Nuclear Medicine in Neurology

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 (e.g., 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.

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.
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. Convenienly for imaging, the gamma rays are emitted at exactly 180 degrees which allows back projection for precise localisation of the source of emission.

Radiopharmaceuticals available

**Planar/SPET**

- 99mTc-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.

- 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).

**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.

Fluorodeoxyglucose (18FDG) and 11CarbonMethionine (11C-Met)
This nucleotide analogue (FLT) and amino acid (11C-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).

18F-Misonidazole (18F-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.

REFERENCES