
<td>92%</td>
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<tr>
<td>&gt;2cm</td>
<td>100%</td>
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</table>

Scintigraphy can assess whether the nodule is solitary or multiple, and the functional status.

10-15% are functioning nodules taking up tracer. This is virtually conclusive evidence that the nodule is benign.
The vast majority, however, are non-functioning nodules (85-90%) with an approximate 5-10% incidence of carcinoma. A non-functioning nodule that is solitary or a dominant nodule in a multinodular gland requires biopsy to exclude malignancy.

3. Thyroiditis
Acute thyroiditis can be associated with biochemical euthyroidism, hyperthyroidism, or hypothyroidism. The thyroid scan in the presence of acute thyroiditis will show diffusely reduced uptake by the thyroid. Thyroid dysfunction is reasonably common in the post partum period and the thyroid scan will allow differentiation of thyroiditis from Graves’s disease as causes of hyperthyroidism.

4. Goitre:

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<td>Diffuse/normal uptake</td>
<td>1. Diffuse non-toxic (simple) goitre</td>
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<tr>
<td>Diffuse/high uptake</td>
<td>1. Diffuse toxic goitre (Graves’s disease)</td>
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<td>2. Lymphocytic thyroiditis (Hashimoto’s)</td>
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<td>- early in disease</td>
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<td>3. Iodine deficiency</td>
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<td>4. Organification defects</td>
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<tr>
<td>Diffuse/low uptake</td>
<td>1. Subacute thyroiditis (De Quervain’s)</td>
</tr>
<tr>
<td></td>
<td>2. Iodine induced goitre</td>
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<tr>
<td></td>
<td>3. Hashimoto’s</td>
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<td></td>
<td>4. Lymphoma</td>
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<tr>
<td>Inhomogenous/normal uptake</td>
<td>1. Simple MNG</td>
</tr>
<tr>
<td></td>
<td>2. Hashimoto’s</td>
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</table>

Other indications:

5. Thyroid cancer - detection, staging and therapy (see page 31)

6. Upper mediastinal mass/retrosternal goitre

7. Developmental anomalies
   Neonatal hypothyroidism
   Masses in mouth/neck

8. Post-thyroidectomy neck masses
**Thyroid**

**Fig 15(a).** Grave’s Disease in young female with goitre and weight loss

**Fig 15(b).** ‘Cold’ nodule in a patient with a single palpable thyroid nodule
1. Parathyroid

The causes of primary hyperparathyroidism are

90% solitary adenoma
9% hyperplasia
1% carcinoma

Multiple adenomas are rare (MEN syndromes associated with parathyroid hyperplasia). Most patients with primary hyperparathyroidism are explored without prior imaging and 90% are cured with a single operation.

**Tc-Sestamibi washout study:**

Dynamic imaging is performed with a large field of view as the parathyroid glands may be located anywhere from the angle of the mandible to the aortic arch. Normal parathyroid glands are not seen. Tc-Sestamibi is taken up by both thyroid and parathyroid tissue but washes out more slowly from parathyroid tissue (this is related to the cell density within the adenoma and metabolic activity). Thyroid adenomas may also show a slow washout so may present diagnostic problems. The test may also be complemented by a pertechnetate subtraction study, as this agent is taken up by the thyroid but not by the parathyroids. SPECT imaging is often used to help with localisation of an abnormal focus.

Detection rates 60-85% (more successful with adenomas than hyperplasia as adenomas usually larger)

*Fig 16. Adenoma of R inferior parathyroid gland*
2. Adrenal cortical tumours
These studies were undertaken with a selenium-labelled cholesterol analogue but since the withdrawal of this agent can no longer be performed.

3. Adrenal medullary tumours
An iodine labelled catecholamine analogue, meta-iodobenzylguanidine (MIBG) is used. To avoid thyroidal uptake Lugol’s iodine is administered before and during the test period.

   - neuroblastoma
   - paraganglioma
   - pheochromocytoma

   Scintigraphy has approximately 85-90% sensitivity. Imaging is usually performed to assist localisation. It can evaluate suspicious adrenal lesions if biochemistry or other modalities such as CT are equivocal and it will also determine whether the lesion is solitary or multiple.
Brain

- differentiation of depression and dementia
- localise seizure foci where surgery is considered
- cerebral perfusion reserve

Technetium-HMPAO (hexamethylpropyl amine oxime) or ECD (ethyl cysteinate dimer) are lipophilic ligands that can be used to image the distribution of regional cerebral blood flow. They are administered intravenously and have a high first pass extraction by the brain. Once taken up by brain cells the tracer is fixed without significant redistribution over the next 6 hours. The pattern of tracer uptake reflects brain perfusion at the time of injection and because of its prolonged retention, imaging can be performed when it is more convenient for the patient.

**Indications:**

1. **Assessment of dementia**

Dementia may be due to a number of different causes, the most common of these are Alzheimer’s disease (presenile dementia of Alzheimer’s type), vascular or multi infarct dementia and the pseudo-dementia of depression. Patterns of perfusion abnormality typical for each of these diagnoses have been described and can assist in their differentiation.

**Alzheimer’s dementia** is associated with parietal and posterior temporal hypoperfusion which may be unilateral or bilateral. Posterior cingulate gyri hypoperfusion has recently been shown to be an early marker for Alzheimer’s disease.

**Vascular or multi infarct dementia** is usually associated with multiple discrete sites of hypoperfusion that do not cross vascular territories.

**Pseudo dementia or major depression** typically causes a reduction in perfusion involving the frontal lobes, usually bilaterally.

As the dementia worsens, hypoperfusion can become more widespread, reducing the ability of the scan to distinguish the different dementia types.

In patients with suspected early cognitive impairment, a normal scan has been shown, on follow up, to have a strong negative correlation with the development of Alzheimer’s disease.

2. **Localisation of seizure foci in the workup of temporal lobe epilepsy**

In the absence of direct clinical and EEG evidence the diagnosis of epilepsy is based primarily on history and the exclusion of other conditions that may mimic epilepsy. CT is often used as a preliminary screening test to exclude structural abnormalities. MRI can identify hippocampal atrophy on the side of the seizure focus in a large proportion of patients with TLE (temporal lobe epilepsy) using coronal T1 imaging. Approximately two thirds of patients with proven epilepsy will be successfully controlled with medication. The remainder may be candidates for surgery.
The most common histological abnormality seen in TLE is mesial temporal sclerosis. In the interictal period cerebral blood flow and metabolism is usually normal or may be reduced. Interictal scanning therefore has a low sensitivity.

During the ictus regional blood flow may increase by up to 300%.

Ictal studies are obtained by injecting the tracer during the seizure or within 30 seconds of completion, which allows visualisation of the blood flow changes occurring due to the high first pass extraction. If the injection is late, it may be given in the post ictal period, during which time regional cerebral blood flow and metabolism are reduced to a greater extent than in the interictal period. A large degree of individual variability in the onset and duration of this post-ictal period of hypoperfusion is recognised.

Extra temporal epilepsy can also be assessed, using the same techniques of ictal and inter ictal imaging.
Brain

3. Assessment of cerebrovascular reserve with Diamox
Assessment of cerebral autoregulatory reserve may be required in the evaluation of patients with known or suspected cerebrovascular disease especially prior to carotid endarterectomy. Diamox (acetazolamide) acts as a vasodilator and pre and post Diamox studies can be used in a manner analogous to the stress/rest protocol for myocardial perfusion imaging.

In a patient with a high-grade carotid artery stenosis, ipsilateral cerebral blood flow may be maintained due to maximal cerebrovascular autoregulation (dependent upon the adequacy of the circle of Willis). Diamox will increase cerebral blood flow in vascular territories that are not dependent on the stenosed carotid vessel for supply. The hemodynamically compromised area that is usually ipsilateral to the stenosis will already have maximal dilatation through auto-regulation and demonstrates relatively decreased perfusion in response to Diamox. The presence and extent of changes reflect the region of brain at risk during a perioperative hypotensive event. Stress and baseline studies are performed on separate days. The Diamox study is performed first as a normal result precludes the need for a baseline study.

This technique can also be used to differentiate vascular from non-vascular causes of reduced regional cerebral perfusion. In neurodegenerative conditions such as Alzheimer’s, areas of reduced perfusion should show a normal response to Diamox vasodilatation unless there is a significant underlying vascular component.

4. CSF studies
Tracers are injected intra-thecally to evaluate ventricular shunt patency, hydrocephalus (communicating, non-communicating and normal pressure) and suspected CSF leaks.

Ventriculo-peritoneal or atrial shunt patency is assessed by administering tracer into the shunt reservoir with serial imaging over the course of the shunt and subsequently of the abdomen. Patency of the distal limb of the shunt is confirmed if activity disperses throughout the peritoneal cavity by 20 minutes. Activity can reflux into the ventricular system and confirm patency of the proximal limb however, many shunts have a one-way valve between the ventricles and the reservoir.

CSF leaks either spontaneous or post traumatic can be assessed. Tracer is administered via lumbar puncture with serial imaging performed. Activity can be shown to track outside the subarachnoid space usually with 24 or 48 hour imaging. Counting of nasal pledgets and comparison with blood activity is a very sensitive test for CSF rhinorrhea.

Hydrocephalus of various types can be assessed by the administration of tracer into the subarachnoid space via a lumbar puncture. Activity ascends to the basal cisterns and disperses over the cerebral convexities or into the ventricles, depending on the pattern of CSF flow.
5. Brain Death

Confirmation of brain death is required for those patients who have been on long term cardiorespiratory support and show no evidence of neurological function. $^{99}$Tc-HMPAO is taken up and retained in perfused and functioning neurological tissue. Planar and SPECT imaging of the head is performed, the absence of cerebral tracer uptake supports clinical testing of brainstem reflexes in the diagnosis of brain death.

6. Tumour recurrence

Following surgery and radiotherapy for brain tumours, gliosis and scar formation can occur which on anatomic imaging can be difficult to differentiate from tumour recurrence. Thallium-201 and $^{99}$Tc-Sestamibi are agents that are taken up by metabolically active cells. Tumours more avidly take up these agents than scar tissue and activity ratios between the suspected recurrence and a similar area in the contralateral uninvolved brain have been used to differentiate these conditions.
Gastro-Intestinal Tract

a. Oesophageal transit studies
   achalasia, dysmotility, chalasia (scleroderma), reflux/aspiration

b. Gastric emptying studies
   diagnosis and follow-up of gastric paresis especially diabetics
   dumping
   post gastric surgery

c. Colonic transit studies
   Gallium citrate drink then image each morning for 3-5 days - distinguishes obstructed defecation from slow transit.

d. GI bleeding
   Acute GI Bleeding: This uses autologous labelled red blood cells. Bleeding is identified on sequential imaging. This will detect bleeding >0.1ml/min and localise it to the upper/lower small bowel or the colon.
   Chronic GI blood loss: This can be evaluated using chromium labelled RBC’s but requires 5 days of stool collection.
   Meckel’s diverticulum: Technetium as sodium pertechnetate is chemically similar to the chloride ion and is concentrated in stomach and ectopic gastric mucosa found in a Meckel’s diverticulum.

e. Malabsorption
   Assessed by various breath tests: steatorrhea, bacterial overgrowth, bile acid and B12 malabsorption

f. Inflammatory bowel disease
   Technetium or indium labelled white blood cells will localise active inflammation and delineate the extent of lesions in Crohn’s disease or ulcerative colitis. It can differentiate inflammatory strictures that may respond to medical therapy from fibrous strictures requiring surgery.

g. Abdominal infection
   Labelled WBC’s or gallium for intra-abdominal collections when other imaging modalities are unhelpful. Labelled leucocytes are a non-specific indicator of inflammation and scanning may be positive in inflammatory bowel disease (see above), suspected acute appendicitis, acute diverticulitis, pelvic inflammatory disease, aortic graft infection, severe gastritis, vasculitis, radiation enteritis, and graft versus host disease.
Fig 18. 99mTc-HMPAO whitecell scan. The patient has terminal ileitis associated with IBD.
Hepatobiliary studies are performed following the intravenous injection of Technetium labelled-IDA (immuno-diaceitic acid). Normally hepatic extraction peaks at 10 minutes and the bile ducts are seen shortly after followed by small intestinal visualisation by 15 to 45 minutes. The gallbladder is normally seen by 60 minutes.

**Indications for biliary imaging:**

1. **Acute and chronic cholecystitis**
   
   HIDA scanning is useful if ultrasound is equivocal. Visualisation of the gallbladder within 4 hours excludes acute cholecystitis with a sensitivity and specificity of >95%. Imaging however is usually only performed for 1 hour after tracer administration. The study can then be augmented with a small dose of morphine if the gallbladder is not visualised. This acts by increasing the pressure in the sphincter of Oddi. Persistent nonvisualisation of the gallbladder confirms acute cholecystitis. Visualisation of the gall bladder after morphine administration is a sign of chronic cholecystitis.

2. **Gall bladder dysfunction**
   
   Gallbladder emptying can be calculated following an infusion of a synthetic analogue of cholecystokinin (Sincalide or Kinevac). A gall bladder ejection fraction of >35% is normal. If gall bladder emptying is impaired chronic cholecystitis is likely.

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**Fig 19 Hepatobiliary scan demonstrating chronic cholecystitis with GBEF of 7% (normal >35%)**
Hepatobiliary

3. Sphincter of Oddi dysfunction

Cholescintigraphy can also be used to assess for sphincter of Oddi dysfunction following cholecystectomy using Sincalide/Kinevac.

4. Other

- bile leaks
- neonatal jaundice and biliary atresia

**Indications for hepatic imaging:**

Focal hepatic lesions are not uncommonly found on abdominal imaging with ultrasound or CT. Nuclear medicine techniques maybe helpful in further defining these lesions prior to FNA.

**Tc-labelled RBC** - Haemangiomas will show a characteristic pattern of increasing accumulation of labelled red blood cells with time. The test is highly specific for lesions greater than 2cm and may show lesions between 1 and 2cm. Lesions close to the portal vessels may be difficult to resolve.

![Tc-labelled RBC](image)

*Fig 20. Large Haemangioma in 5th segment of live (red arrow) with a smaller focus (black arrow) superiorly. Activity shown on the earlier images (a) becomes more prominent at 2hrs post injection (b)*

**Tc-sulphur colloid** - Colloidal particles are taken up by Kupffer cells and theoretically focal nodular hyperplasia will show normal uptake of colloid whereas adenomas and metastases will show absent uptake. The specificity is however low.
Other

a. Spleen

Denatured autologous RBC’s are avidly taken up by the spleen, allowing the sensitive and specific identification of splenic tissue. This can be used to assess masses seen around the spleen suspected to be splenunculi, for recurrent splenic tissue post-splenectomy (eg relapsed ITP), and splenic infarcts.

b. Lacrimal/Salivary

Lacrimal drainage can be assessed by instilling drops of $99^{m}$Tc-pertechnetate into one eye at a time and then imaging as activity passes down the lacrimal duct into the nasopharynx. Patency of the tear duct can be confirmed in a non-invasive physiological manner.

Salivary function can be assessed using $99^{m}$Tc-pertechnetate. Normally there is rapid uptake by the salivary glands (appearing along with the thyroid) with prompt, almost complete clearance of activity following gustatory stimulation (eg. lemon drink). This test can be used in the diagnosis of Sjogren’s disease as there is impairment of uptake and slow excretion of activity from both the major and minor salivary glands.

c. Tumours

Gallium and thallium for lymphoma – used for staging prior to therapy and in the assessment of residual bulk disease post therapy. Low grade lymphomas may show poor gallium uptake and in this setting thallium tends to be used.

Gallium, Thallium, Sestamibi, DMSA-V and even the bone seeking tracer MDP show non-specific uptake in a wide variety of tumour types. These include; sarcomas, mesothelioma, gliomas, melanoma and also differentiated thyroid carcinoma and breast carcinoma.

Other- $^{111}$Indium Octreotide (somatostatin analogue – carcinoid, islet cell tumours), $^{123}$I MIBG (catecholamine precursor – pheochromocytoma, medullary thyroid carcinoma) and radiolabelled monoclonal antibodies (eg Prostascint) are more specific tumour diagnostic agents.

d. Lymphoscintigraphy

Lymphedema vs. venous obstruction

Sentinel node studies

Lymphoscintigraphy is the imaging modality of choice for evaluating lymphatic function. It is a simple technique that uses radiocolloids to image regional lymph drainage.

For the evaluation of the swollen limb the injection is made intradermally into the first interdigital space of the foot or the second or third web-space in the hand.
Qualitative interpretation includes evaluation of the injection site (number and size of lymph vessels), lymph collectors (collateral vessels, dermal back-flow), lymph nodes (number, distribution pattern) and liver and spleen uptake. Quantitative assessment is not routinely performed.

The indications for performing the study are:

A) Investigation of the swollen limb when lymphedema, venous disease or lipedema is considered and other imaging investigations have been unhelpful.

B) Confirm diagnosis in primary and secondary lymphedema to distinguish peripheral obstruction from proximal lymph node obstruction and to determine residual lymphatic function and drainage pathways.

(Cannot differentiate between primary and secondary lymphedema)

Sentinel node studies

Lymphoscintigraphy has been used to map drainage basins in the surgical management of certain malignancies eg melanoma, breast, vulval and penile carcinoma. Pathologic examination of the first draining node (sentinel node) has been shown to be predictive of tumour spread and this is now being used in surgical planning of melanoma and breast carcinoma.

e. Haematology

Tc-Sestamibi is currently being evaluated in the assessment of Myeloma and other haematological malignancies.

Laboratory tests

- RBC volume, plasma volume – true verses relative polycythemia
- red cell and platelet survival, Fe, Cu, and B12 studies
Radionuclide Therapy

Therapeutic Nuclear Medicine is a growing area with many new compounds being labelled with therapeutic radionuclides. One of the most exciting areas is the labelling of monoclonal antibodies, for the treatment of B cell lymphomas. The rates of complete and partial remission in chemotherapy resistant and low grade lymphomas are very encouraging.

Benign Thyroid Disease

Graves’s disease, toxic multinodular goitre or solitary toxic nodules can be effectively treated with I-131. Euthyroid patients with multinodular goitre can also be treated however this is less effective as the aim of treatment is to reduce the size of the goitre.

Thyroid Carcinoma

I-131 has been used in the treatment of thyroid carcinoma since the 1940s. Following thyroidectomy and/or surgical debulking if required patients at intermediate or high risk for recurrent thyroid carcinoma are given 4-6 GBq of I-131 orally. This treatment has been shown to reduce the rates of recurrence.

Painful bony metastases

Strontium-89 and more recently Samarium-153 have become available as palliative treatment in patients with painful bony metastases. They can be used following failure of hormonal therapy and where external beam radiotherapy is inappropriate due the metastases being widespread. Both agents are available for the treatment of prostate carcinoma, and there is also HIC approval for the use of samarium for the treatment of breast carcinoma.

Radioimmunotherapy for B-Cell Non-Hodgkin’s Lymphoma (RIT)

Eighty percent of lymphomas are of B cell origin and can be divided into Low Grade, Intermediate Grade and High Grade. Symptomatic early stage NHL is treated with radiotherapy, while the higher grades are treated with a variety of chemotherapeutic and immuno-therapeutic regimes. Immunotherapy with “cold” Rituximab leads to partial or complete responses in 50% of patients with low grade NHL with usually only partial responses in 30% of patients with higher grade NHL. These regimes tend to have high initial response rates but virtually all patients relapse with subsequently lower response rates and shorter response durations. Patients that have relapsed after standard treatment regimes are candidates for RIT. Treatment with a number of $^{131}$I and more recently $^{90}$Y labelled antibodies has lead to overall response rates of 60-80% with complete responses in 20-30% of patients. Currently radioimmunotherapy in combination with chemotherapy regimes and its use as initial treatment or earlier in the treatment algorithm is being investigated.
**Positron Emission Tomography (PET)**

**Introduction**

Standard nuclear medicine studies use radionuclides that decay by releasing gamma photons from the nucleus, whereas PET uses positron emitting isotopes. PET agents are usually produced in a cyclotron and tend to be of low atomic weight and short lived. Positrons are positively charged electrons that rapidly annihilate with nearby negatively charged electrons releasing two geometrically opposed 511KeV gamma rays. The short half-life allows a high photon flux for imaging with good dosimetry. A crystal array surrounding the patient collects these photons simultaneously (coincidence detection) and from these incidents forms an image.

The most commonly used agent is the glucose analogue fluorodeoxyglucose (FDG). The positron emitting isotope fluorine-18 is substituted for a hydroxyl group in the glucose molecule. FDG uptake and subsequent retention is a marker of cellular glycolytic activity. The higher metabolic activity of tumours and their preference for glucose as an energy substrate and its non insulin dependent uptake leads to the high sensitivity and specificity of this agent in oncology, which is the main area of use. Many other PET radiopharmaceuticals are available which can be used to look at various biological processes. An example of this is C-11 methionine which is a labelled amino acid that is taken up and retained depending upon rates of cellular protein synthesis.

A local cyclotron has been established in WA to produce FDG and other tracers, and PET imaging is now available.

**Indications**

PET imaging has a potential application for a wide range of clinical situations. The indications currently being reimbursed in Australia include:

- Staging of non small cell lung carcinoma
- Solitary pulmonary nodule
- Recurrent melanoma
- Recurrent colorectal carcinoma
- Tumour response to treatment
- Staging newly diagnosed oesophageal carcinoma
- Staging and re-staging head and neck carcinoma
- Recurrent glioma and assessment of brain tumours
- Staging newly diagnosed gastric carcinoma
- Re-staging of Ovarian Carcinoma
- Staging of Cervical Carcinoma
- Epilepsy in Patients being considered for surgery
- Myocardial Viability Assessment
- Initial Staging of Sarcoma

Other applications may include:

- Infection imaging – FDG is taken up by activated leukocytes
- Cognitive impairment - Alzheimer’s
- Neuropsychiatric testing – brain activation studies using O-15 water
- In vivo imaging of gene therapy – used as a marker of reporter gene activity
Fig 21. Widespread metastatic disease in a patient with malignant melanoma
Paediatric Nuclear Medicine

Nuclear medicine has an important role in the evaluation of a broad range of pathology in children. Nuclear medicine procedures are safe, generally non-invasive and are well tolerated. Patient cooperation can be more difficult than in adults however reassurance, distraction, and immobilisation with an imaging jacket will usually be sufficient. Sedation is seldom required.

1. **Bone**
   - Trauma including non accidental injury
   - Limp/Non weight bearing
   - PUO/Septicaemia
   - Tumour evaluation and monitoring

2. **Renal**
   - Evaluation of suspected obstruction to drainage
   - Evaluation and follow up of urinary tract infection and vesicoureteric reflux
   - Transplant evaluation

3. **Gastrointestinal**
   - Gastric emptying and gastro-oesophageal reflux
   - White cell imaging in the management of inflammatory bowel disease
   - Colonic transit in the evaluation of constipation

4. **Hepato-biliary**
   - Conjugated hyperbilirubinemia in newborn infants – biliary atresia/neonatal hepatitis
   - Acute and chronic cholecystitis
   - Hepatocellular dysfunction in patients with cystic fibrosis

4. **Thyroid**
   - Congenital hypothyroidism/ectopic thyroid tissue
   - Goitre/thyroiditis/hyperthyroidism
   - Thyroid cancer

6. **Lung imaging**
   - Suspected pulmonary embolism
   - Differential lung perfusion in patients with congenital lung and cardiac anomalies

7. **Cardiac**
   - Myocardial perfusion imaging in patients with suspected coronary artery disease eg congenital anomalies, post Kawasaki’s disease
   - Gated blood pool study for the evaluation of left ventricular function in patients on cardiotoxic chemotherapy.

8. **Cerebral perfusion**
   - Evaluation of patients with refractory epilepsy who are being considered for epilepsy surgery.
Paediatric Nuclear Medicine - Bone

Three phase scintigraphy is routinely employed in the evaluation of the peripheries. Short periods of inactivity will result in a significant reduction in blood flow and uptake in the affected limb so it is critically important to evaluate the history and physical findings before attempting to interpret the bone scan.

Tomographic (SPECT) imaging is of most use in the evaluation of the spine but may be difficult to perform due to the requirement for prolonged immobilisation.

a) Trauma

Useful when radiological images are negative but significant bone injury is suspected. Increased bone uptake is seen with bone bruising, stress fracture and with overt fracture. The time since injury and the relative intensity of uptake give a guide to the most likely diagnosis.

Multiple trauma/non-accidental injury - Scintigraphy is particularly useful in demonstrating rib fractures as these are difficult to visualise on plain films and are indicative of a significant amount of force having been used in the production of the injury (generally occurring in infants who have been squeezed and shaken).

The bone scan will generally be positive after 24 hours and may show a persisting abnormality for between 3 and 6 months.

Stress injuries - may be seen in children and adolescent athletes. Sites involved include the pars interarticularis of the vertebrae (most commonly L4 or L5). Genetic factors are involved but this injury is more common in individuals involved in ballet, gymnastics, football and cricket. Spondylolysis may be recognised on planar bone images but is more accurately localised with tomography.

Accidental injuries recognised in toddlers include spiral fractures of the tibiae (so called Toddler's fracture), and fractures of the calcaneum and the cuboid.

b) Infection

Osteomyelitis is relatively common in the paediatric age group and most frequently affects children under 5 years of age.

usually results from haematogenous spread associated with bacteremia

Staphylococcus aureus is the most common organism

usually unifocal but can be multifocal particularly in neonates

Group B beta haemolytic in approx 30% neonates

long bones are predominantly affected (75%) of cases

metaphyses are the most common site of involvement

Abnormalities are evident on scintigraphy within 24-72 hours of symptom onset

Sensitivity and specificity approximate 95%
Paediatric Nuclear Medicine - Bone

Septic arthritis

involves the knee or hip in 70% of paediatric cases
bone scan shows increased periarticular uptake on all three phases
a tense hip effusion may reduce uptake within the femoral capital epiphysis as a result of tamponade of the intracapsular epiphyseal vessels. Although reduced uptake within the epiphysis may be seen with viral or transient synovitis this is more commonly seen with bacterial (septic) arthritis. A repeat bone scan following hip drainage is useful in demonstrating a return of normal vascularity.

Vertebral osteomyelitis and discitis

similar manifestations
discitis more commonly affects the younger child from 6 months to 4 years while vertebral osteomyelitis tends to occur in older children
tomography increases the sensitivity and specificity for this diagnosis.

c) Limp/Non weight bearing

The evaluation of the child presenting with a limp or non weight bearing can represent a significant diagnostic dilemma. Apart from trauma and infection other causes of non weight bearing include Perthe’s disease, Kohler’s disease (AVN of the head of the femur and of the tarsal navicular respectively) and primary or secondary bone tumours. Radiographic correlation is generally indicated following identification of an abnormality on scintigraphy.

![Image of Kohler's Disease (AVN) left navicular in 5yr old boy with limp](image)
d) PUO/Septicaemia
Skeletal scintigraphy can be informative in children with PUO or unexplained septicaemia. In these patients careful review of the spine should be undertaken looking for signs of discitis or vertebral osteomyelitis.

e) Tumour evaluation and monitoring
Skeletal scintigraphy is routinely undertaken in the evaluation of children presenting with solid tumours as well as with primary bone tumours. In the evaluation of solid tumours the bone scan is principally used to screen for the presence of skeletal metastases. In the evaluation of primary bone tumours the bone scan gives information about the associated vascularity, extent and the presence of skip lesions as well as the presence of skeletal metastases. Occasionally disseminated skeletal metastatic disease due to neuroblastoma will be identified in the child with suspected osteomyelitis.

Fig 22. Teenager with R knee pain and swelling. X-ray shows mass lesion, and bone scan shows no metastatic disease
Paediatric Nuclear Medicine - Urinary Tract

a) Evaluation of suspected obstruction

Suspected when urinary tract dilatation shown antenatally on ultrasound, or postnatally in the evaluation of the child with abdominal symptoms or a history of urinary tract infection (UTI)

The differential diagnosis includes
- vesicoureteric reflux
- obstruction to drainage
- dilatation without reflux or obstruction (non obstructed, non refluxing megasystems)

Diuretic renography is used to evaluate obstruction. Where there is dilatation of the ureter or demonstrated reflux placement of a draining bladder catheter is helpful.

b) Evaluation of urinary tract infection

All confirmed urinary tract infections in childhood require investigation of the renal tract to assess for underlying abnormalities.

Significant pyrexia associated with UTI is a good indicator of pyelonephritis. In the acute phase renal involvement is demonstrated most sensitively with DMSA scanning. Some protocols obtain a DMSA scan first which is used to determine the need for further investigations.

Alternatively investigation may consist of an early ultrasound, followed by an MCU and a DMSA study to assess for scarring at 3-4 months post infection.

Fig 23. 6yr F with history of R reflux nephropathy. DMSA scan shows scarring of R kidney tissue and reduced function of 27%
c) Vesicoureteric reflux

If vesicoureteric reflux is demonstrated on MCU and medical management is undertaken with long term prophylactic antibiotics follow up studies with nuclear cystograms at 1-2 yearly intervals are used to assess for spontaneous resolution. This is less likely to occur with higher grades of reflux or with associated anatomical abnormalities. The nuclear cystogram is preferred as the gonadal radiation dose is approximately 1/10 the radiation dose for an MCU. Sensitivity is slightly better with the nuclear cystogram however anatomical definition is not as great and so is less suitable for primary evaluation. Nuclear cystograms are also used in the evaluation of siblings under 5 years old as the incidence of reflux is reported at 25-30%.

Direct nuclear cystogram

Follow up of children with known reflux to assess for resolution and for sibling studies. The estimated gonadal radiation dose is approximately one tenth that for a radiological MCU

Indirect nuclear cystogram

An initial renogram is performed and imaging continued until tracer has cleared from the kidneys. Once the bladder is full a voiding study is performed and the kidneys are reviewed to determine if there is increasing activity to indicate reflux. This is not as sensitive in the detection of reflux as the direct cystogram however significant reflux is readily identified. It is suitable for older children or those who have had antireflux surgery assessment. Additional information with regard to renal function and drainage is obtained.

d) Transplant evaluation (see adult section)

Paediatric Nuclear Medicine - Gastro-intestinal Tract

a) Gastroesophageal reflux and gastric emptying

Gastroesophageal reflux and gastric emptying can be evaluated in infants with a milk scan. The patient is given a feed of labelled milk and continuous imaging is performed for an hour. Episodes of reflux can be identified on image review. Pulmonary aspiration is infrequently identified. The rate of gastric emptying can also be measured. In older children gastric emptying for solids can be evaluated following ingestion of a standard test meal.

b) Colonic transit for the evaluation of constipation

Constipation is a relatively common problem in children. It is frequently transitory and responds well to dietary modification and short-term laxative treatment. When it presents in infants an organic cause such as Hirschsprung's disease (rectal aganglionosis) needs exclusion. Older children occasionally present with a gradually worsening history of constipation resistant to treatment. In these children evaluation may include a colonic transit study which assesses the pattern and rate of transit through the colon. The study is performed over a 5 or 7 day period following ingestion of water containing a small amount of radioactive Gallium (half-life approx 3 days). Imaging commences at 6 hours. At this stage most tracer lies within the terminal ileum or within the caecum. The study can distinguish between slow transit and delayed (obstructed) defecation constipation. Normal colonic transit may occasionally be seen in patients with a history of constipation.
c) **White cell imaging in the evaluation of inflammatory bowel disease**

Autologous white cells are separated from whole blood by centrifugation and are then labelled with Tc-99° HMPAO. White cell imaging can demonstrate active inflammation within the small bowel as this portion of the bowel is not visible with endoscopy or colonoscopy. It can also monitor disease activity in patients with known inflammatory bowel disease. Because of uptake within the normal liver and spleen white cell imaging is less sensitive in the demonstration of hepatic and splenic abscesses.

d) **Meckel's scan**

25-40% present with painless PR bleeding before 2 years of age

approximately 50% of Meckel’s diverticula contain ectopic gastric mucosa. Acid production by these may cause ulceration and bleeding.

Tc 99° pertechnetate is selectively secreted by mucoid cells of the gastric mucosa and this allows visualisation of ectopic mucosa within the Meckel’s diverticulum.

The reported overall sensitivity is 85% and specificity 95%. Results are aided by pre-treatment with H2 receptor antagonists (cimetidine or ranitidine) for 48 hours prior to scanning. In a child presenting with active bleeding this can be given intravenously 4 hours before imaging. Imaging is performed for 30 minutes following tracer injection with delayed images being obtained at 3-4 hours delay.

**Paediatric Nuclear Medicine - Hepatobiliary**

a) **Jaundice**

Jaundice in newborn infants is most often physiological. Hemolytic causes are the next most common and the primary biochemical feature of these conditions is an unconjugated (prehepatic) hyperbilirubinemia.

Conjugated hyperbilirubinemia is much less common and any increase in the level of conjugated bilirubin above normal is cause for concern. In the newborn the differential diagnosis is primarily biliary atresia or neonatal hepatitis. Less common causes are choledochal cysts, alpha 1-antitrypsin deficiency and TPN related cholestasis in premature infants.

Choledochal cysts are commonly demonstrated on ultrasound and these may be demonstrated antenatally. The presence of a gall bladder does not exclude biliary atresia although the gall bladder is commonly not seen with biliary atresia.

The hepatobiliary scan is used to distinguish between biliary atresia and neonatal hepatitis. With biliary atresia there is good tracer extraction by the liver with no transit of tracer through to the bowel even at 24 hours. In neonatal hepatitis there is poor tracer extraction by the liver however tracer does transit through to the small bowel. Delayed images are necessary as transit may not be apparent until 24 hours. Pre-treatment with phenobarbitone for 5-7 days prior to scanning enhances uptake and excretion.
b) Acute and chronic cholecystitis
Although these conditions are less common in children compared with adults, cholecystitis should be considered in the differential diagnosis of the child presenting with upper abdominal pain. An ultrasound should be the initial investigation as this has a high sensitivity in the detection of cholelithiasis. If the ultrasound is negative a hepatobiliary scan can be used to diagnose acute cholecystitis. Gall bladder function can be assessed by measuring emptying following a fatty meal or an infusion of cholecystokinin. Abnormal function (dysmotility) is a useful marker of chronic cholecystitis.

c) Hepatocellular function
The hepatobiliary study can be used to assess hepatocellular function by measuring the rate of clearance of injected tracer. This has been used as an early marker of liver involvement in patients with cystic fibrosis.

Paediatric Nuclear Medicine - Thyroid

a) Congenital hypothyroidism
Thyroid scintigraphy has a limited role in the assessment of the hypothyroidism in the newborn, however this can show ectopic thyroid tissue and confirm normal uptake of tracer when there is an organification defect present.

b) Neck masses
The thyroid scan can be used to demonstrate the relationship of a neck mass to the thyroid. The anatomical relationship is best demonstrated with ultrasound however the thyroid scan can demonstrate uptake where ectopic thyroid tissue is suspected.

c) Goitre
Most goitres presenting in infancy are due to an organification defect in T4 synthesis or due to maternal ingestion of goitrogens. Most goitres presenting in late childhood or adolescents are due to Hashimoto’s disease.

d) Thyroiditis
Hashimoto’s thyroiditis (chronic autoimmune lymphocytic thyroiditis) is the most common cause of juvenile hypothyroidism. This is unusual before 5 years of age and the incidence increases during puberty. The most common presentation is with euthyroid goitre. Subacute thyroiditis is rare in children.

e) Hyperthyroidism
Most children with thyrotoxicosis have Graves’ disease and present with a diffuse goitre. Thyroid scintigraphy typically shows diffuse increased uptake. Chronic hyperthyroidism refractory to treatment can be treated with surgery or with radioactive I-131 ablation.

f) Thyroid Cancer
Thyroid cancer is rare in children and is managed similar to adults with thyroidectomy and post-operative thyroid ablation with I-131.
Paediatric Nuclear Medicine

Lung

a) Pulmonary embolism
Pulmonary embolism is infrequent in children compared with adults, however is seen following multiple trauma, associated with malignancy and with disorders of clotting. A chest x-ray followed by ventilation-perfusion imaging is used for diagnosis. The ventilation study is more often normal than in adults and this makes interpretation of the perfusion study more straightforward.

b) Evaluation of differential lung perfusion
Patients with congenital heart disease commonly have associated pulmonary artery abnormalities, which may limit lung perfusion. Differential lung perfusion can be measured with perfusion scintigraphy and this can be used to measure improvement post stenting.

Cardiac

a) Perfusion Imaging
Coronary artery disease due to atherosclerosis is rare in childhood however coronary artery lesions are seen as a result of congenital abnormalities and as a sequelae to Kawasaki disease (Mucocutaneous lymph node syndrome).

Perfusion is performed using either thallium, sestamibi, or tetrofosmin and may consist of rest or combined stress/rest imaging.

b) Gated Blood Pool Imaging
Gated blood pool imaging following reinjection of labelled red blood cells is used to accurately measure left ventricular ejection fraction. This is predominantly used in patients who require serial assessment of left ventricular function. These patients include those on cardiotoxic chemotherapy and those with cardiomyopathy.

Brain

a) Epilepsy
Cerebral perfusion imaging with Tc 99m HMPAO is used in the workup of patients with refractory epilepsy who are being considered for epilepsy surgery. An ictal study is performed by injecting the patient at the time of a typical seizure through a pre-sited IV line. This procedure is done as an adjunct to video EEG monitoring and may require inpatient monitoring for up to a week to capture a suitable seizure (see adult section).

b) Systemic Lupus Erythematosis
Cerebral lupus involvement can be sensitively demonstrated with cerebral perfusion imaging and can be used as a guide to treatment.
Technetium-99m

Technetium-99m is obtained from a portable generator by the radioactive decay of Molybdenum-99. The Technetium is removed by eluting the column with sodium chloride to obtain sodium pertechnetate. This is taken up by glandular tissue such as the thyroid, salivary glands, choroid plexus, and stomach and is promptly excreted by the kidneys.

Sodium pertechnetate has a chemical valency of seven but by simple reduction-oxidation reactions can be reduced to a valency of four that enables it to be bound to cellular components or chemical ligands. eg.

- HDP or MDP (phosphate compounds) for bone imaging
- DTPA or DMSA - renal uptake
- Macro aggregates of albumin - lung perfusion
- HMPAO (a lipophilic agent) transports Technetium into cells and across the blood brain barrier

Tc-DMSA

This localises in the renal cortex by binding to proximal tubules. It can assess the functional mass of the kidney and will provide differential uptake, even in renal failure.

It is primarily used in children allowing accurate assessment of renal scarring. It is also useful in the evaluation of pseudomasses found by other modalities eg prominent columns of Bertin and dromedary humps and for congenital renal malformations.

Tc-DTPA or Tc-MAG3

Functional images similar to an IVP provide information about perfusion, uptake and excretion. A time-activity curve, the renogram, is also derived. This can be quantified to derive cortical and whole kidney transit times to assist diagnosis. DTPA is solely filtered so estimates G.F.R. MAG3 is secreted by the renal tubules so estimates effective renal plasma flow.

Gallium

This is a radio-active metal that is handled similarly to iron. It is transported by transferrin and ferritin and reaches inflammatory sites via these plasma proteins, by lactoferrin in neutrophils, or through direct uptake by bacterial siderophores. It is used to image inflammation, infection and some tumours. Excretion via the colon can limit its use in assessing abdominal infections.

Thallium

This is also a radio-active metal that is handled similarly to potassium. It is transported into the cell by the Na/K ATPase pump and washes out over time. It is used predominantly to image viable myocardium but has a role in the investigation of some tumours eg thyroid, lymphoma and glioma as well as benign abnormalities of the parathyroid.
Iodine-131

This agent has both beta particle emission and gamma emission and because of the beta emission delivers a high dose to the patient. It is no longer used to image benign thyroid disease as this can be effectively achieved with sodium pertechnetate. It is used for imaging in thyroid cancer (both for the initial post-operative evaluation and for follow-up), as well as for therapy of benign and malignant thyroid disorders. It is the imaging component of MIBG, a compound used to image some neuroectodermal tumours.
Bioeffects and radiation dose

Technetium $^{99m}$ is a pure emitter of gamma rays (similar to x-rays). The half life is 6 hours, therefore, in the 24 hours following administration the Technetium will undergo 4 half lives of decay leaving 6.25% of the initial radioactivity remaining. For most compounds the additional effect of biological excretion will mean that less than this amount will remain after 24 hours.

For most studies involving Technetium as the radioactive agent the amount of radiation the patient receives will be approximately the same as that received by having a CT scan. Most diagnostic nuclear medicine studies will require an intravenous injection. Radioactive tracer compounds are administered in trace amounts and, as a result, adverse side effects including anaphylaxis are extremely unusual.

The calculation of radiation exposure following a diagnostic nuclear medicine scan requires consideration of the type of tracer administered, its biodistribution, and the physical and biological half lives of the compound. Radiation exposures are measured in units of milli Sieverts (mSv). The average exposure from background radiation in Australia is 2 - 3 mSv per year. Radiation workers are allowed an annual exposure of 20 mSv and members of the public 1 mSv.

No special precautions are necessary for family members or members of the public following a diagnostic nuclear medicine study. Pregnancy is a relative contraindication to a nuclear study and breast feeding may need to be ceased for a 24 hour period. Expression of breast milk and resumption of breast feeding after 24 hours is encouraged.

Comparative radiation exposures for nuclear medicine and radiological procedures are as follows (in mSv).

<table>
<thead>
<tr>
<th>Nuclear Medicine</th>
<th>CT Scan</th>
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<tbody>
<tr>
<td>Bone Scan</td>
<td>Brain</td>
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<tr>
<td>Lung Perfusion</td>
<td>Chest</td>
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<tr>
<td>Myocardial Perfusion (Thallium)</td>
<td>Abdomen</td>
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<tr>
<td>DTPA Renal Study</td>
<td>Pelvis</td>
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<tr>
<td>DMSA Renal Study</td>
<td></td>
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</tbody>
</table>

**Plain X-ray**
- Chest 0.02          
- IVP 4.6             
- Lumbar Spine 2.4    
- Barium
  - Oesophagus 2.0     
  - Stomach 5.0        
  - Small Bowel 6.0    
  - Large Bowel 9.0

*from Nuclear Medicine Science and Safety, pg 83, A C Perkins, John Libbey & Company 1995 (with permission)*
Nuclear Medicine Sites at Perth Radiological Clinic

**BENTLEY**
Bentley Health Service (B Block)  
Mills Street  
Ph: 9458 1373  Fax: 9350 5644  
Mon-Fri 8.30am - 5.00pm  Sat 8.30am - 12.00noon  
Multislice CT · OPG  
Dentascan · Lat Ceph  
X-ray · Ultrasound  
Mammogram · Doppler  
FNA · Nuclear Medicine  
Bone Densitometry

**JOONDALUP**
Nuclear Medicine WA  
Joondalup Health Campus Shenton Ave  
Ph: 9400 9830 (Appointments)  
Fax: 9400 9833  
Mon-Fri 8.30am - 5.00pm  
Service available to emergency department patients after hours

**MIDLAND**
Victoria Street Radiology  
21-23 Victoria St  
Ph: 9250 2829  Fax: 9250 2254  
Mon-Fri 8.30am - 5.00pm  Sat 8.30am - 12.00noon  
Multislice CT · OPG  
Dentascan · Lat Ceph  
X-ray · Ultrasound  
Mammogram · Doppler  
FNA · Nuclear Medicine  
Bone Densitometry

**ROCKINGHAM**
215 Willmott Dve  
Walwick  
Ph: 9592 1222  Fax: 9592 9893  
Mon-Fri 8.30am - 5.00pm  Sat 8.30am - 12.00noon  
OPG · Lat Ceph · Xray  
Ultrasound · Multislice CT  
Mammogram · FNA  
Doppler · Nuclear Medicine  
Bone Densitometry

**SUBIACO**
Magnetic Resonance Centre  
127 Hamersley Rd  
Ph: 9380 4888  Fax: 9380 4188  
Mon-Fri 8.30am - 5.00pm  
64-Slice CT  
MRI · Ultrasound · Doppler  
Dentascan · OPG · Lat Ceph · FNA · X-ray  
Tendon Shock Wave Therapy