

Nuclear Medicine in Neurology



Dr Justin Cross

trained in neuroradiology at Addenbrooke's Hospital, Cambridge UK and at the University of Toronto, Canada. He has a special interest in paediatric neuroradiology and has published articles on the measurement of cerebral tumour volume, carotid imaging and the use of spectroscopy in clinical practice.

Dr HK Cheow,

Consultant in Nuclear Medicine at Addenbrooke's Hospital. HK is trained in both radiology and nuclear medicine and has published widely on the applications of radioisotope imaging to clinical medicine.

Correspondence to:

Dr Justin Cross,
Department of Radiology,
Box 218,
Addenbrooke's Hospital,
Hills Road,
Cambridge CB2 0QQ, UK.

Principles of Nuclear Medicine

Nuclear Medicine (NM) imaging is a modality which utilises radioactivity emitted by a radiopharmaceutical to generate an image. Most of the radiopharmaceuticals are made up of a radioactive element (isotope) bound to a biologically active molecule (ligand). They are typically injected intravenously. The advantage of NM over many other methods of imaging is that physiological processes can be investigated (eg blood flow, glucose uptake, binding of neurotransmitters). The main disadvantage is that the images obtained are of lower spatial resolution than computed tomography (CT) or magnetic resonance imaging (MRI).

Physical and physiological considerations of a nuclear medicine study

Gamma-camera (Figure 1)

Traditional nuclear medicine uses a crystal detector NaI(Tl) which scintillates (gives out a short burst of light) on exposure to radiation. Photomultiplier tubes or photodiodes positioned adjacent to the crystal will amplify and convert the weak light signal emitted by the scintillator crystal to electrons. These electrons are then fed into a computer to generate an image. The collimator is a device to channel the radiation (gamma rays or photons) produced by the radiopharmaceutical in an appropriate direction to the crystal detector.

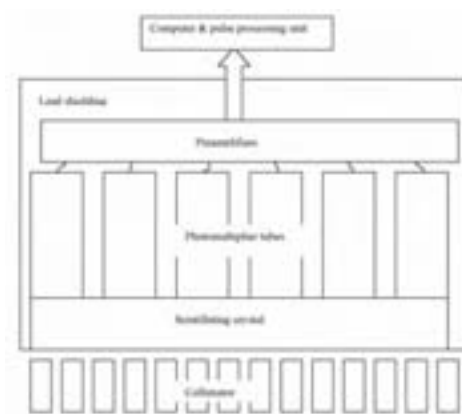


Figure 1: Cross-section through the detector head of a gamma camera.

Photon energy

The optimum energy for detection of photons is around 150 keV using the conventional gamma camera. In practice, the useful energy is between 50 keV and 300 keV. Below this energy, much of the emitted radiation is absorbed within the patient. Photons which are too high in energy will penetrate a standard scintillator crystal without producing a useful image. A thicker and denser crystal will be needed.

Half life

The radioactive half life can be defined as the time in which radiation emission decreases by a half and is an important feature in NM. It governs the ideal time to image and the dose of radiopharmaceutical given to the patients. By understanding the half life of a radiopharmaceutical, one can utilise its property to study various physiological process. Materials with a very short half life can be imaged instantaneously but require a high initial dose given to the patients. The disadvantage of such reagents with a short half life is that their production must be close to the patient. This makes them costly and inconvenient to use. Materials with a very long half life are useful in imaging over a period of time. However, patients remain radioactive for a considerable time and the initial dose of the radiopharmaceutical has to be kept low which could compromise the quality of the images.

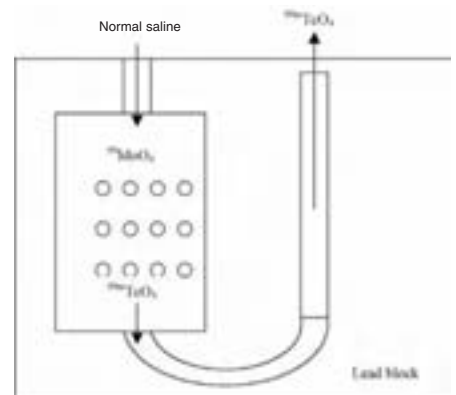


Figure 2a: Technetium-99m is produced from a generator which contains ⁹⁹MolybdenumO₄ adsorbed onto beads in column. The generator produces sufficient activity for about one week's supply of Tc-99m. The Tc-99m is eluted from the column by the addition of a solution of normal saline. The more soluble ^{99m}TcO₄ is preferentially released from the beads. The generator can be eluted once every six hours.

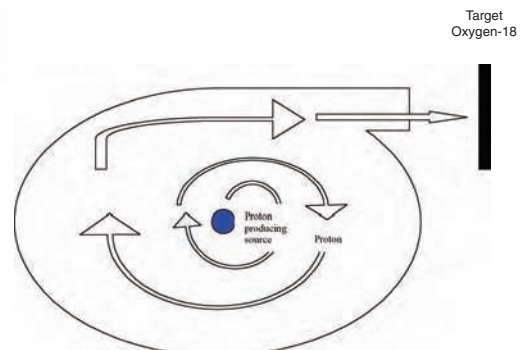


Figure 2b: Fluoride-18 and a neutron are produced by a cyclotron by the collision of Oxygen-18 with a proton.

Production of radiopharmaceutical (Figure 2)

The isotope most commonly used in conventional NM is Technetium-99m (^{99m}Tc) because it emits gamma radiation of an easily detectable energy (140keV) and has a biologically useful half life (six hrs). It is produced from a molybdenum-99/ technetium-99m generator. The generator is portable; it can be purchased and stored in a secured unit in the hospital.

Production of PET isotopes requires an expensive, large machine called a cyclotron which accelerates subatomic particles to nearly the speed of light. The particles or protons then collide against a target to produce an unstable positron emitter isotope.

Imaging (Figure 3)

Planar – This is a useful method to give an overview to large parts of the body, e.g. bone, lung and renal scintigram, but brain imaging requires more precise definition. Therefore planar view is rarely used in routine brain studies.

Single photon emission tomography, SPET – (also known as single photon emission computed tomography, SPECT) is a method using data from gamma radiation obtained in 360 degrees for multiplanar reconstructions similar to MR images.

Positron emission tomography, PET – is a technique which uses isotopes which undergo an annihilation reaction. Certain nuclei of the radioactive material emit positrons (anti-electrons). On collision with electrons, both the positron and electron are annihilated and two gamma rays are emitted, each with energy of 511 keV. Conveniently for imaging, the gamma rays are emitted at exactly 180 degrees which allows back projection for precise localisation of the source of emission.

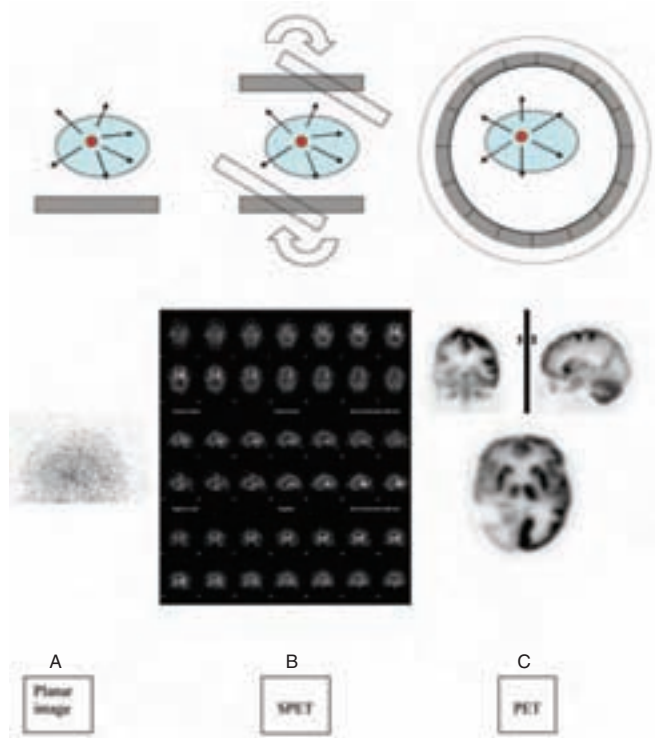


Figure 3: Nuclear Medicine imaging
 A. Planar image. The scintillating crystal detects radiation (gamma rays or photons) emitted from the patient in one direction. Radiation that is not directed in the direction of the crystal is lost.
 B. Single photon emission tomography. Two detectors are rotated around the patient. This method results in a more efficient radiation capture and allows reconstruction of multiplanar images.
 C. Positron emission tomography. A ring of detectors around the patient detects radiation from all directions. Each annihilation event results in two photons being emitted along the same line at approximately same time, a coincidence circuit will be able to pick the correct signals within a fixed coincidence time window. Signals outside this time frame are rejected. The location of the annihilation event can then be traced back along the line of response.

Radiopharmaceuticals available

Planar/SPET

^{99m}Tc- Hexa-Methyl-Propylene-Amine-Oxime (HMPAO)

This is a non specific radiopharmaceutical which is able to cross the blood-brain barrier because of its lipophilic property. It is extracted from the bloodstream into the cerebral parenchyma and is dependent on the cerebral blood flow. This has a role in the imaging of neurodegenerative conditions with characteristic findings in Alzheimer's disease and frontotemporal dementia as well as other neurological conditions (Figure 4). It has also been used in epilepsy and shows increased uptake in focal seizures when injected during the seizure (ictal imaging). Hypoperfusion may be demonstrated on interictal imaging.

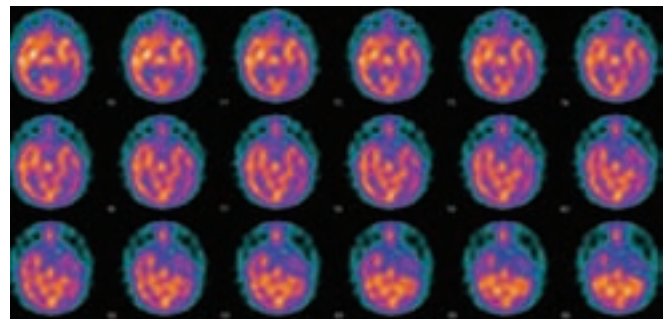


Figure 4: ^{99m}Tc-HMPAO SPET brain images of a patient with Alzheimer's dementia. There is reduced perfusion seen in the left temporoparietal region.

¹²³I-ioflupane (Dopamine transporter, DaTSCAN)

This is a specific radiopharmaceutical which is taken up by dopamine specific transporters found in the presynaptic nerve terminal. These transporters are found most abundance in the basal ganglia. In Parkinson's disease, parkinsonian syndromes (multiple system atrophy, progressive supranuclear palsy & corticobasal degeneration) and Lewy body dementia, the uptake is reduced significantly in the basal ganglion (Figure 5). In drug-induced Parkinson's disease or essential tremor, uptake is not affected (Figure 6).

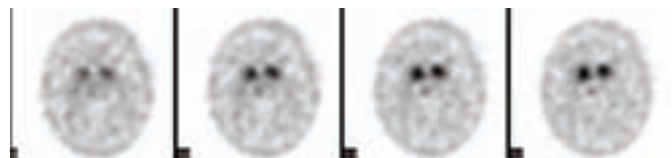


Figure 5: ¹²³I-ioflupane (DaTSCAN) SPET brain images of a patient with parkinsonian syndrome. There is bilateral reduction in the tracer uptake seen in the basal ganglion.



Figure 6: ¹²³I-ioflupane (DaTSCAN) SPET brain images of a normal patient.

PET

¹⁸F Deoxy Glucose (18FDG)

¹⁸FDG is a non specific positron emitting radiopharmaceutical. Its uptake in tissue is directly related to cellular glycolytic activity. Because of this property, infection, inflammation or tumour can be difficult to differentiate one from the other. Glucose is the only source of fuel for the brain; therefore ¹⁸FDG is taken up avidly by the brain. Grey matter shows relatively higher ¹⁸FDG tracer uptake as compared to the white matter. A focal reduction in tracer uptake can be seen in several neurodegenerative conditions (Figure 7). This method has better spatial resolution than

HMPAO SPET. Primary brain tumour or metastasis can sometimes be identified by this method (Figure 8). However, low grade malignancy can be missed and benign lesion such as meningioma, pituitary adenoma can show avid tracer uptake.



Figure 7: ^{18}F FDG PET brain images in a patient with frontal lobe dementia. There is reduction in tracer uptake seen in the frontal lobe (arrow) (courtesy of M O'Doherty, Clinical PET Centre, London).



Figure 8: ^{18}F FDG PET brain images in a patient with a brain tumour (arrow) (courtesy of M O'Doherty, Clinical PET Centre, London).

^{18}F FluoroThymidine (^{18}F FLT) and ^{11}C CarbonMethionine (^{11}C -Met)

This nucleotide analogue (FLT) and amino acid (^{11}C -Met) shows promise in diagnosis of cerebral tumours and uptake correlates with cellular proliferation. Tumour recurrence can be identified in the region of the brain where previous surgery or radiotherapy has been taken place (Figure 9).

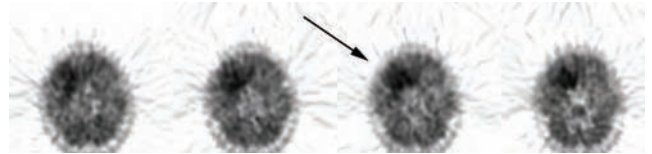


Figure 9: ^{11}C -methionine PET brain images in a patient who had undergone surgery for oligoastrocytoma. PET images show region of increased tracer uptake consistent with recurrent disease (arrow) (courtesy of M O'Doherty, Clinical PET Centre, London).

^{18}F Misonidazole (^{18}F -MISO)

This compound accumulates in hypoxic tissues and may be of use in predicting tumour recurrence following radiotherapy and other oncological treatments in conditions such as carcinoma of lung and glioblastoma.

Pittsburgh Compound B (PiB)

This tracer is taken up in cells containing beta amyloid and may be useful in detecting pathology such as Alzheimer's disease at an early stage.

Conclusion

Nuclear medicine is an important part of the medical imaging specialty in both clinical and research settings. With better understanding of human physiology, new tracers and techniques will no doubt continue to evolve and flourish.

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Key note speakers to include:

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