An introduction to nuclear medicine

Abstract Nuclear medicine is the injection, ingestion or inhalation of a radiopharmaceutical for the purpose of diagnosis or therapy. It shares imaging synergies with both planar / general x-ray and to computed tomography (CT) in its acquisition methods. Nonetheless, the prime difference is that the focus of planar x-ray and CT is on morphology or anatomy while nuclear medicine has a focus on the evaluation of function or physiology. The history of nuclear medicine follows similar timelines to that of x-ray. Nuclear medicine, however, had a slower recognition and clinical permeation of its imaging / treatment methods and strengths as well as a delayed recognition of the dangers of these forms of ionising radiation. Both planar x-ray and planar nuclear medicine, and x-ray CT and single photon emission computed tomography (SPECT) have emerged with greater integration in order provide improved diagnostic utility of each modality; the whole is greater than the sum of its parts. The strengths of x-ray imaging modalities and the treatment approaches used in radiation therapy are well understood by diagnostic radiographers and radiation therapists. An understanding of the technical and clinical aspects of nuclear medicine and its imaging and treatments strengths can provide improved service provision and patient care.

Keywords: history, imaging principles, nuclear medicine, radionuclides.

JM Wheat[1,2]
BAppSci(RT), MMedRadSc(NM), MHlthSc(HM), DHlthSc

GM Currie[1,2]
MMedRadSc, MAppMngt, MBA, PhD

R Davidson[1]
BBus, MAppSc(MI), PhD

H Kiat[1,2]
MBBS, FRACP, FACP

[1]School of Dentistry and Health Sciences, Faculty of Science, Charles Sturt University, Wagga Wagga, New South Wales 2650, Australia.

[2]Australian School of Advanced Medicine, Macquarie University, Sydney, New South Wales 2109, Australia.

Correspondence to jwheat@csu.edu.au

Introduction

This article is designed to provide a broad introduction to general nuclear medicine. General nuclear medicine includes single photon emission computed tomography (SPECT) studies. While positron emission tomography (PET) shares some similar principles to general nuclear medicine, PET represents a unique modality that requires separate consideration; analogous perhaps to magnetic resonance imaging (MRI) as an extension beyond general x-ray principles.

Nuclear medicine is the injection, ingestion or inhalation of a radiopharmaceutical for the purpose of diagnosis or therapy. A gamma camera is utilised to detect and quantitate the invivo biodistribution

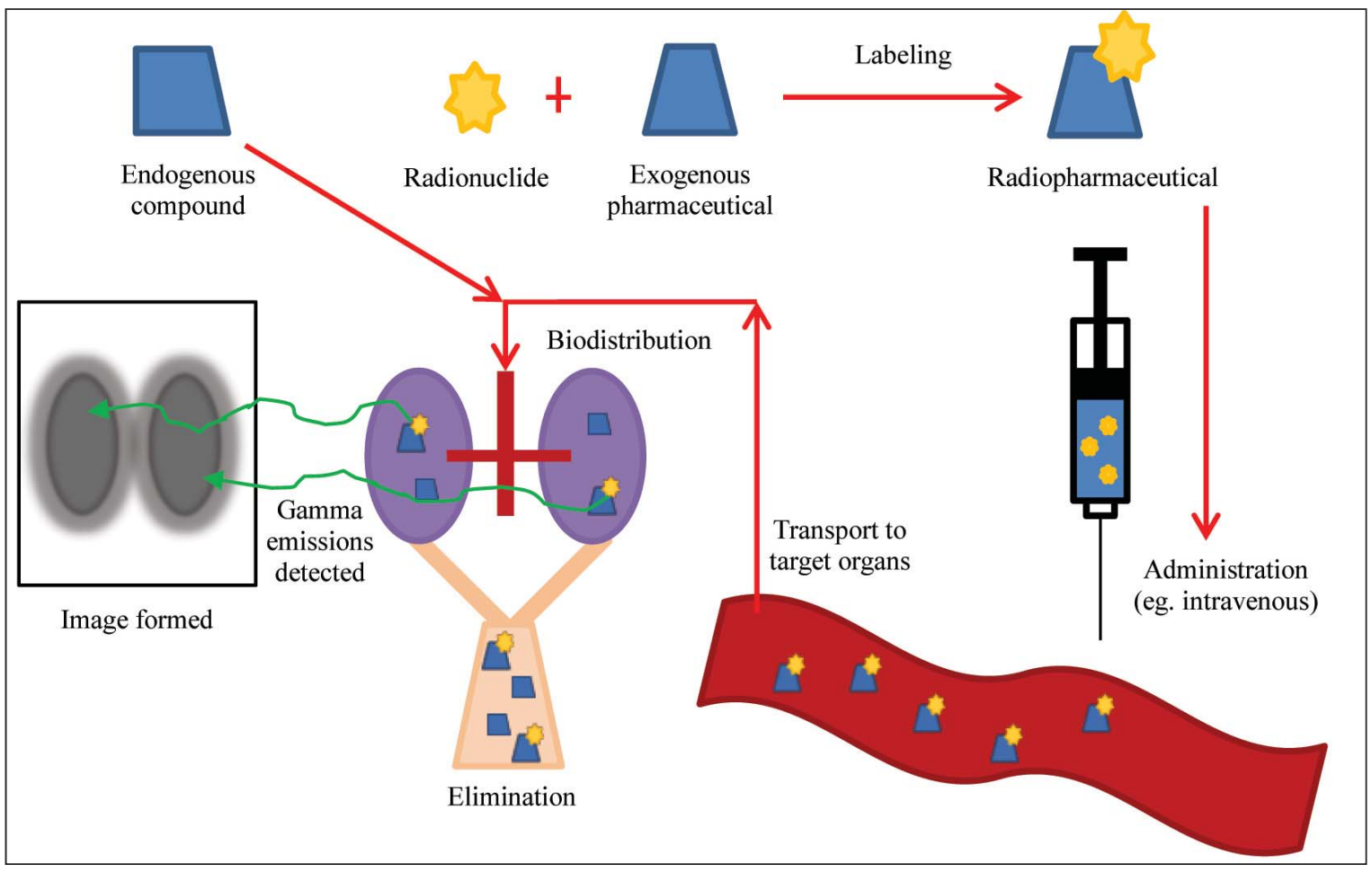

Figure 1: Schematic representation of the basic principles of nuclear medicine. An exogenous version of a naturally occurring endogenous compound is produced to localise in a particular physiological manner (eg. phosphate metabolism into bone). A radionuclide is tagged or labelled to the exogenous compound to produce a radiopharmaceutical. The radiopharmaceutical is introduced to the biological compartment (eg. intravenous injection) and biodistribution follows. The exogenous compound distributes and competes with the endogenous versions. The gamma emission associated with the radiopharmaceutical allows external detection and, thus, imaging of its biodistribution. The radiopharmaceutical is generally eliminated in the same manner as the endogenous variety.

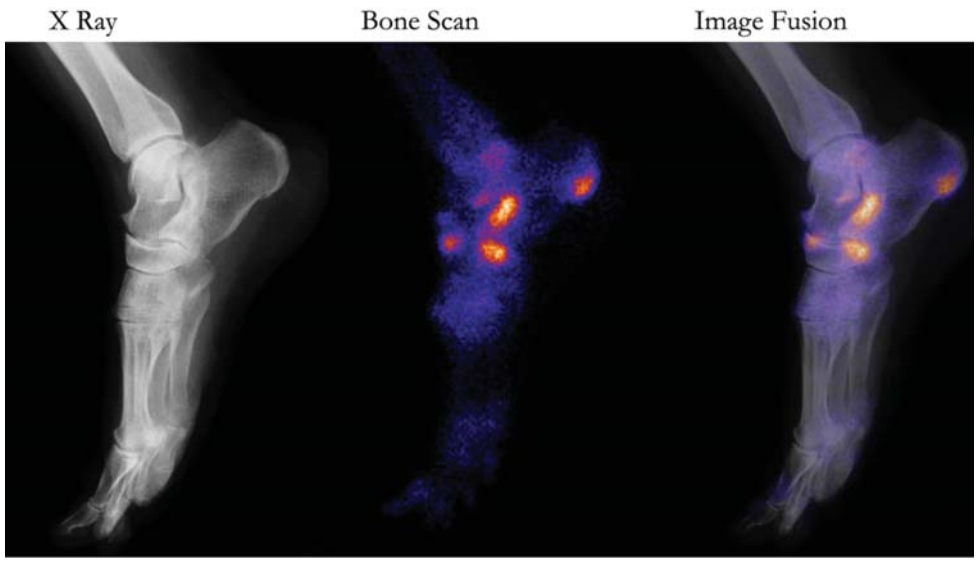

Figure 2: Anatomy (x-ray) and physiology (bone scan).

of the radiopharmaceuticals. It is important to note that the biological processes take place with or without the radiopharmaceutical, the radiopharmaceutical only makes it possible to image this physiologic or pathophysiologic process by tagging or labelling the appropriate compound (Figure 1). Since nuclear medicine employs compounds (or their analogues) that are found naturally within the body, it is extremely rare for a patient to have an adverse reaction to the radiopharmaceutical. Exceptions to this do exist with some specific innovative tracers like monoclonal antibodies that may elicit an immune response. Otherwise, sensations experienced by patients at the time of administration (particularly intravenously) are on the continuum describing a vasovagal reaction.

How does nuclear medicine differ from x-ray? Fundamentally, nuclear medicine principally evaluates the function (ie. physiology or pathophysiology) of organs and systems while x-ray chiefly evaluates form or morphology (ie. anatomy). It is true that x-ray, computed tomography (CT), and MRI can image function and likewise nuclear medicine can image morphology or structure. But it is fair to say that x-ray technology is far better equipped to image anatomy than scintigraphy and that scintigraphy provides a different level of physiological evaluation (Figure 2). Nuclear medicine is capable of tracing the most intricate biological pathways by simply taking a compound that is known to (or should) behave in a certain way within the body (ie. follow a particular biological pathway) and attach it to a radioactive substance.

The history of nuclear medicine

The history of the individual disciplines that comprise the medical radiation sciences are intertwined. The discovery and harnessing of the x-ray and gamma rays in diagnosis and therapy have had a profound impact on medicine and, indeed, the way people live their lives. From the irradiation of food through to global security, the application of radiation has become an integral part of our lives. The historical discoveries outlined briefly below represent key events in transforming modern medicine and, indeed, in the subsequent evolution and revolution that is enjoyed in medicine today.

While most of the scientific community were focusing their attention on x-rays and the cathode tube, the French scientist Henri Becquerel discovered radioactivity in 1896; spawning nuclear medicine. Unlike x-rays (that were almost immediately and universally applied to medical practice), some time would pass before any semblance of the industry referred to as nuclear medicine developed. While working with uranium, Becquerel noticed that photographic material would be exposed (fogged) if in close proximity to uranium.[1] The main difference between the discovery of x-rays and radioactivity was that, unlike x-ray, other scientists had not made similar observations. For Roentgen, his findings provided science to the anecdotal evidence of many others and, was intuitive and immediately adopted. Moreover, the very visual evidence conjured immediate scientific, social and medical applications. Becquerel, however, was not able to generate the same degree of enthusiasm for his discovery. Several years later (1898), the Polish Marie Curie and her French husband Pierre discovered radium and interest in radioactivity became more widespread.[1] Radium very quickly replaced x-rays for industrial radiography. In 1899 Rutherford discovered alpha and beta particles and in 1900 Villard discovered gamma rays.[1]

Alexander Graham Bell briefly dabbled in nuclear medicine, suggesting the use of radioactive sources to treat tumours in 1903 and in 1913 it was reported as useful for various diseases.[1] While these activities represent the pioneering days in nuclear medicine, they also represent the early years of radiotherapy. Nonetheless, radionuclide therapy remains a central activity in nuclear medicine quite independent of the applications of radiotherapy today.

Nuclear medicine itself tends to be characterised by the functional assessment of a biological and metabolic process. In the 1920s, radioactive phosphorus was used in animals to, for the first time, show metabolic processes in an intact animal – the bone scan.[1] Not long after, phosphorus-32 (^{32}P) was used to treat a patient with leukemia. ^{32}P remains a popular radionuclide for therapy and the bone scan (albeit without phosphorus) is the most common nuclear medicine procedure today. Radioactive iodine was used to study thyroid physiology in the late 1930s and is used today for therapy and imaging.[1] Strontium-89 (^{89}Sr) was first evaluated in 1939 and is still used today for palliation of painful bone metastases.[1] While beta emissions are very useful for therapy, they are not particularly good for imaging and radionuclides with gamma emissions were required for nuclear medicine to make any advances.

The key breakthrough in nuclear medicine came in 1939 with the discovery of Technetium-99m (^{99m}Tc) by Italian Emilio Segre and American Glenn Seaborg.[1] This allowed crude functional assessment (eg. inject in left arm and measure intensity and timing for transit to right arm with a detector). In 1951 the first scanner was developed by Cassen (rectilinear scanner). A number of other key milestones in nuclear medicine include; the first annual meeting of the Society of Nuclear Medicine in 1954, the emergence of the scintillation camera in 1958 (basis of current technology), commercial availability of ^{99m}Tc generators in 1960, introduction of emission tomography in 1962, and commercially available SPECT cameras in 1976.[1] The emergence of digital technology, computer technology, reconstruction algorithms, multiple detector cameras and hybrid SPECT/CT devices, combined with radiopharmaceutical developments, have all enhanced the capabilities of nuclear medicine while the underlying principle remains fairly constant since the late 1970s.

Since the discovery of x-rays and radium, knowledge / attitude toward radiation safety has been pendulous; at the peril of patient and health practitioner alike. While the mis-use of x-ray is well reported (hair removal in beauty salons, shoe fittings, x-ray portraits, and even party games), abuse of radium was more liberal in the early years.[2] Radium was popular as an ingested tonic, socialites served radium cocktails,

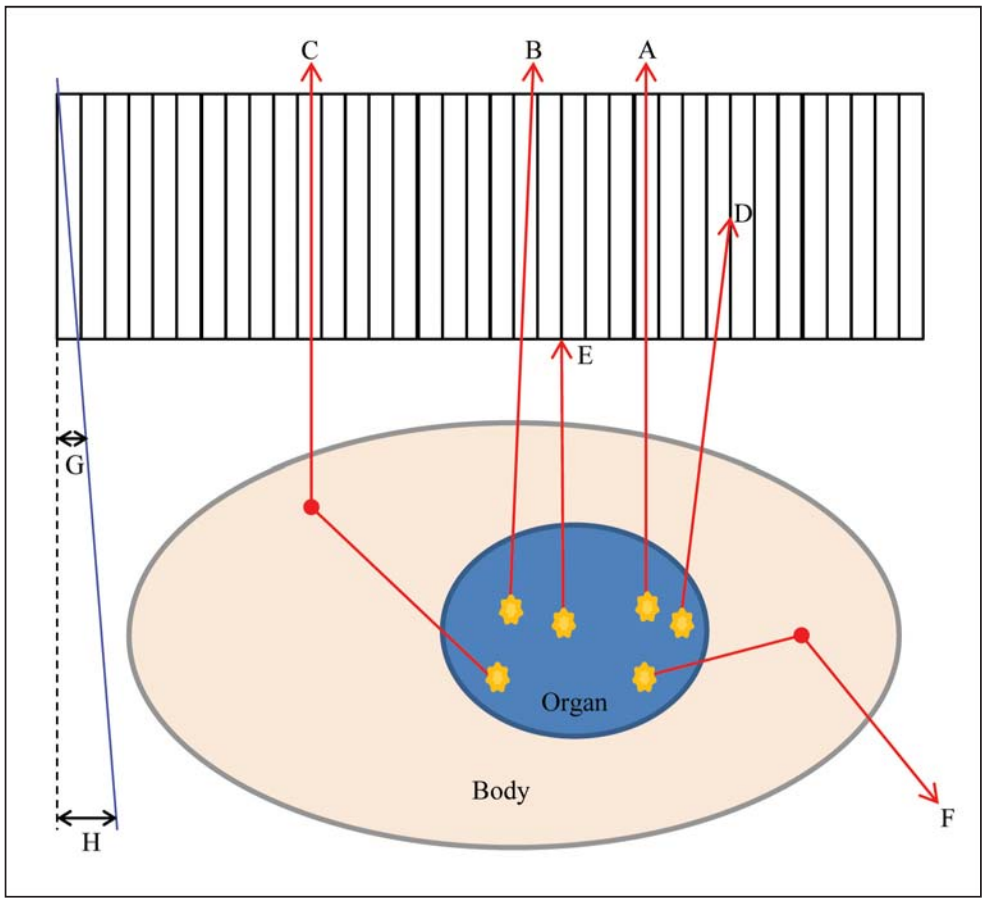

Figure 3: Depiction of the operation of the collimator. The collimator is the interface between the patient and the detector system; serving as a physical discriminator of photons based on their angle of incidence. Photons incident perpendicular to the imaging plane (A) generally pass through the collimator to interact with the detector. Photons incident at a small angle defined by the septal length and the 'hole' size are also detected (B). It is possible for events that are scattered to be incident perpendicular to the detector (C) and this will mis-register the location of the event if included in the image. Photons incident outside the small window about 90 degrees (D) will be absorbed by the septa. Sensitivity of the system can be reduced through smaller 'holes' (increased resolution) because it increases the cross sectional surface area of the septa for elimination of events incident perpendicular to the detector but 'in line' with the septa (E). Other events, including those that might otherwise be incident perpendicular to the detector, may undergo scatter events that take the event outside the field of view of the detector (F). Clearly, lengthening the septa or adding septa (smaller 'holes') will convert event B to a type D event. The impact of the acceptable range of incident angles can be seen to the left of the figure with the mis-registration error increasing with distance from the detector (G to H; front of body to back of body) which highlights the importance of imaging an organ as close to the detector as possible (see also Figure 4).

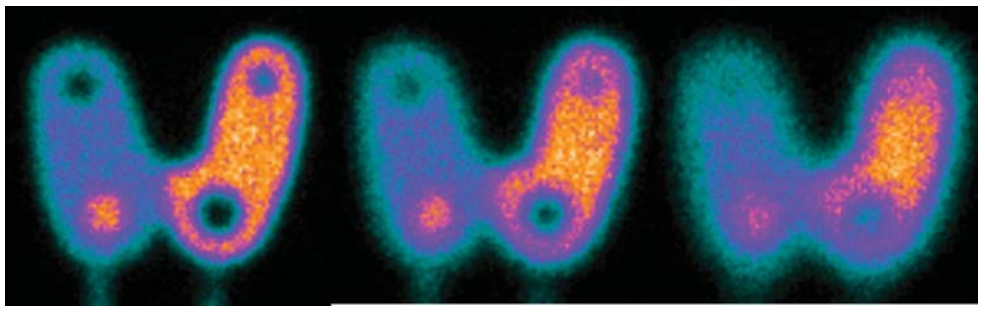

Figure 4: A series of images of a thyroid phantom with various size 'nodules', positioned identically but positioned with the detector 0 cm (left), 5 cm (middle) and 10 cm (right) from the phantom. It is clear from these otherwise identical images that a significant degradation in resolution and contrast results from increasing the object to detector distance. This is evident in the 'blurred' boundaries, decreasing lesion size and eventual lack of lesion detection.

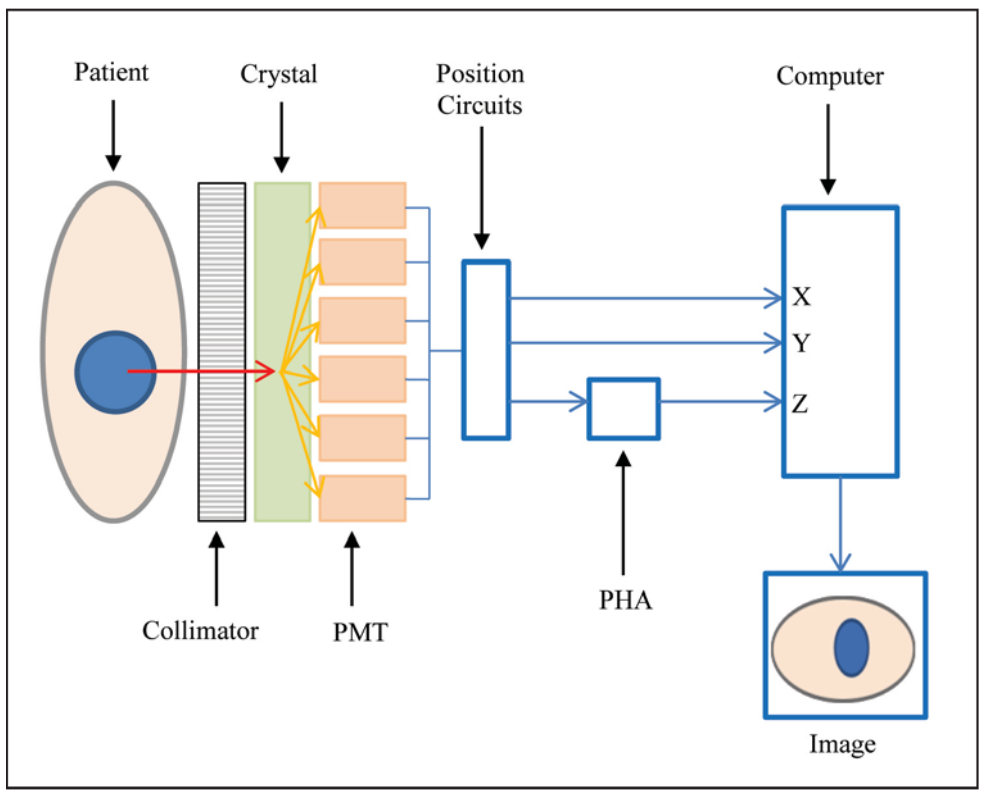

Figure 5: Schematic representation of the basic operation of a gamma camera. Photons emitted from the body incident perpendicular to the detector are 'trapped' in the crystal; converting the energy to a light emission. The light is detected by the photocathode of the photomultiplier tube (PMT) and converted to an electrical impulse which is amplified through the PMT. Position circuitry provides an X and Y coordinate for each event and that event is registered in the image if a Z signal is also received from the pulse height analyser (PHA) where scatter events are eliminated.

radium toothpaste and radium contraceptive jelly were available, and these represent but a fraction of the commercial exploitation of radium.[2] The popularity of radium is perhaps typified by the use of radium paint throughout the 1920s to produce luminescence; watch dials, dolls eyes, religious artifacts to list but a few applications.[2]

Basic imaging principles

The basic principle of the gamma camera is to externally detect the biodistribution of the administered radiopharmaceutical. Emission of radioactivity, usually a gamma emission, facilitates this process. A revision of the interactions of gamma, alpha and beta emission in tissue (or matter) is beyond the scope of this article, however, it is an important basis for the following discussion. Photons emitted from the patient first encounter the collimator which acts as a physical discriminator to eliminate photons from the resulting image whose angle of incidence varies from approximately 90 degrees to the image plane (Figure 3). Thus, a single image reflects a 'planar' image. That is, one might expect the origin of a detected photon to originate at some point along the line projected back through the patient at 90 degrees to the detector face. The emission of a photon from an unstable nuclei is random in direction and the lead or tungsten septa of the collimator is designed to absorb photons not incident at approximately 90 degrees. The size and/or length of the 'hole' or space between septa (generally a hexagonal array) govern the variation from 90 degrees of the accepted angle of incidence (larger and/or shorter holes have a larger window) and, thus, impact on image resolution and sensitivity. The distance the object is from the detector has a significant bearing on image resolution (Figure 3 and Figure 4).

Incident photons passing through the collimator interact with the crystal. In the traditional gamma camera the crystal is inorganic sodium iodide although there have been recent advances in solid state or semiconductor detectors (eg. CZT or cadmium zinc telluride). The energy of the incident photon causes excitation in the crystal which, on de-excitation,

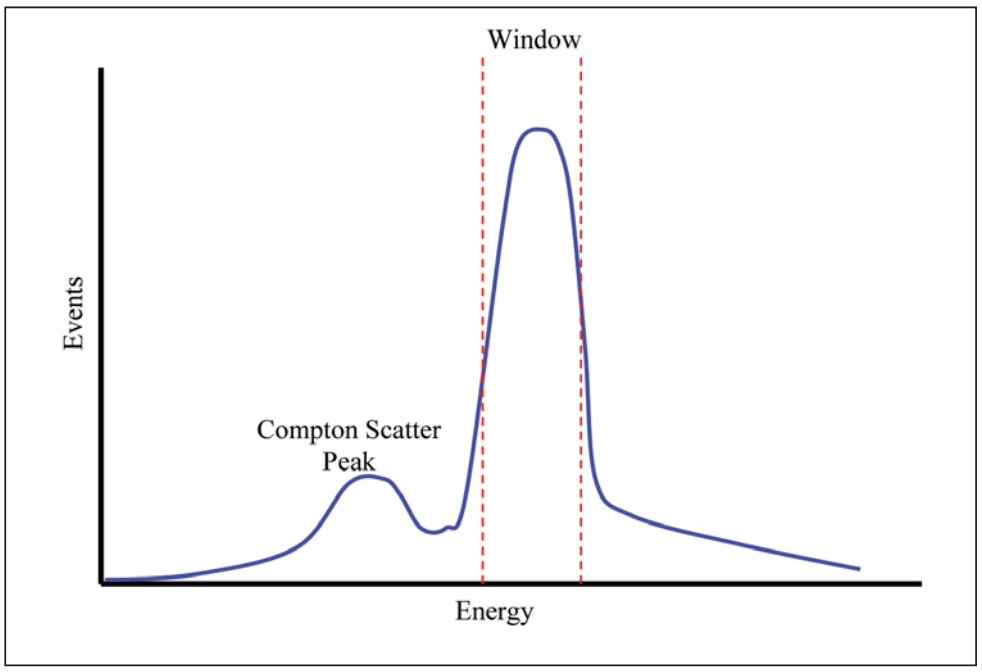

Figure 6: Schematic representation of the energy photopeak. Application of a narrow acceptance window will eliminate scatter events that are incident perpendicular to the detector but which have previously undergone a scatter event.

releases energy in the form of light; hence the term scintillation detector. The amount of light emitted is proportional to the energy of the incident photon which facilitates energy discrimination later in the process.

The emitted light is detected by an array of photomultiplier tubes (PMTs). PMTs are tubes that convert weak light outputs into amplified electrical impulses (Figure 5). One end of the tube couples to the crystal and is coated with a material which emits electrons in response to incident visible light photons and is known as the photocathode. The signal is amplified through the tube using dynodes until an impulse exits at the anode.

Positioning circuitry provides an X,Y set of coordinates for the incident photon and this coordinate is registered when a Z signal is received. The X,Y coordinate represents a single 'dot' registered in the image. Each image is comprised upwards of 500000 separate events yet there are billions of other events that go undetected. A 200 MBq (megabecqueral) dose, for example, represents 200 million events or disintegrations every second. Doses in nuclear medicine are in the order, typically, of 150 MBq to 1000 MBq. The Z signal is produced by the pulse height analyser (PHA) when the incident energy is within an acceptance window and, thus, the PHA is an energy discriminator (Figure 6). The role of the PHA is to eliminate events that are incident perpendicular to the detector after a scatter event (event C in Figure 3). Following scatter, energy is lost and thus the amount of light and subsequent signal amplitude is lower than the target events.

Advances in nuclear medicine imaging

Single photon emission computed tomography (SPECT)

Since its introduction into clinical nuclear medicine in the late 1970s SPECT, has become a routine tool in the nuclear medicine. A significant part of that transition was the advent of sufficient computing power for data collection and subsequent reconstruction. In the late 1980's in Australia, the majority of gamma cameras in clinical departments did not have SPECT capability. By the early 1990s in Australia, virtually all new gamma cameras being purchased were SPECT systems. Nonetheless, the early SPECT systems were based on modified planar cameras and these were not optimised for SPECT creating reliability issues. Moreover, the limitations associated with computing space and power meant sub-optimal acquisition parameters were employed. The real value of SPECT emerged with the

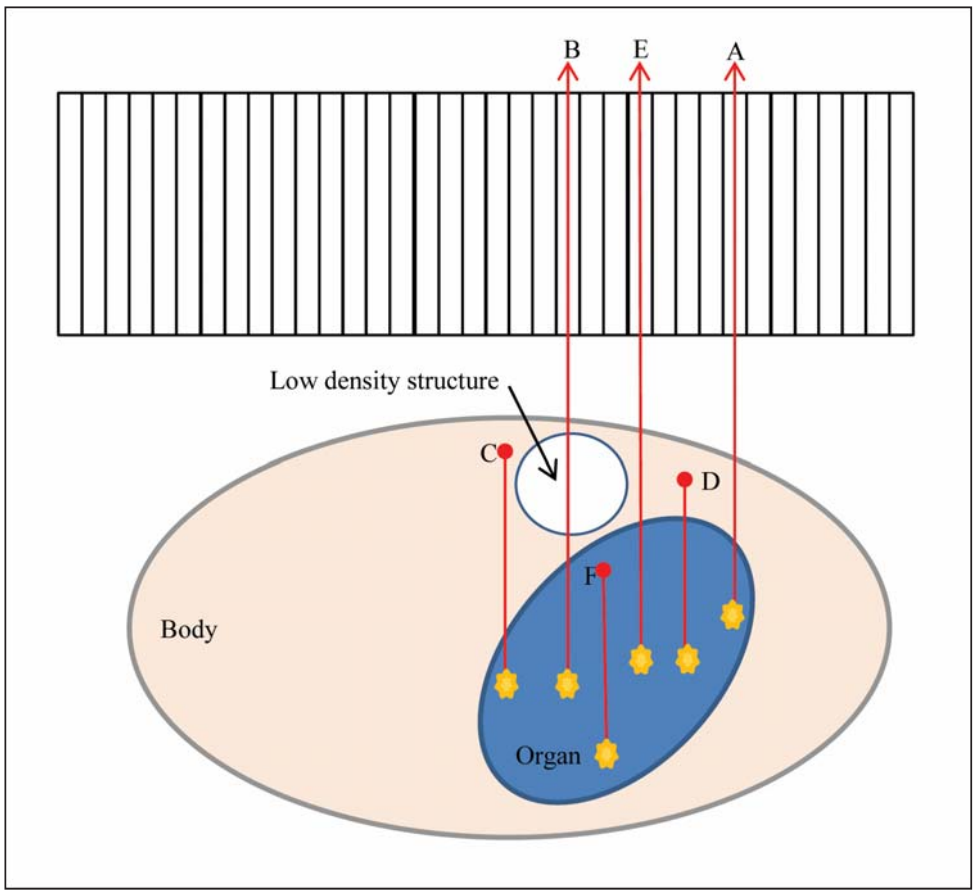

Figure 7: Schematic representation of the impact of attenuation on gamma emissions that would otherwise be incident perpendicular to the detector. The organ may be of greater or lesser density than surrounding body tissues and, indeed, some structures will have very lower density or attenuation (eg. lung or gas pockets in the colon). Some events pass from an organ structure, through surrounding body tissues and are detected without attenuation (A). Events originating at the same depth within a structure will have variable attenuation based on whether the pathway is through a lower density structure (B) or normal tissues (C). Independent of variations in the density along the photon pathway, events originating from the same (or similar) locations within a structure, based on probability, may be attenuated (D) or detected (E). In a dense organ of interest, some events are attenuated within the organ itself (F), particularly if the event originates deeper with the structure. Clearly in this schematic, imaging the patient either posterior or laterally will change the fates of each of the hypothetical events. The point of attenuation correction is to apply a uniform field along a series of lines of response and estimate the probability of an event being attenuated along that pathway, and then subsequently corrected for those loses.

advances in computer technology and gantry configurations

Computer technology allowed the use of optimal imaging parameters (e.g. matrix) due to overcoming data storage limitations. Computing power has significantly shortened reconstruction time from hours to seconds which has allowed multiple re-slice. Certainly the advances in computing power have allowed the introduction of gated SPECT which revolutionised cardiac imaging in the late 1990s. The reconstruction process has been refined (pre- and post-filter functions) which has allowed improved image quality. New reconstruction approaches, like iterative reconstruction, are possible with the improved computing technology. The use of 180 degree data collection and reconstruction algorithms essentially halved the acquisition time.

Cameras were constructed with dedicated SPECT gantries which have allowed greater physical integrity of the data collection (eg. less centre of rotation issues typical of older generation cameras) and the introduction of elliptical orbits to maximise spatial resolution. The introduction of digital head technology has improved image quality. The duration of the imaging time has been reduced with the introduction of multi-detector technologies and cardiac configurations (90 degree). Image quality has been refined with the development of high resolution/sensitivity collimator designs

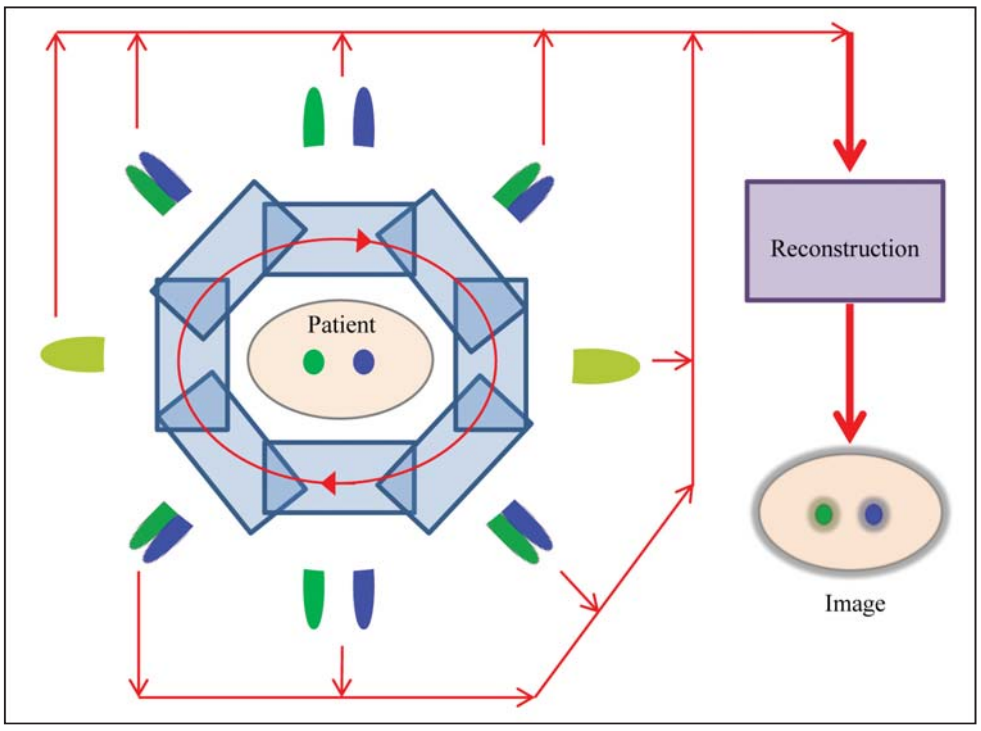

Figure 8: Schematic representation of the principals of SPECT. Individual planar projections are acquired at regular intervals around the patient's body (typically 60-120) for either 360 or 180 degrees depending on the organ of interest. The subsequent image profiles are fed into the reconstruction algorithm (typically filtered backprojection or iterative reconstruction) to reconstruct the object of interest. The object generally suffers some loss of detail over the object like CT or even a photograph.

(eg. fan beam). The emergence of CT based attenuation correction has improved image quality through attenuation correction of the data (Figure 7) while improving lesion localisation. More recently the introduction of solid state detectors has improved resolution and sensitivity substantially and subsequently reduced images times to a fraction of traditional SPECT systems (eg. 20 minute SPECT reduced to just 3–5 minutes without loss of quality). SPECT is a technique for generating images of single planes within a volume of radioactivity from projections of that volume obtained at a number of different angles.[3] The principle is similar to that of PET and CT (Figure 9). In a more practical sense, SPECT is a method of separating overlying and underlying tissue from the source or target of interest by reconstructing cut sections of the object, (traditionally transverse, sagittal and coronal, but in cardiology, short axis, vertical long axis and horizontal long axis). Unlike planar projections, SPECT does not have the problem of superimposition of other structures in front of or behind the organ of interest, thus improving image contrast and allowing smaller defects to be accurately diagnosed. The advantages of SPECT over planar imaging are the same as those for performing CT over x-ray. Clearly there will be situations where SPECT (or CT) provides better quality images than the planar equivalent without actually changing the outcome or patient management. The difference is that the addition of CT to the patient work-up significantly increases the radiation dose. For SPECT, there is no additional radiation dose over that which was given for the planar study.

Single photon emission computed tomography/ computed tomography (SPECT/CT)

While hybrid imaging requires a dedicated article to adequately address its emergence and role in clinical practice, in the context of this discussion SPECT/CT represents an important development in nuclear medicine. The boundaries demarcating the line between disciplines have been blurred in the past; the original CT devices were rotating radionuclide sources, the origins of radiation therapy and

Figure 9: High resolution CT, poor resolution Indium-111 (^{111}In) octreotide SPECT and fusion SPECT/CT for neuroendocrine tumour detection and localisation.

radionuclide therapy are common and some modalities like MRI are not a classical fit in either discipline. In recent times, there has been a noticeable convergence to exploit synergies in diagnosis and therapy to improve outcomes. Radiography has always been anatomy based and nuclear medicine always been strongly physiology based. Advances in instrumentation in both areas have seen significant clinical improvements but also the emergence of hybrid systems where a single device operates as both a SPECT system and CT, PET and CT or more recently PET and MRI. These hybrid systems demand uniquely qualified individuals and represent the cutting edge and future of imaging technology. As indicated in Figure 9, the fusion of SPECT and CT has added a new dimension allowing nuclear medicine to have anatomical definition and CT to have sensitive physiological information.

Radiopharmacy

The radiopharmacy is an important aspect of all nuclear medicine departments but not all nuclear medicine departments have a fully functional radiopharmacy with on site ^{99m}Tc generator. Some departments will accept delivery of radionuclides (^{99m}Tc) from a centralised radiopharmacy and reconstitute their own radiopharmacueticals (kits) on site for use on a daily basis. Others rely on unit dose deliveries from a centralised pharmacy. Still others rely on a mix of the two.

The main radiopharmaceutical used in general nuclear medicine is ^{99m}Tc and this is produced by a generator from decay from the Molybdenum-99 (^{99}Mo) parent. A single generator tends to provide sufficient radionuclide activity for one week because the parent nuclide has a half-life of approximately 67 hours (^{99m}Tc has a 6 hour half-life). The half-life is one of the key issues in nuclear medicine. It governs how long a radioactive source is useful for imaging. Every half-life, the activity is halved. Thus, for ^{99m}Tc our imaging window is typically around 6 hours and by 24 hours there is very little to image. One needs to consider that the half-life is but one issue, once administered to the patient, elimination (e.g. urinary system) introduces the biological half-life which can further reduce the effective window for imaging. A bone scan has relatively slow biological clearance and consequently the patient is imaged several hours after administration and a long window of opportunity for imaging (many hours) is available. Conversely, renal imaging using perfusion tracers are rapidly excreted (by the nature of the test) and imaging is performed immediately upon administration and in a narrow window exists (minutes).

^{99}Mo and some other radionuclides used in nuclear medicine (eg. Iodine-131 [^{131}I]) are produced in a fission nuclear reactor like the one at Lucas Heights in Sydney. Others are produced by a cyclotron (Iodine-123 [^{123}I], Gallium-67 [^{67}Ga], Thallium-201 [^{201}Tl]); these are imported to Australia commercially since the de-commission of Australia national medical cyclotron. The cyclotrons operational in Australia are small (lower

Table 1: Radionuclides typically employed in nuclear medicine.[4,5] The table includes PET radionuclides but excludes radionuclide therapy.

Nuclide		Emission	Gamma energy for imaging (MeV)	Half-life	Maximum particle energy (MeV)	Production
Technetium	^{99m}Tc	Gamma	0.140	6 hours	–	^{99}Mo/^{99m}Tc generator
Thallium	^{201}Tl	Gamma	0.80 & 0.167	73 hours	–	Cyclotron
Gallium	^{67}Ga	Gamma	0.093, 0.184 & 0.296	78 hours	–	Cyclotron
Indium	^{111}In	Gamma	0.173 & 0.247	2.8 days	–	Cyclotron
Iodine	^{123}I	Gamma	0.159	13.3 hours	–	Cyclotron
Iodine	^{131}I	Gamma	0.364	8 days	0.61	Fission
Fluorine	^{18}F	Positron	0.511	109 min	0.64	Cyclotron
Carbon	^{11}C	Positron	0.511	20 min	0.97	Cyclotron
Nitrogen	^{13}N	Positron	0.511	10 min	1.20	Cyclotron
Oxygen	^{15}O	Positron	0.511	2 min	1.73	Cyclotron
Gallium	^{68}Ga	Positron	0.511	68 min	2.919	^{68}Ge/^{68}Ga generator
Rubidium	^{82}Rb	Positron	0.511	75 seconds	3.15	^{82}Sr/^{82}Rb generator
Xenon	^{133}Xe	Beta & Gamma	0.080	5.2 days	0.364	Fission
Krypton	^{81m}Kr	Gamma	0.190	13 seconds	1.29	^{81}Rb/^{81m}Kr generator

maximum energy) and geared toward production of PET radionuclides (eg. Flourine-18 [^{18}F], Nitrogen-13 [^{13}N]) only. Some radionuclide therapy sources are produced in a nuclear reactor by neutron activation (eg. ^{32}P, ^{89}Sr).

One of the key strengths of nuclear medicine has been the innovation of various radiopharmaceuticals. While the radionuclides have been fairly static (Table 1), the biological products labelled to those radionuclides has progressed rapidly. ^{99m}Tc labelling of somatostatin receptor tracers is one example that has revolutionised the imaging of neuroendocrine tumours. The development of tracers that cross the blood brain barrier reinvented cerebral imaging and, indeed, broadened the clinical efficacy and utility. Well established tracers, like ^{201}Tl chloride for myocardial perfusion imaging, have had limitations associated with physical properties (eg. half-life, photon energy) overcome by development of perfusion tracers labelled to ^{99m}Tc. Even the humble bone scan has seen refinement of radiophamraceuticals for improved localisation, improved target to background ratios and more rapid localisation (earlier imaging times). Radiopharmacy is a dynamic and very liquid environment that ensures nuclear medicine remains cutting edge, providing an integrative and adjunctive nexus to both radiography and radiation therapy.

There are several key strategies for safety in the radiopharmacy. Time, distance and shielding (TDS) reduces radiation exposure to staff and other visitors to the department. Reduce the time exposed, increase the distance from the source and use shielding between yourself and the source. As low as reasonably achievable (ALARA) is a concept that protects patients and staff. In essence, and not too dissimilar to approaches in x-ray, the lowest dose that can be reasonably used to provide diagnostic quality results is used. While minimal, the risk of a radiation based adverse effect is generally of greater importance in managing the patients than the risk of adverse reaction to the radiopharmaceutical (with the notable exception of monoclonal antibodies). The concepts of justification, optimisation and limitation are also applied. Contrary to popular belief outside nuclear medicine, the radiation doses to patients and staff are very low. For many procedures, the radiation dose to the patient is lower than the x-ray equivalent; especially if that equivalent is fluoroscopy, angiography or CT. Doses to staff are typically higher than that of a general radiographer or radiation therapist but only a fraction of the occupational exposure limits.

Clinical indications

There are a number of key reasons for choosing a general nuclear medicine procedure either as an adjunct to other imaging modalities or as an alternative to them (Table 2). These include, without being limited to:

- Diagnosis (detection and localisation) of conditions or diseases which for some reason have gone undetected by other simpler imaging techniques (e.g. fractures may not be visible on x-ray if there is no separation of the bone and in small or complex structures).
- In some cases, nuclear medicine offers a simple, cost effective alternative to more invasive, high-risk procedures (e.g. myocardial perfusion study instead of a coronary angiogram).
- Nuclear medicine is extremely sensitive and in some cases can detect and localise disease processes that other imaging modalities cannot successfully image (e.g. cerebral perfusion studies where the radiopharmaceutical actually crosses the blood brain barrier and is trapped in the brain cells to allow perfusion mapping).
- Nuclear medicine studies can offer lower radiation doses than traditional alternatives. This can be of significant advantage in paediatrics, women of child bearing age, pregnant patients and patients having repeated follow up studies (e.g. radionuclide cystogram versus the radiographic cystogram and the ventilation / perfusion (V/Q) lung scan versus CT pulmonary angiography).

Table 2: A summary of the clinical indications of major nuclear medicine procedures.[4,5] The list is not exhaustive but rather provides a snapshot of the main clinical procedures performed in Australian nuclear medicine departments. The tabulated summary excludes PET, radionuclide therapy, research procedures and emerging techniques. There are a number of procedures that can be modified for other purposes that are also not listed. Routes of administration are intravenous (IV) unless otherwise indicated.

Organ / Pathology	Radiopharmaceutical	Indications
Bone	^{99m}Tc MDP or HDP	Metastases, metabolic disease (eg. Paget's), trauma (particularly when xray is normal or difficult), infection, sports injuries (eg. pars articularis, osteitis pubis, shin splints, stress fractures), avascular necrosis, assess prosthetic joints for loosening or infection, degenerative change or arthritis, pain in bone or joints, reflex sympathetic dystrophy to name a few.
Bone marrow	^{99m}Tc sulphur colloid	Define marrow distribution in tumour, biopsy, harvest and post joint replacement.
Brain	^{99m}Tc DTPA flow ^{99m}Tc HMPAO or ECD perfusion	The flow study is used to assess the integrity of the blood brain barrier (BBB). It is useful although superseded by CT and SPECT perfusion in; cerebrovascular accident, tumour, other mass, infection and brain death. Cerebral perfusion SPECT uses tracers that cross the BBB and are useful for functional assessment in epilepsy, stroke, transient ischaemic attacks, carotid artery stenosis, infection and brain death.
Lacrimal glands	^{99m}Tc pertechnetate or DTPA – drops on eye surface	Epiphora. The procedure is non invasive and assess the actual physiology without application of a catheter or pressure.
Salivary	^{99m}Tc pertechnetate	Functional evaluation of salivary glands in suspected tumour, Sjogren's syndrome or infection.
Thyroid	^{99m}Tc pertechnetate although 123I is used more so in the USA	Grave's disease, assess functional status of nodules, detect ectopic tissue, quantitate and differentiate causes of hyper- and hypothyroidism, determine thyroid uptake for assessment and therapy planning, response to therapy.
Parathyroid	^{99m}Tc pertechnetate in combination with ^{99m}Tc MIBI or ^{201}Tl chloride	Pre-operative localisation of hyperfunctioning parathyroid tissue (adenoma or hyperplasia). Locate residual hyperfunctioning parathyroid tissue, including ectopic.
Oesophagus	^{99m}Tc sulphur colloid labelled in orange juice or egg whites (liquid versus solid) - oral ^{99m}Tc pertechnetate - IV	Oesophageal transit (eg. spasm, achalasia), lung aspiration and oesophageal reflux studies for detection and quantitation. Barrett's oesophagus.
Stomach	^{99m}Tc sulphur colloid labelled in orange juice or egg whites (liquid versus solid) - oral	Solid and liquid gastric empty studies to evaluate rapid or delayed transit. Physical or functional obstruction. Reflux studies can be performed in conjunction.
Liver	^{99m}Tc sulphur colloid ^{99m}Tc red blood cells ^{99m}Tc IDA derivative (HIDA, DIDA, DISIDA etc)	Liver / spleen scan to determine size and shape of each, functional abnormalities of reticloendothelial system, focal nodular hyperplasia, trauma and accessory spleen. Haemangioma and focal nodular hyperplasia. Assessment of biliary function including gallbladder ejection fraction following a fatty meal intervention. Detection of obstruction in the cystic duct or common bile duct.
Colon	^{67}Ga citrate – oral ^{99m}Tc red blood cells - IV ^{99m}Tc pertechnetate - IV	Colon transit for constipation. Gastrointestinal haemorrhage. Meckel's diverticulum
Kidneys	^{99m}Tc DTPA or MAG3 (renogram) ^{99m}Tc DMSA	Differential function and assessment of blood supply. Can be used instead of CT if contrast is contraindicated. Diuretic intervention for assessment and quantitation of obstructive uropathy. Captopril intervention for detection of renal artery stenosis. Cortical morphology imaging for assessment of pyelonephritis, scarring, trauma, space occupying lesion and in patients where contrast is contraindicated.
Bladder	^{99m}Tc DTPA – instilled in bladder (direct method) or IV (indirect)	Radionuclide cystogram is very sensitive and low doses radiation alternative to micturating cystogram for the detection and quantitation of vesico-uretal reflux.
Testes	^{99m}Tc pertechnetate	Evaluation of the acute scrotum for diagnosis of torsion. Largely superseded by ultrasound.
Heart	^{99m}Tc MIBI ^{99m}Tc red blood cells	Myocardial perfusion study to assess coronary flow reserve in known or suspect coronary artery disease. Includes quantitation of chamber volumes and ejection fraction. The blood pool study provides accurate quantitation of the left ventricular function, including volumes and ejection fraction. It can also be employed to evaluation cardiac shunts (first pass study).
Lung	^{99m}Tc MAA (perfusion - IV) and ^{99m}Tc technegas (ventilation - inhalation) although ^{99m}Tc DTPA aerosols are also used in Australia.	Detection of pulmonary embolism (PE). Virtually 100% positive and negative predictive value. Intermediate probability generally need CT angiogram. Differentiate old and new PE. Quantitative differential studies pre-surgical resection for emphysema. Can be sued to detect and quantitate right to left cardiac shunts.
Sentinel node	^{99m}Tc antimony sulphur colloid - sub cutaneous, inter-tumoural, peri-tumoural	Identification of lymphatic sentinel node prior to breast cancer surgery.
Breast	^{99m}Tc MIBI or 201Tl chloride	Scintimammography is a powerful tool for differentiating benign and malignant breast lesions. Particularly useful in monitoring response to non surgical therapy. Is effective in assessing those not suitable for mammography.
CSF	^{99m}Tc DTPA (triple filtered) – intra-portal or intrathecal	Hydrocephalis, shunt patency, cerebrospinal fluid (CSF) leak.
Lymphatics	^{99m}Tc antimony sulphur colloid - sub cutaneous	Bilateral or unilateral lymphoedema, typically arms or legs but it has been performed in other structures (eg. penis or vulva).
Infection	^{67}Ga citrate ^{99m}Tc white blood cells	Fever of unknown origin, osteomyelitis, lung infection (eg. pneumocystis pneumonia in immune suppression). Fever of unknown origin, infected joint prosthesis, inflammatory bowel disease, graft infection, abscess, diabetic infections.
Tumour	^{67}Ga citrate ^{111}In octreotide ^{123}I MIBG	Non-Hodgkin's lymphoma and to a lesser extent Hodgkin's disease. The latter superseded by PET. Neuroendocrine tumours. Pheochromocytomas, neuroblastoma, carcinoid tumours.

- Computer quantitation of function is possible and is often the only clue to detection of an abnormal process (eg. renograms in renal artery stenosis and myocardial perfusion polar maps).
- Outside of trauma, many pathologies begin as a functional change and that functional change eventually produces the structural change seen in anatomical imaging. While widespread screening is neither cost effective nor safe, nuclear medicine is capable of detecting disease before the structural changes are apparent.
- Functional imaging allows earlier detection of disease, risk stratification, tailoring of patient management, differentiation of pathology (eg. benign or malignant) and assessment of response to therapy. For example, response of a tumour to therapy can be immediate from a functional perspective despite no 'shrinkage' on anatomical imaging (indeed there can be some enlargement).
- Therapeutic doses can be performed for the treatment of a variety of conditions. Scintigraphy can be used to map biodistribution of therapeutic tracers before therapy is undertaken.
- Advanced tools like SPECT and SPECT/CT offer additional advantages which have been discussed above.

Conclusion

Nuclear medicine provides an important tool for an integrative approach to medical radiation science. The synergies between nuclear medicine and both radiography and radiation therapy are evident historically and in the emergence of current best practice. An understanding of the technical and clinical aspects of integrated modalities affords advantage to clinical practitioners in all disciplines of the medical radiation sciences. This article provides a basic insight into nuclear medicine to extend the capabilities of radiographers, radiation therapists and other health care professions engaged in the diagnostic imaging industry.

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