Basic physics

A stable nucleus is one where the number of protons and neutrons are equal or nearly equal. However, this equilibrium can be disturbed by adding an extra neutron, a process that occurs in a nuclear reactor, or removing a neutron, which occurs in a cyclotron. The resulting nuclide (or isotope) is unstable and will decay to a more stable state by emitting energy (radiation), such as alpha, beta and gamma rays. This process is called radioactive decay and its application in medicine is for both diagnostic and therapeutic purposes.

Diagnostic nuclear medicine involves injecting a radioactive agent, intravenously. The agent is then taken up by organs and radioactive decay within the patient begins. Emitted gamma rays have high energy and a significant proportion leaves the body and can be detected and measured by a gamma camera. The majority of those radiopharmaceuticals used in diagnostic imaging are gamma emitters.

A gamma camera is a device that contains crystals that will react to particles of radiation producing a point light source (scintillation). The light is multiplied by a photomultiplier tube and recorded. The images are acquired over a period of time that ranges from a few minutes to half an hour depending on the amount of radiation emitted. The camera is placed next to the patient who will need to remain still for the duration of the study. As radiation is partly absorbed by tissues, it is usually necessary to image the area of interest from different angles and directions in each study.

Alpha and beta particles have much less energy and most of the energy will be absorbed by the patient. Radiopharmaceuticals that use alpha or beta radioactive decay as a marker will lead to much higher radiation dose than a gamma-emitting compound. Alpha and beta rays are charged...
particles which are directly ionising, causing damage to DNA. These particles are therefore potentially more dangerous. However, this property can also be used, under controlled conditions, to target cells (e.g. Y\(^{90}\) synovectomy). Currently, alpha and beta particle emitting agents have no useful role in diagnostic imaging.

The most widely used nuclide in diagnostic nuclear medicine is the metastable isotope of Technetium (Tc\(^{99m}\)). Its main advantages are that it is a pure gamma emitter and has a half-life of only 6 h which is long enough to perform a diagnostic study such as bone scintigraphy, but short enough to keep patient dose to a minimum. Tc\(^{99m}\) can be labelled with a variety of compounds called chelators, which stabilise the nuclide and direct it to the part of the body that needs to be imaged. For example, methyl diphosphonate (MDP) is taken up by osteoblasts and therefore Tc\(^{99m}\)-MDP is used for bone scintigraphy. Areas which have higher osteoblastic activity (e.g. metastatic deposits) will therefore take up more isotope and show up as hot areas on scintigraphy. However, a tumour that does not cause significant bone reaction (e.g. multiple myeloma) can be invisible on bone scan.

Single-photon emission computed tomography (SPECT) is a tomographic examination achieved by rotating the gamma camera 360\(^\circ\) around a patient who has been injected with a radioisotope. The camera stops at regular intervals (every 6\(^\circ\)), to detect and measure the gamma ray emissions. Computations allow the construction of an image that represents a slice of tissue in a similar way to a conventional CT scanner. However, compared to CT the resolution and noise are significantly worse. SPECT can improve the sensitivity for detecting small lesions by improving contrast and anatomic localisation compared to planar imaging. Its main applications are in bone scintigraphy, cerebral and myocardial perfusion imaging.

The basic physics of PET scanning

Positron emission tomography (PET) scanning is one of the most recent developments in imaging and although currently limited in availability in the UK, the number of PET scanners is likely to increase rapidly over the next few years.

The most widely used nuclide in PET scanning is deoxyglucose labelled with \(^{18}\)Fluorine. This isotope is taken up by metabolically active cells, most avidly by malignant cells. Radioactive decay then occurs with a half-life of 112 min. The radioactive decay produces two photons of gamma radiation of exactly 511 keV emitted simultaneously at 180\(^\circ\) to each other. This energy is detected and measured by a coincidence camera. Modern machines allow combined PET-CT imaging. This provides attenuation correction improving lesion detection at depth and providing anatomic localisation.

Bone scintigraphy

Radionuclide examination of the skeletal system remains a useful diagnostic method. Bone-seeking radiopharmaceuticals are used, most commonly Tc\(^{99m}\)-MDP (mono-diphosphonate). The initial accumulation of the technetium-labelled radiopharmaceutical in bone is primarily related to blood supply, although other factors such as the quantity of mineralisable bone, bone turnover, as well as hormonal influences play a part.

Factors that may be responsible for greater-than-usual activity are:

1. Increased osteoid formation
2. Increased blood flow
3. Increased mineralisation of osteoid
4. Interrupted sympathetic nerve supply

The converse is also true. Thus, in cases of cardiac failure and reduced cardiac output, bone scintigraphy may be of poor quality due to reduced delivery of radiopharmaceutical.

The normal study

It varies markedly in appearance between children and adults. In the child, areas of active epiphyseal growth are “hot” on bone scintigraphy. In the adult, skeletal uptake can be somewhat patchy in relation to the patient’s age; the older the patient, and the more osteoporotic, the patchier the uptake is likely to be. In addition, age-related degenerative changes within joints, discs, etc. can lead to foci of increased bone uptake. Areas of tendon insertion, constant stress and osseous remodelling will show increased activity. On the anterior view, there is prominent visualisation of the sternum, sterno-clavicular joints, shoulders, iliac crests and hips. Anterior views are, however, poor at demonstrating posterior structures as the radiation emitted from these areas will be largely absorbed by the body before it reaches the camera. As a consequence, it is important to use different views and to recognise that only those structures within 15–20 cm of the surface will be well visualised.
Indications for bone scintigraphy

1. Detection and staging of metastatic disease
2. Bone pain in patients with normal radiographs
3. Investigation of abnormal X-ray findings
4. Assessment of possible arthropathy
5. Prosthetic joints for signs of infection or loosening (together with MRI)
6. Differentiation between osteomyelitis and cellulitis

The principal use of bone scintigraphy is in searching for metastatic disease as it has a high sensitivity for this purpose. Bone scintigraphy typically will demonstrate metastases weeks or months before plain radiography. However, some tumours may produce false-negative bone scintigraphy. This phenomenon occurs most commonly with multiple myeloma deposits. Breast cancer metastases are occasionally cold on bone scintigraphy. Approximately 80% of patients with known malignancy and bone pain will have metastases documented by bone scintigraphy.

The abnormal study (Fig. 1)

Most metastases are multiple and relatively easy to detect by scintigraphy. However, in the case of solitary lesions, interpretation may be difficult. A single focus of increased uptake is usually secondary to benign disease. In the thorax, if two consecutive ribs are involved, this is most likely secondary to trauma. However, if multi-focal non-contiguous areas of increased uptake are detected, these are more likely due to metastatic disease.

Diffuse involvement of the axial skeleton by metastases can be deceptive; it may look simply like a remarkably good bone scan, with uniform uptake throughout. Closer inspection will show relative lack of renal uptake indicating the excessive bone activity; this constitutes a "Super-scan", and is most commonly due to metastatic prostate carcinoma.

When searching for metastatic disease, cold lesions on bone scintigraphy are also important. If the tumour is extremely aggressive and there is disruption to blood supply or if there is significant marrow involvement, then photon-deficient lesions may occur.

Some causes of hot lesions on bone scintigraphy

- Metastatic disease
- Primary malignant bone tumour (Fig. 2)

Figure 1 Anterior and posterior views of a radioisotope bone scan showing multiple areas of increased tracer uptake throughout the bony skeleton consistent with multiple metastases in a patient with prostate cancer.

- Osteomyelitis
- Trauma including stress fractures, non-accidental injury, loose prosthesis
- Osteoid osteoma
- Paget’s disease
- Fibrous dysplasia
- Arthritis
- Locally increased blood flow

Generalised:

- Primary hyperparathyroidism
- Renal osteodystrophy
- Multiple metastases (prostate, lung, breast)
- Haematologic disorders

Some causes of cold lesions on bone scintigraphy

- Overlying artefact from, e.g. pacemaker, barium, etc.
- Radiation therapy
Local vascular compromise, e.g. infarction, early aseptic necrosis
Early osteomyelitis
Tumour, e.g. Myeloma, plasmacytoma, breast carcinoma

Bone scintigraphy is of limited value in the local staging of primary malignant bone tumours such as osteosarcoma, since the assessment of tumour extent is usually complicated by reactive hyperaemia and thus markedly increased tracer uptake in much of the affected limb. In this situation, MRI is the examination of choice.

In the case of benign bone tumours, bone scintigraphy is even less useful since these do not usually accumulate tracer. The major exception to this is in osteoid osteomas, which demonstrate intense activity at the site of the nidus.

Soft tissue uptake
On occasion, soft tissue visualisation may be a confusing issue. There are various potential causes for this, the most important being:

- Poor radiopharmaceutical preparation
- Renal failure
- Urine contamination
- Tissue infarction
- Myositis ossificans and other causes of soft tissue calcification/ossification

Figure 2  (a) Plain X-ray of the left humerus in a 13-year-old shows an aggressive bone-forming lesion in the proximal humeral diaphysis. (b) Radioisotope bone scan shows an area of markedly increased tracer uptake corresponding to the abnormality seen on plain film. This was biopsied and histology showed an osteosarcoma. The foci of increased uptake in both proximal humeri represent normal activity around the growth plates.
Amyloidosis

Certain soft tissue tumours, e.g. mucinous ovarian, colon, uterine fibroids, hepatic mets.

Use of bone scintigraphy in trauma

In general, an examination will be abnormal within 24 h after a fracture, and usually remains active for a length of time, which is variable and age-dependant. Typically, bone scintigraphy has been used in the assessment of subtle trauma such as that from stress fractures which are often difficult to identify on plain film, and also in the detection of occult scaphoid fractures. Nuclear medicine studies will only be reliable a few days after the injury as the bone needs time to react to the insult to change in its vascular supply and to alter the metabolic turn over. On the other hand, MRI will detect fractures as soon as they occur and it has greater resolution. For these reasons, MR is superseding bone scintigraphy in trauma.

In the case of the suspected non-accidental injury in children, bone scintigraphy is of limited use in excluding areas of increased bone activity that may represent fractures. Interpretation must be cautious, however, in view of the markedly increased activity around the growth plates.

Scintigraphy is particularly useful for detecting stress or fatigue fractures, which are among the most common skeletal injuries in physically active patients, when most stress fractures result from repetitive local stress on normal bone that causes excessive bone resorption, collapse of the bony trabeculae, and micro-fracture. Insufficiency fractures result from routine physical stress on a weakened bone (Fig. 3). Osteoporosis, corticosteroid therapy, and metabolic bone diseases are common predisposing factors for insufficiency fractures. In addition to the vertebrae, the sacrum is a common site for an insufficiency fracture that can cause unexplained low-back pain, especially in elderly women with osteoporosis. The bone scintigraphy typically demonstrates bilateral linear uptake in the region of the sacral alae with transverse uptake in the mid-sacrum which appear as an H shape on the posterior image and this is described as a “Honda” sign. All these lesions may be detected by MRI.

Assessment of joint prostheses

In the initial post-surgical period, activity is noted around the prosthesis, although this usually decreases rapidly and returns to normal within 12 months around the hip, and 18 months around the knee. Persistent activity around the tip of the prosthesis may be taken as an indication of loosening. More generalised activity can be due to infection around the prosthesis. This issue may be studied further by means of labelled white cell scintigraphy which will be positive in the case of infection. However, aspiration of the joint and instillation of local anaesthetic is also an efficient way of detecting sepsis, that will additionally identify the organism and prove that it is the joint that hurts. In many practices, joint puncture has replaced scintigraphy as the primary means of diagnosis in potentially infected prostheses.

Use of bone scintigraphy in benign, non-neoplastic disease

Paget’s disease of bone classically displays marked increased activity in the involved skeleton. Scintigraphy may be used to search for occult disease but is not normally indicated in the routine management of this condition.

Fibrous dysplasia, will be active on bone scintigraphy; therefore the technique may be a useful tool in searching for polyostotic involvement.

Diagnosis of osteomyelitis

Three-phase skeletal scintigraphy, consisting of a radionuclide angiogram, an immediate post-injection “blood-pool” image, and 2–3 h delayed images can be used when the diagnosis of osteomyelitis is in question. In these cases, increased tracer uptake will be observed during both the angiographic and the blood pool images at the site of infection.
However, MRI has virtually replaced scintigraphy for this indication.

**Bone marrow scintigraphy**

This may be used to identify bone marrow replacement by tumour or locate active sites for biopsy. It has also been used to assess femoral head blood supply. 99mTc-sulphur colloid is used, which localises to marrow since it is phagocytosed by the native reticuloendothelial cells. Again MR is generally the preferred imaging method for tumours and marrow involvement.

**SPECT (single-photon emission computed tomography)**

The development of SPECT has enhanced the contrast resolution of bone scintigraphy by screening out overlying or underlying tissue. This results in improved detection and localisation of small abnormalities, especially in the spine, pelvis, and knees. In some cases, increased activity not clearly seen on the planar images can be definitively demonstrated with SPECT. Tc\(^{99m}\)-MDP is employed, and the use of SPECT makes it possible to generate tomographic, multi-planar images of skeletal structures within the field of view of the camera.

**White blood cell (WBC) imaging**

This examination technique involves labelling the patient’s own WBCs with the radioactive tracer. The agents used most often for labelling are indium and Tc\(^{99m}\)-hexamethyl propylenamineoxime. Labelled WBCs usually accumulate in areas of infection but not in areas of increased bone turnover. Due to the increasing use of MRI in diagnosing bone and joint infection, WBC imaging is mainly used in the case of suspected multi-focal infection. The delineation of infected prostheses is also a potential use. When the appearance of the white cell scan is controversial, further information may be obtained by performing a marrow scan using technetium labelled with sulphur colloid. This will show up any areas of marrow “rests” which have been implanted during surgery.

**PET (positron emission tomography)**

Better diagnosis and follow up of bone and soft-tissue infections, particularly in joint replacement patients, are major benefits of PET.

A patient undergoing a PET scan is injected with the radiopharmaceutical 18-fluorodeoxyglucose about 45 min before the examination. The radiopharmaceutical tracer emits signals which are picked up by the PET scanner. A computer then reformats the signals into images that display the distribution of metabolic activity as an anatomic image. The more metabolic areas show up more brightly on the scan. The most important emerging use of PET in skeletal radiology is in the assessment of metallic implant-associated infection, owing to its superior spatial resolution. The role for PET is, however, limited by the fact that prosthetic joint loosening can give rise to a positive PET scan as can degenerative joint change. WBC scanning is certainly more specific for infection and joint aspiration has a primary role in most cases.