PET scan

Principle of action:

To conduct the scan, a short-lived radioactive tracer isotope ,which decays by emitting a positron, is used, in a form which can be chemically incorporated into a metabolically active molecule, is injected into the living subject (usually into blood circulation).

There is a waiting period while the metabolically active molecule becomes concentrated in tissues of interest; then the research subject or patient is placed in the imaging scanner.

As the radioisotope undergoes decay ,it emits a positron ,which after travelling up to a few millimeters encounters and annihilates with an electron, producing a pair of annihilation (gamma) photons moving in almost opposite directions.

These are detected when they reach a scintillator material in the scanning device, creating a burst of light which is detected by photomultiplier tubes or silicon avalanche photodiodes (Si APD).

The technique depends on simultaneous or coincident detection of the pair of photons; photons which do not arrive in pairs (i.e., within a few nanoseconds) are ig nored .The most significant fraction of electron-positron decays result in two 511 keV gamma photons being emitted at almost 180 degrees to each other; hence it is possible to localize their source along a straight line of coincidence (also called formally the "line of response" or LOR).

Using statistics collected from tens-of-thousands of coincidence events, a set of simultaneous equations for the total activity of each parcel of tissue along many LORs can be solved by a number of techniques, and thus a map of radioactivities as a function of location for parcels or bits of tissue ("voxels"), may be constructed and plotted. The resulting map shows the tissues in which the molecular probe has become concentrated, and can be interpreted by nuclear medicine physician or radiologist in the context of the patient's diagnosis and treatment plan.

Commonly used radiotracers:

The molecule most commonly used for this purpose is fluorodeoxyglucose (FDG), a sugar, for which the waiting period is typically an hour.

Radionuclides used in PET scanning are typically isotopes with short half lives such as ^{11}C (~20 min), ^{13}N (~10 min), ^{15}O (~2 min), and ^{18}F (~110 min). Due to their short half lives, the radionuclides must be produced in a cyclotron which is not too far away in delivery-time to the PET scanner. These radionuclides are incorporated into compounds normally used by the body such as glucose, water or ammonia and then injected into the

body to trace where they become distributed. Such labelled compounds are known as radiotracers.

PET scanners:

PET imaging is best performed using a dedicated PET scanner. However, it is possible to acquire PET images using a conventional dual-head gamma camera fitted with a coincidence detector. The quality of gamma-camera PET is considerably lower, and acquisition is slower. However, for institutions with low demand for PET, this may allow on-site imaging, instead of referring patients to another center, or relying on a visit by a mobile scanner.

PET-CT/MR integration:

Because PET imaging is most useful in combination with anatomical imaging, such as CT, modern PET scanners are now available with integrated high-end multi-detector-row CT scanners. Because the two scans can be performed in immediate sequence during the same session, with the patient not changing position between the two types of scans, the two sets of images are more-precisely registered, so that areas of abnormality on the PET imaging can be more perfectly correlated with anatomy on the CT images. This is very useful in showing detailed views of moving organs or structures with higher amounts of anatomical variation, such as are more likely to occur outside the brain.

Limitations:

(1) High costs of cyclotrons needed to produce the short-lived radionuclides for PET scanning and the need for specially adapted on-site chemical synthesis apparatus to produce the radiopharmceuticals. Few hospitals and universities are capable of maintaining such systems, and most clinical PET is supported by third-party suppliers of radio-tracers which can supply many sites simultaneously. This limitation restricts clinical PET primarily to the use of tracers labelled with ^{18}F, which has a half life of 110 minutes and can be transported a reasonable distance before use, or to ^{82}Rb, which can be created in a portable generator and is used for myocardial perfusion studies.

(2) Because the half-life of ^{18}F is about two hours, the prepared dose of a radiopharmaceutical bearing this radionuclide will undergo multiple half-lives of decay during the working day. This necessitates frequent recalibration of the remaining dose (determination of activity per unit volume) and careful planning with respect to patient scheduling.

Radiation exposure:

The total dose of radiation is small, however, usually around 7 mSv. This can be compared to 2.2 mSv average annual background radiation in the UK, 0.02 mSv for a chest X-Ray, up to 8 mSv for a CT scan of the chest, 2-6 mSv per annum for aircrew.

Applications:

PET is a valuable technique for some diseases and disorders, because it is possible to target the radio-chemicals used for particular bodily functions.

1. Oncology: PET scanning with the tracer (^{18}F) fluorodeoxyglucose (FDG, FDG-PET) is widely used in clinical oncology. This tracer is a glucose analog that is taken up by glucose-using cells and phosphorylated by hexokinase (whose mitochondrial form is greatly elevated in rapidly-growing malignant tumours). A typical dose of FDG used in an oncological scan is 200-400 MBq for an adult human. Because the oxygen atom which is replaced by ^{18}F to generate FDG is required for the next step in glucose metabolism in all cells, no further reactions occur in FDG. Furthermore, most tissues (with the notable exception of liver and kidneys) cannot remove the phosphate added by hexokinase. This means that FDG is trapped in any cell which takes it up, until it decays, since phosphorylated sugars (due to their ionic charge) cannot exit from the cell. This results in intense radiolabeling of tissues with high glucose uptake, such as the brain, the liver, and most cancers. As a result, FDG-PET can be used for diagnosis, staging, and monitoring treatment of cancers, particularly in Hodgkin's disease, non Hodgkin's lymphoma, and lung cancer. Many other types of solid tumors will be found to be very highly labeled on a case-by-case basis-- a fact which becomes especially useful in searching for tumor metastasis, or for recurrence after a known highly-active primary tumor is removed. Oncology scans using FDG make up over 90% of all PET scans in current practice.

   Recently PET scans fused with CT scans have also started to be used for radiotherapy planning.

2. PET scan of the human brain.

   Neurology: PET neuroimaging is based on an assumption that areas of high radioactivity are associated with brain activity. What is actually measured indirectly is the flow of blood to different parts of the brain, which is generally believed to be correlated, and has been measured using the tracer oxygen (^{15}O). However, because of its 2-minute half-life ^{15}O must be piped directly from a medical cyclotron for such uses, and this is difficult. In practice, since the brain is normally a rapid user of glucose, and since brain pathologies such as Alzheimer's disease greatly decrease brain metabolism of both glucose and oxygen in tandem, standard FDG-PET of the brain (which measures regional glucose use) may also

be successfully used to differentiate Alzheimer's disease from other dementing processes, and also to make early diagnosis of Alzheimer's disease. The advantage of FDG-PET for these uses is its much wider availability.

Several radiotracers (i.e. radioligands) have been developed for PET that are ligands for specific neuroreceptor subtypes (e.g. dopamine D2, serotonin 5-HT1A, etc.), transporters (such as [(11)C]McN5652, [(11)C]DASB or other novel tracer ligands for serotonin in this case), or enzyme substrates (e.g. 6-FDOPA for the AADC enzyme).

3. Cardiology, atherosclerosis and vascular disease study: In clinical cardiology FDG-PET can identify so-called "hibernating myocardium", but its cost-effectiveness in this role versus SPECT is unclear. Recently, a role has been suggested for FDG-PET imaging of atherosclerosis to detect patients at risk of stroke
4. Neuropsychology / Cognitive neuroscience: To examine links between specific psychological processes or disorders and brain activity.
5. Psychiatry: Numerous compounds that bind selectively to neuroreceptors of interest in biological psychiatry have been radiolabeled with ^{11}C or ^{18}F. Radioligands that bind to dopamine receptors (D1,D2, reuptake transporter), serotonin receptors (5HT1A, 5HT2A, reuptake transporter) opioid receptors (mu) and other sites have been used successfully in studies with human subjects. Studies have been performed examining the state of these receptors in patients compared to healthy controls in schizophrenia, substance abuse, mood disorders and other psychiatric conditions.
6. Pharmacology: In pre-clinical trials, it is possible to radio-label a new drug and inject it into animals. The uptake of the drug, the tissues in which it concentrates, and its eventual elimination, can be monitored far more quickly and cost effectively than the older technique of killing and dissecting the animals to discover the same information. PET scanners for rats and apes are marketed for this purpose. (The technique is still generally too expensive for the veterinary medicine market, however, so very few pet PET scans are done). Drug occupancy at the purported site of action can also be inferred indirectly by competition studies between unlabeled drug and radiolabeled compounds known apriori to bind with specificity to the site.