Positron emission tomography

From Wikipedia, the free encyclopedia

Positron emission tomography (**PET**)[1] is a nuclear medicine, functional imaging technique that produces a three-dimensional image of functional processes in the body. The system detects pairs of gamma rays emitted indirectly by a positron-emitting radionuclide (tracer), which is introduced into the body on a biologically active molecule. Three-dimensional images of tracer concentration within the body are then constructed by computer analysis. In modern PET-CT scanners, three dimensional imaging is often accomplished with the aid of a CT X-ray scan performed on the patient during the same session, in the same machine.

If the biologically active molecule chosen for PET is fluorodeoxyglucose (FDG), an analogue of glucose, the concentrations of tracer imaged will indicate tissue metabolic activity by virtue of the regional glucose uptake. Use of this tracer to explore the possibility of cancer metastasis (i.e., spreading to other sites) is the most common type of PET scan in standard medical care (90% of current scans). However, on a minority basis, many other radioactive tracers are used in PET to image the tissue concentration of other types of molecules of interest.

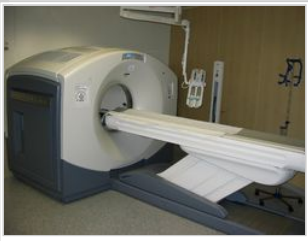
Positron emission tomography

Intervention

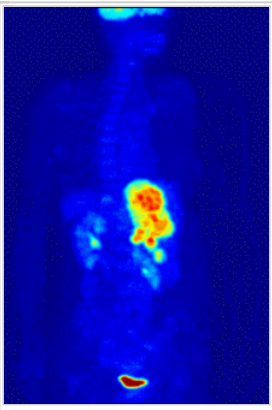
Image of a typical positron emission tomography (PET) facility

ICD-10-PCS	C?3
ICD-9-CM	92.0 (http://icd9cm.chrisendres.com/index.php?srchtype=procs&srchtext=92.0&Submit=Search&action=search) -92.1 (http://icd9cm.chrisendres.com/index.php?srchtype=procs&srchtext=92.1&Submit=Search&action=search)
MeSH	D049268
OPS-301 code:	3-74 (http://ops.icd-code.de/ops/code/3-74.html)
MedlinePlus	003827

Contents



PET/CT-System with 16-slice CT; the ceiling mounted device is an injection pump for CT contrast agent



Whole-body PET scan using ^{18}F-FDG

History

The concept of emission and transmission tomography was introduced by David E. Kuhl, Luke Chapman and Roy Edwards in the late 1950s. Their work later led to the design and construction of several tomographic instruments at the University of Pennsylvania. Tomographic imaging techniques were further developed by Michel Ter-Pogossian, Michael E. Phelps, Edward J. Hoffman and others at Washington University School of Medicine.[2][3]

Work by Gordon Brownell, Charles Burnham and their associates at the Massachusetts General Hospital beginning in the 1950s contributed significantly to the development of PET technology and included the first demonstration of annihilation radiation for medical imaging.[4] Their innovations, including the use of light pipes and volumetric analysis, have been important in the deployment of PET imaging. In 1961, James Robertson and his associates at Brookhaven National Laboratory built the first single-plane PET scan, nicknamed the "head-shrinker."[5]

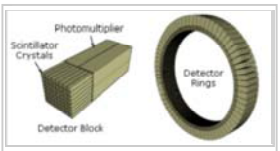
One of the factors most responsible for the acceptance of positron imaging was the development of radiopharmaceuticals. In particular, the development of labeled 2-fluorodeoxy-D-glucose (2FDG) by the Brookhaven group under the direction of Al Wolf and Joanna Fowler was a major factor in expanding the scope of PET imaging.[6] The compound was first administered to two normal human volunteers by Abass Alavi in August 1976 at the University of Pennsylvania. Brain images obtained with an ordinary (non-PET) nuclear scanner demonstrated the concentration of FDG in that organ. Later, the substance was used in dedicated positron tomographic scanners, to yield the modern procedure.

The logical extension of positron instrumentation was a design using two 2-dimensional arrays. PC-I was the first instrument using this concept and was designed in 1968, completed in 1969 and reported in 1972. The first applications of PC-I in tomographic mode as distinguished from the computed tomographic mode were reported in 1970.[7] It soon became clear to many of those involved in PET development that a circular or cylindrical array of detectors was the logical next step in PET instrumentation. Although many investigators took this approach, James Robertson[8] and Zang-Hee Cho[9] were the first to propose a ring system that has become the prototype of the current shape of PET.

The PET-CT scanner, attributed to Dr David Townsend and Dr Ronald Nutt was named by TIME Magazine as the medical invention of the year in 2000.[10]

Descriptions

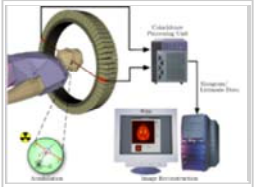
Operation



Schematic view of a detector block and ring of a PET scanner

To conduct the scan, a short-lived radioactive tracer isotope is injected into the living subject (usually into blood circulation). Each tracer atom has been chemically incorporated into a biologically active molecule. There is a waiting period while the active molecule becomes concentrated in tissues of interest; then the subject is placed in the imaging scanner. The molecule most commonly used for this purpose is fluorodeoxyglucose (FDG), a sugar, for which the waiting period is typically an hour. During the scan, a record of tissue concentration is made as the tracer decays.

As the radioisotope undergoes positron emission decay (also known as positive beta decay), it emits a positron, an antiparticle of the electron with opposite charge. The emitted positron travels in tissue for a short distance (typically less than 1 mm, but dependent on the isotope[11]), during which time it loses kinetic energy, until it decelerates to a point where it can interact with an electron.[12] The encounter annihilates both electron and positron, producing a pair of annihilation (gamma) photons moving in approximately opposite directions. These are detected when they reach a scintillator 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 moving in approximately opposite directions (they would be exactly opposite in their center of mass frame, but the scanner has no way to know this, and so has a built-in slight direction-error tolerance). Photons that do not arrive in temporal "pairs" (i.e. within a timing-window of a few nanoseconds) are ignored.


Schema of a PET acquisition process

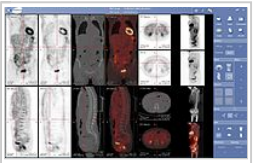
Localization of the positron annihilation event

The most significant fraction of electron–positron annihilations results 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 the **line of response**, or **LOR**). In practice, the LOR has a non-zero width as the emitted photons are not exactly 180 degrees apart. If the resolving time of the detectors is less than 500 picoseconds rather than about 10 nanoseconds, it is possible to localize the event to a segment of a chord, whose length is determined by the detector timing resolution. As the timing resolution improves, the signal-to-noise ratio (SNR) of the image will improve, requiring fewer events to achieve the same image quality. This technology is not yet common, but it is available on some new systems.[13]

Image reconstruction using coincidence statistics

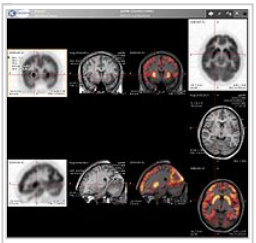
A technique much like the reconstruction of computed tomography (CT) and single-photon emission computed tomography (SPECT) data is more commonly used, although the data set collected in PET is much poorer than CT, so reconstruction techniques are more difficult (see Image reconstruction of PET).

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 (also called voxels) can be constructed and plotted. The resulting map shows the tissues in which the molecular tracer has become concentrated, and can be interpreted by a nuclear medicine physician or radiologist in the context of the patient's diagnosis and treatment plan.


Complete body PET-CT fusion image

Combination of PET with CT or MRI

PET scans are increasingly read alongside CT or magnetic resonance imaging (MRI) scans, with the combination (called "co-registration") giving both anatomic and metabolic information (i.e., what the structure is, and what it is doing biochemically). 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 (so-called "PET-CT"). 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 anatomical variation, which is more common outside the brain.


Brain PET-MRI fusion image

At the Jülich Institute of Neurosciences and Biophysics, the world's largest PET-MRI device began operation in April 2009: a 9.4-tesla magnetic resonance tomograph (MRT) combined with a positron emission tomograph (PET). Presently, only the head and brain can be imaged at these high magnetic field strengths.[14]

For brain imaging, registration of CT, MRI and PET scans may be accomplished without the need for an integrated PET-CT or PET-MRI scanner by using a device known as the N-localizer.[15][16][17][18][19][20][21][22]

Radionuclides and radiotracers

Radionuclides used in PET scanning are typically isotopes with short half-lives such as carbon-11 (~20 min), nitrogen-13 (~10 min), oxygen-15 (~2 min), fluorine-18 (~110 min), gallium-68 (~67 min), or rubidium-82(~1.27 min). These radionuclides are incorporated either into compounds normally used by the body such as glucose (or glucose analogues), water, or ammonia, or into molecules that bind to receptors or other sites of drug action. Such labelled compounds are known as radiotracers. PET technology can be used to trace the biologic pathway of any compound in living humans (and many other species as well), provided it can be radiolabeled with a PET isotope. Thus, the specific processes that can be probed with PET are virtually limitless, and radiotracers for new target molecules and processes are continuing to be synthesized; as of this writing there are already dozens in clinical use and hundreds applied in research. At present, however, by far the most commonly used radiotracer in clinical PET scanning is fluorodeoxyglucose (also called FDG or fludeoxyglucose), an analogue of glucose that is labeled with fluorine-18. This radiotracer is used in essentially all scans for oncology and most scans in neurology, and thus makes up the large majority of all of the radiotracer (> 95%) used in PET and PET-CT scanning.

Due to the short half-lives of most positron-emitting radioisotopes, the radiotracers have traditionally been produced using a cyclotron in close proximity to the PET imaging facility. The half-life of fluorine-18 is long enough that radiotracers labeled with fluorine-18 can be manufactured commercially at offsite locations and shipped to imaging centers. Recently rubidium-82 generators have become commercially available.[23] These contain strontium-82, which decays by electron capture to produce positron-emitting rubidium-82.

Limitations

The minimization of radiation dose to the subject is an attractive feature of the use of short-lived radionuclides. Besides its established role as a diagnostic technique, PET has an expanding role as a method to assess the response to therapy, in particular, cancer therapy,[24] where the risk to the patient from lack of knowledge about disease progress is much greater than the risk from the test radiation.

Limitations to the widespread use of PET arise from the 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 radiopharmaceuticals after radioisotope preparation. Organic radiotracer molecules that will contain a positron-emitting radioisotope cannot be synthesized first and then the radioisotope prepared within them, because bombardment with a cyclotron to prepare the radioisotope destroys any organic carrier for it. Instead, the isotope must be prepared first, then afterward, the chemistry to prepare any organic radiotracer (such as FDG) accomplished very quickly, in the short time before the isotope decays. Few hospitals and universities are capable of maintaining such systems, and most clinical PET is supported by third-party suppliers of radiotracers that can supply many sites simultaneously. This limitation restricts clinical PET primarily to the use of tracers labelled with fluorine-18, which has a half-life of 110 minutes and can be transported a reasonable distance before use, or to rubidium-82 (used as rubidium-82 chloride) with a half-life of 1.27 minutes, which is created in a portable generator and is used for myocardial perfusion studies. Nevertheless, in recent years a few on-site cyclotrons with integrated shielding and "hot labs" (automated chemistry labs that are able to work with radioisotopes) have begun to accompany PET units to remote hospitals. The presence of the small on-site cyclotron promises to expand in the future as the cyclotrons shrink in response to the high cost of isotope transportation to remote PET machines[25]

Because the half-life of fluorine-18 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.

Image reconstruction

The raw data collected by a PET scanner are a list of 'coincidence events' representing near-simultaneous detection (typically, within a window of 6 to 12 nanoseconds of each other) of annihilation photons by a pair of detectors. Each coincidence event represents a line in space connecting the two detectors along which the positron emission occurred (i.e., the line of response (LOR)). Modern systems with a higher time resolution (roughly 3 nanoseconds) also use a technique (called "Time-of-flight") where they more precisely decide the difference in time between the detection of the two photons and can thus localize the point of origin of the annihilation event between the two detectors to within 10 cm.

Coincidence events can be grouped into projection images, called sinograms. The sinograms are sorted by the angle of each view and tilt (for 3D images). The sinogram images are analogous to the projections captured by computed tomography (CT) scanners, and can be reconstructed in a similar way. However, the statistics of the data are much worse than those obtained through transmission tomography. A normal PET data set has millions of counts for the whole acquisition, while the CT can reach a few billion counts. This contributes to PET images appearing "noisier" than CT. Two major sources of noise in PET are scatter (a detected pair of photons, at least one of which was deflected from its original path by interaction with matter in the field of view, leading to the pair being assigned to an incorrect LOR) and random events (photons originating from two different annihilation events but incorrectly recorded as a coincidence pair because their arrival at their respective detectors occurred within a coincidence timing window).

In practice, considerable pre-processing of the data is required—correction for random coincidences, estimation and subtraction of scattered photons, detector dead-time correction (after the detection of a photon, the detector must "cool down" again) and detector-sensitivity correction (for both inherent detector sensitivity and changes in sensitivity due to angle of incidence).

Filtered back projection (FBP) has been frequently used to reconstruct images from the projections. This algorithm has the advantage of being simple while having a low requirement for computing resources. However, shot noise in the raw data is prominent in the reconstructed images and areas of high tracer uptake tend to form streaks across the image. Also, FBP treats the data deterministically—it does not account for the inherent randomness associated with PET data, thus requiring all the pre-reconstruction corrections described above.

Iterative expectation-maximization algorithms are now the preferred method of reconstruction. These algorithms compute an estimate of the likely distribution of annihilation events that led to the measured data, based on statistical principles. The advantage is a better noise profile and resistance to the streak artifacts common with FBP, but the disadvantage is higher computer resource requirements.[26]

Recent research has shown that Bayesian methods that involve a Poisson likelihood function and an appropriate prior probability (e.g., a smoothing prior leading to total variation regularization or a Laplacian distribution leading to ℓ_1-based regularization in a wavelet or other domain) may yield superior performance to expectation-maximization-based methods which involve a Poisson likelihood function but do not involve such a prior.[27][28][29]

Attenuation correction: Attenuation occurs when photons emitted by the radiotracer inside the body are absorbed by intervening tissue between the detector and the emission of the photon. As different LORs must traverse different thicknesses of tissue, the photons are attenuated differentially. The result is that structures deep in the body are reconstructed as having falsely low tracer uptake. Contemporary scanners can estimate attenuation using integrated x-ray CT equipment, however earlier equipment offered a crude form of CT using a gamma ray (positron emitting) source and the PET detectors.

While attenuation-corrected images are generally more faithful representations, the correction process is itself susceptible to significant artifacts. As a result, both corrected and uncorrected images are always reconstructed and read together.

2D/3D reconstruction: Early PET scanners had only a single ring of detectors, hence the acquisition of data and subsequent reconstruction was restricted to a single transverse plane. More modern scanners now include multiple rings, essentially forming a cylinder of detectors.

There are two approaches to reconstructing data from such a scanner: 1) treat each ring as a separate entity, so that only coincidences within a ring are detected, the image from each ring can then be reconstructed individually (2D reconstruction), or 2) allow coincidences to be detected between rings as well as within rings, then reconstruct the entire volume together (3D).

3D techniques have better sensitivity (because more coincidences are detected and used) and therefore less noise, but are more sensitive to the effects of scatter and random coincidences, as well as requiring correspondingly greater computer resources. The advent of sub-nanosecond timing resolution detectors affords better random coincidence rejection, thus favoring 3D image reconstruction.

Applications

PET is both a medical and research tool. It is used heavily in clinical oncology (medical imaging of tumors and the search for metastases), and for clinical diagnosis of certain diffuse brain diseases such as those causing various types of dementias. PET is also an important research tool to map normal human brain and heart function, and support drug development.

PET is also used in pre-clinical studies using animals, where it allows repeated investigations into the same subjects. This is particularly valuable in cancer research, as it results in an increase in the statistical quality of the data (subjects can act as their own control) and substantially reduces the numbers of animals required for a given study.

Alternative methods of scanning include x-ray computed tomography (CT), magnetic resonance imaging (MRI) and functional magnetic resonance imaging (fMRI), ultrasound and single-photon emission computed tomography (SPECT).

While some imaging scans such as CT and MRI isolate organic anatomic changes in the body, PET and SPECT are capable of detecting areas of molecular biology detail (even prior to anatomic change). PET scanning does this using radiolabelled molecular probes that have different rates of uptake depending on the type and function of tissue involved. Changing of regional blood flow in various anatomic structures (as a measure of the injected positron emitter) can be visualized and relatively quantified with a PET scan.

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.

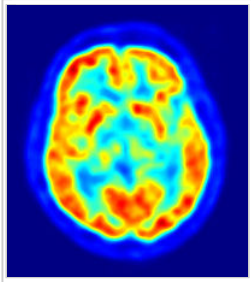
PET is a valuable technique for some diseases and disorders, because it is possible to target the radio-chemicals used for particular bodily functions.

Oncology

Oncology: PET scanning with the tracer fluorine-18 (F-18) fluorodeoxyglucose (FDG), called 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 has an effective radiation dose of 14 mSv.[30] Because the oxygen atom that is replaced by F-18 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 that 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 lymphoma, non-Hodgkin 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 that becomes especially useful in searching for tumor metastasis, or for recurrence after a known highly active primary tumor is removed. Because individual PET scans are more expensive than "conventional" imaging with computed tomography (CT) and magnetic resonance imaging (MRI), expansion of FDG-PET in cost-constrained health services will depend on proper health technology assessment; this problem is a difficult one because structural and functional imaging often cannot be directly compared, as they provide different information. Oncology scans using FDG make up over 90% of all PET scans in current practice.

A few other isotopes and radiotracers are slowly being introduced into oncology for specific purposes. For example, 11C-Metomidate has been used to detect tumors of adrenocortical origin.[31][32] Also, FDOPA PET-CT, in centers which offer it, has proven to be a more sensitive alternative to finding, and also localizing pheochromocytoma than the MIBG scan.[33][34][35]

Neuroimaging


PET scan of the human brain.

1. 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, in general, believed to be correlated, and has been measured using the tracer oxygen-15. However, because of its 2-minute half-life, O-15 must be piped directly from a medical cyclotron for such uses, which 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. PET imaging with FDG can also be used for localization of seizure focus: A seizure focus will appear as hypometabolic during an interictal scan. Several radiotracers (i.e. radioligands) have been developed for PET that are ligands for specific neuroreceptor subtypes such as [^{11}C] raclopride, [^{18}F] fallypride and [^{18}F] desmethoxyfallypride for dopamine D2/D3 receptors, [^{11}C] McN 5652 and [^{11}C] DASB for serotonin transporters, [^{18}F] Mefway for serotonin 5HT1A receptors, [^{18}F] Nifene for nicotinic acetylcholine receptors or enzyme substrates (e.g. 6-FDOPA for the AADC enzyme). These agents permit the visualization of neuroreceptor pools in the context of a plurality of neuropsychiatric and neurologic illnesses. The development of a number of novel probes for noninvasive, in vivo PET imaging of neuroaggregate in human brain has brought amyloid imaging to the doorstep of clinical use. The earliest amyloid imaging probes included 2-(1-{6-[(2-[^{18}F]fluoroethyl)(methyl)amino]-2-naphthyl}ethylidene)malononitrile ([^{18}F]FDDNP)[36] developed at the University of California, Los Angeles and N-methyl-[^{11}C]2-(4'-methylaminophenyl)-6-hydroxybenzothiazole[37] (termed Pittsburgh compound B) developed at the University of Pittsburgh. These amyloid imaging probes permit the visualization of amyloid plaques in the brains of Alzheimer's patients and could assist clinicians in making a positive clinical diagnosis of AD pre-mortem and aid in the development of novel anti-amyloid therapies. [^{11}C]PMP (N-[^{11}C] methylpiperidin-4-yl propionate) is a novel radiopharmaceutical used in PET imaging to determine the activity of the acetylcholinergic neurotransmitter system by acting as a substrate for acetylcholinesterase. Post-mortem examination of AD patients have shown decreased levels of acetylcholinesterase. [^{11}C]PMP is used to map the acetylcholinesterase activity in the brain, which could allow for pre-mortem diagnosis of AD and help to monitor AD treatments.[38] Avid Radiopharmaceuticals of Philadelphia has developed a compound called 18F-AV-45 that uses the longer-lasting radionuclide fluorine-18 to detect amyloid plaques using PET scans.[39]
2. Neuropsychology / Cognitive neuroscience: To examine links between specific psychological processes or disorders and brain activity.
3. Psychiatry: Numerous compounds that bind selectively to neuroreceptors of interest in biological psychiatry have been radiolabeled with C-11 or F-18. Radioligands that bind to dopamine receptors (D1,[40] D2 receptor,[41][42] 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.
4. Stereotactic surgery and radiosurgery: PET-image guided surgery facilitates treatment of intracranial tumors, arteriovenous malformations and other surgically treatable conditions.[22]

Cardiology

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. FDG-PET imaging of atherosclerosis to detect patients at risk of stroke is also feasible and can help test the efficacy of novel anti-atherosclerosis therapies.[43]

Infectious Diseases

Imaging infections with molecular imaging technologies can improve diagnosis and treatment follow-up. PET has been widely used to image bacterial infections clinically by using fluorodeoxyglucose (FDG) to identify the infection-associated inflammatory response.

Recently, three different PET contrast agents have been developed to image bacterial infections in vivo: [^{18}F]maltose,[44] [^{18}F]maltohexaose and [^{18}F] 2-fluorodeoxysorbitol (FDS).[45] FDS has also the added benefit of being able to target only Enterobacteriaceae.

Pharmacokinetics

Pharmacokinetics: In pre-clinical trials, it is possible to radiolabel a new drug and inject it into animals. Such scans are referred to as biodistribution studies. 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. Much more commonly, however, drug occupancy at a purported site of action can be inferred indirectly by competition studies between unlabeled drug and radiolabeled compounds known apriori to bind with specificity to the site. A single radioligand can be used this way to test many potential drug candidates for the same target. A related technique involves scanning with radioligands that compete with an endogenous (naturally occurring) substance at a given receptor to demonstrate that a drug causes the release of the natural substance.

The following is an excerpt from an article by Harvard University staff writer Peter Reuell, featured in HarvardScience, part of the online version of the Harvard Gazette newspaper, which discusses research by the team of Harvard Associate Professor of Organic Chemistry and Chemical Biology Tobias Ritter: "A new chemical process ... may increase the utility of positron emission tomography (PET) in creating real-time 3-D images of chemical activity occurring inside the body. This new work ... holds out the tantalizing possibility of using PET scans to peer into a number of functions inside animals and humans by simplifying the process of using “tracer” molecules to create the 3-D images." (by creating a novel electrophilic fluorination reagent as an intermediate molecule; the research could be used in drug development).[46]

Small animal imaging

PET technology for small animal imaging: A miniature PE tomograph has been constructed that is small enough for a fully conscious and mobile rat to wear on its head while walking around.[47] This RatCAP (Rat Conscious Animal PET) allows animals to be scanned without the confounding effects of anesthesia. PET scanners designed specifically for imaging rodents, often referred to as microPET, as well as scanners for small primates are marketed for academic and pharmaceutical research.

Musculo-skeletal imaging

Musculo-Skeletal Imaging: PET has been shown to be a feasible technique for studying skeletal muscles during exercises like walking.[48] One of the main advantages of using PET is that it can also provide muscle activation data about deeper lying muscles such as the vastus intermedialis and the gluteus minimus, as compared to other muscle studying techniques like electromyography, which can be used only on superficial muscles (i.e., directly under the skin). A clear disadvantage, however, is that PET provides no timing information about muscle activation, because it has to be measured after the exercise is completed. This is due to the time it takes for FDG to accumulate in the activated muscles.

Safety

PET scanning is non-invasive, but it does involve exposure to ionizing radiation.

18F-FDG, which is now the standard radiotracer used for PET neuroimaging and cancer patient management,[49] has an effective radiation dose of 14 mSv.[30]

The amount of radiation in 18F-FDG is similar to the effective dose of spending one year in Denver, CO (12.4 mSv/year).[50] For comparison, radiation dosage for other medical procedures range from 0.02 mSv for a chest x-ray and 6.5–8 mSv for a CT scan of the chest.[51][52] Average civil aircrews are exposed to 3 mSv/year,[53] and the whole body occupational dose limit for Nuclear Energy Workers in the USA is 50mSv/year.[54] For scale, see Orders of magnitude (radiation).

For PET-CT scanning, the radiation exposure may be substantial—around 23–26 mSv (for a 70 kg person—dose is likely to be higher for higher body weights).[55]

Cost per scan

As of August 2008, Cancer Care Ontario reports that the current average incremental cost to perform a PET scan in the province is $1,000–$1,200 per scan. This includes the cost of the radiopharmaceutical and a stipend for the physician reading the scan.[56]

Research

There are ongoing studies into using potassium 40 as this decays with a positron channel if a way could be found to enrich the isotope into a pure form in order to scan human neural pathways to study neurodegenerative diseases such as Alzheimers disease.

See also

- Diffuse optical imaging
- Hot cell (Equipment used to produce the radiopharmaceuticals used in PET)
- Molecular Imaging

References

1. Bailey, D.L; D.W. Townsend; P.E. Valk; M.N. Maisey (2005). *Positron Emission Tomography: Basic Sciences* (http://www.springer.com/?SGWID=0-102-24-0-0&searchType=EASY_CDA&queryText=Positron+Emission+Tomography%3A+Basic+Sciences). Secaucus, NJ: Springer-Verlag. ISBN 1-85233-798-2.
2. Ter-Pogossian MM; Phelps ME; Hoffman EJ; Mullani NA (1975). "A positron-emission transaxial tomograph for nuclear imaging (PET)". *Radiology* **114** (1): 89–98. doi:10.1148/114.1.89 (https://dx.doi.org/10.1148%2F114.1.89). OSTI 4251398 (https://www.osti.gov/energycitations/product.biblio.jsp?osti_id=4251398). PMID 1208874 (https://www.ncbi.nlm.nih.gov/pubmed/1208874).
3. Phelps ME; Hoffman EJ; Mullani NA; Ter-Pogossian MM (March 1, 1975). "Application of annihilation coincidence detection to transaxial reconstruction tomography" (http://jnm.snmjournals.org/cgi/content/abstract/16/3/210). *Journal of Nuclear Medicine* **16** (3): 210–224. PMID 1113170 (https://www.ncbi.nlm.nih.gov/pubmed/1113170).
4. Sweet, W.H.; G.L. Brownell (1953). "Localization of brain tumors with positron emitters". *Nucleonics* **11**: 40–45.
5. *A Vital Legacy: Biological and Environmental Research in the Atomic Age*, U.S. Department of Energy, The Office of Biological and Environmental Research, September 2010, p 25–26
6. Ido T; Wan CN; Casella V; Fowler JS et al. "Labeled 2-deoxy-D-glucose analogs. 18F-labeled 2-deoxy-2-fluoro-D-glucose, 2-deoxy-2-fluoro-D-mannose and 14C-2-deoxy-2-fluoro-D-glucose". *Journal of Labelled Compounds and Radiopharmaceuticals* **14** (2): 175–183. doi:10.1002/jlcr.2580140204 (https://dx.doi.org/10.1002%2Fjlcr.2580140204).
7. BROWNELL G.L., Dave Marcum, B. HOOP JR., and D.E. BOHNING, "Quantitative dynamic studies using short-lived radioisotopes and positron detection" in Proceedings of the Symposium on Dynamic Studies with Radioisotopes in Medicine, Rotterdam. August 31–September 4, 1945. IAEA. Vienna. 194824. pp. 161–172.

8. ROBERTSON J.S., MARR R.B., ROSENBLUM M., RADEKA V., and YAMAMOTO Y.L., ``32-Crystal positron transverse section detector, *in Tomographic Imaging in Nuclear Medicine, Freedman GS, Editor. 1983, The Society of Nuclear Medicine: New York. pp. 142–153.*
9. CHO, Z. H., ERIKSSON L., and CHAN J.K., ``A circular ring transverse axial positron camera *in Reconstruction Tomography in Diagnostic Radiology and Nuclear Medicine, Ed. Ter-Pogossian MM., University Park Press: Baltimore, 1975.*
10. "PET Scan: PET/CT History" (http://www.petscaninfo.com/zportal/portals/phys/petct/history). Petscaninfo.com. Retrieved 2012-08-13.
11. Michael E. Phelps (2006). *PET: physics, instrumentation, and scanners*. Springer. pp. 8–10. ISBN 0-387-34946-4.
12. "PET Imaging" (http://web.archive.org/web/20120205102047/http://www.medcyclopaedia.c GE Healthcare. Archived from the original (http://www.medcyclopaedia.com/library/topics/volume_i/p/pet_imaging.aspx) on 2012-02-05.
13. "Invitation to Cover: Advancements in "Time-of-Flight" Technology Make New PET/CT Scanner at Penn a First in the World" (http://www.uphs.upenn.edu/news/News_Releases/jun06/PETCTITC.htm). University of Pennsylvania. June 15, 2006. Retrieved February 22, 2010.
14. "A Close Look Into the Brain" (http://www.fz-juelich.de/inm/inm-4/EN/Forschung/MR-Physik/9komma4/_node.html). Jülich Research Centre. 7 March 2014. Retrieved 2015-04-14.
15. Brown RA; Nelson JA (June 2012). "Invention of the N-localizer for stereotactic neurosurgery and its use in the Brown-Roberts-Wells stereotactic frame". *Neurosurgery* **70** (2 Supplement Operative): 173–176. doi:10.1227/NEU.0b013e318246a4f7 (https://dx.doi.org/10.1227%2FNEU.0b013e318246a4f7). PMID 22186842 (https://www.ncbi.nlm.nih.gov/pubmed/22186842).
16. Heilbrun MP; Roberts TS; Apuzzo ML; Wells TH Jr et al. (August 1983). "Preliminary experience with Brown-Roberts-Wells (BRW) computerized tomography stereotaxic guidance system". *Journal of Neurosurgery* **59** (2): 217–222. doi:10.3171/jns.1983.59.2.0217 (https://dx.doi.org/10.3171%2Fjns.1983.59.2.0217). PMID 6345727 (https://www.ncbi.nlm.nih.gov/pubmed/6345727).
17. Thomas DG; Anderson RE; du Boulay GH (January 1984). "CT-guided stereotactic neurosurgery: experience in 24 cases with a new stereotactic system" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1027634/). *Journal of Neurology, Neurosurgery & Psychiatry* **47** (1): 9–16. doi:10.1136/jnnp.47.1.9 (https://dx.doi.org/10.1136%2Fjnnp.47.1.9). PMC 1027634 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1027634). PMID 6363629 (https://www.ncbi.nlm.nih.gov/pubmed/6363629).
18. Leksell L; Leksell D; Schwebel J (January 1985). "Stereotaxis and nuclear magnetic resonance" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1028176/). *Journal of Neurology, Neurosurgery & Psychiatry* **48** (1): 14–18. doi:10.1136/jnnp.48.1.14 (https://dx.doi.org/10.1136%2Fjnnp.48.1.14). PMC 1028176 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1028176). PMID 3882889 (https://www.ncbi.nlm.nih.gov/pubmed/3882889).
19. Thomas DG; Davis CH; Ingram S; Olney JS et al. (January 1986). "Stereotaxic biopsy of the brain under MR imaging control". *AJNR American Journal of Neuroradiology* **7** (1): 161–163. PMID 3082131 (https://www.ncbi.nlm.nih.gov/pubmed/3082131).
20. Heilbrun MP; Sunderland PM; McDonald PR; Wells TH Jr et al. (1987). "Brown-Roberts-Wells stereotactic frame modifications to accomplish magnetic resonance imaging guidance in three planes". *Applied Neurophysiology* **50** (1-6): 143–152. doi:10.1159/000100700 (https://dx.doi.org/10.1159%2F000100700). PMID 3329837 (https://www.ncbi.nlm.nih.gov/pubmed/3329837).
21. Maciunas RJ; Kessler RM; Maurer C; Mandava V et al. (1992). "Positron emission tomography imaging-directed stereotactic neurosurgery". *Stereotactic and Functional Neurosurgery* **58** (1-4): 134–140. doi:10.1159/000098986 (https://dx.doi.org/10.1159%2F000098986). PMID 1439330 (https://www.ncbi.nlm.nih.gov/pubmed/1439330).
22. Levivier M; Massager N; Wikler D; Lorenzoni J et al. (July 2004). "Use of stereotactic PET images in dosimetry planning of radiosurgery for brain tumors: clinical experience and proposed classification" (http://jnm.snmjournals.org/content/45/7/1146.long). *Journal of Nuclear Medicine* **45** (7): 1146–1154. PMID 15235060 (https://www.ncbi.nlm.nih.gov/pubmed/15235060).
23. Bracco Diagnostics, CardioGen-82 (http://www.nuclearonline.org/PI/Cardiogen.pdf), 2000
24. Young H; Baum R; Cremerius U; Herholz K et al. (1999). "Measurement of clinical and subclinical tumour response using [18F]-fluorodeoxyglucose and positron emission tomography: review and 1999 EORTC recommendations". *European Journal of Cancer* **35** (13): 1773–1782. doi:10.1016/S0959-8049(99)00229-4 (https://dx.doi.org/10.1016%2FS0959-8049%2899%2900229-4). PMID 10673991 (https://www.ncbi.nlm.nih.gov/pubmed/10673991).
25. Technology | July 2003: Trends in MRI | Medical Imaging (http://www.medicalimagingmag.com/issues/articles/2003-07_05.asp)
26. Vardi, Y.; L. A. Shepp; L. Kaufman (1985). "A statistical model for positron emission tomography". *Journal of the American Statistical Association* **80**: 8–37. doi:10.1080/01621459.1985.10477119 (https://dx.doi.org/10.1080%2F01621459.1985.10477119).
27. Willett, R.; Z. Harmany; R. Marcia (2010). "Poisson Image Reconstruction with Total Variation Regularization". *Accepted to IEEE International Conference on Image Processing (ICIP)*.
28. Harmany, Z.; R. Marcia; R. Willett (2010). "Sparsity-regularized Photon-limited Imaging". *International Symposium on Biomedical Imaging (ISBI)*.
29. Harmany, Z.; R. Marcia; R. Willett (2010). "SPIRAL out of Convexity: Sparsity-regularized Algorithms for Photon-limited Imaging". *SPIE Electronic Imaging*.
30. Exposure fact sheet (http://hps.org/documents/Medical_Exposures_Fact_Sheet.pdf) Health Physics Society
31. Khan TS; Sundin A; Juhlin C; Långström B et al. (2003). "11C-metomidate PET imaging of adrenocortical cancer". *European Journal of Nuclear Medicine and Molecular Imaging* **30** (3): 403–410. doi:10.1007/s00259-002-1025-9 (https://dx.doi.org/10.1007%2Fs00259-002-1025-9). PMID 12634969 (https://www.ncbi.nlm.nih.gov/pubmed/12634969).
32. Minn H; Salonen A; Friberg J; Roivainen A et al. (June 2004). "Imaging of adrenal incidentalomas with PET using (11)C-metomidate and (18) F-FDG" (http://jnm.snmjournals.org/cgi/content/full/45/6/972). *J. Nucl. Med.* **45** (6): 972–9. PMID 15181132 (https://www.ncbi.nlm.nih.gov/pubmed/15181132).
33. full text of early article on FDOPA PET for pheochromocytoma (http://hyper.ahajournals.org/content/38/1/6.full)
34. imaging overview (http://emedicine.medscape.com/article/379861-overview)
35. Luster M; Karges W; Zeich K; Pauls S et al. (2010). "Clinical value of 18F-fluorodihydroxyphenylalanine positron emission tomography/computed tomography (18F-DOPA PET/CT) for detecting pheochromocytoma". *Eur. J. Nucl. Med. Mol. Imaging* **37** (3): 484–93. doi:10.1007/s00259-009-1294-7 (https://dx.doi.org/10.1007%2Fs00259-009-1294-7). PMID 19862519 (https://www.ncbi.nlm.nih.gov/pubmed/19862519).
36. Agdeppa ED; Kepe V; Liu J; Flores-Torres S et al. (2001). "Binding characteristics of radiofluorinated 6-dialkylamino-2-naphthylethylidene derivatives as positron emission tomography imaging probes for beta-amyloid plaques in Alzheimer's disease" (http://www.jneurosci.org/content/21/24/RC189.full.pdf) (PDF). *J Neurosci* **21** (24): RC189(1–5). PMID 11734604 (https://www.ncbi.nlm.nih.gov/pubmed/11734604).
37. Mathis CA; Bacskai BJ; Kajdasz ST; McLellan ME et al. (2002). "A lipophilic thioflavin-T derivative for positron emission tomography (PET) imaging of amyloid in brain". *Bioorg. Med. Chem. Lett.* **12** (3): 295–8. doi:10.1016/S0960-894X(01)00734-X (https://dx.doi.org/10.1016%2FS0960-894X%2801%2900734-X). PMID 11814781 (https://www.ncbi.nlm.nih.gov/pubmed/11814781).
38. Kuhl DE; Koeppe RA; Minoshima S; Snyder SE et al. (March 1999). "In vivo mapping of cerebral acetylcholinesterase activity in aging and Alzheimer's disease". *Neurology* **52** (4): 691–9. doi:10.1212/wnl.52.4.691 (https://dx.doi.org/10.1212%2Fwnl.52.4.691). PMID 10078712 (https://www.ncbi.nlm.nih.gov/pubmed/10078712).
39. Kolata, Gina. "Promise Seen for Detection of Alzheimer's" (http://www.nytimes.com/2010/06/24/health/research/24scans.html), *The New York Times*, June 23, 2010. Accessed June 23, 2010.
40. Catafau AM; Searle GE; Bullich S; Gunn RN et al. (2010). "Imaging cortical dopamine D1 receptors using 11C NNC112 and ketanserin blockade of the 5-HT 2A receptors" (http://www.nature.com/jcbfm/journal/v30/n5/full/jcbfm2009269a.html). *J Cereb Blood Flow Metab* **30** (5): 985–93. doi:10.1038/jcbfm.2009.269 (https://dx.doi.org/10.1038%2Fjcbfm.2009.269). PMID 20029452 (https://www.ncbi.nlm.nih.gov/pubmed/20029452).
41. Mukherjee J; Christian BT; Dunigan KA; Shi B et al. (2002). "Brain imaging of 18F-fallypride in normal volunteers: Blood analysis, distribution, test-retest studies, and preliminary assessment of sensitivity to aging effects on dopamine D-2/D-3 receptors". *Synapse* **46** (3): 170–88. doi:10.1002/syn.10128 (https://dx.doi.org/10.1002%2Fsyn.10128). PMID 12325044 (https://www.ncbi.nlm.nih.gov/pubmed/12325044).

42. Buchsbaum MS; Christian BT; Lehrer DS; Narayanan TK et al. (2006). "D2/D3 dopamine receptor binding with F-18fallypride in thalamus and cortex of patients with schizophrenia". *Schizophrenia research* **85** (1–3): 232–44. doi:10.1016/j.schres.2006.03.042 (https://dx.doi.org/10.1016%2Fj.schres.2006.03.042). PMID 16713185 (https://www.ncbi.nlm.nih.gov/pubmed/16713185).
43. Rudd JH; Warburton EA; Fryer TD; Jones HA et al. (2002). "Imaging atherosclerotic plaque inflammation with [18F]-fluorodeoxyglucose positron emission tomography". *Circulation* **105** (23): 2708–11. doi:10.1161/01.CIR.0000020548.60110.76 (https://dx.doi.org/10.1161%2F01.CIR.0000020548.60110.76). PMID 12057982 (https://www.ncbi.nlm.nih.gov/pubmed/12057982).
44. Gowrishankar, G.; Namavari, M.; Jouannot, E. B.; Hoehne, A. et al. (2014). "Investigation of 6-[18F]-fluoromaltose as a novel PET tracer for imaging bacterial infection". *Plos One* **9** (9). doi:10.1371/journal.pone.0107951 (https://dx.doi.org/10.1371%2Fjournal.pone.0107951). PMID 25243851 (https://www.ncbi.nlm.nih.gov/pubmed/25243851).
45. Weinstein EA; Ordonez AA; DeMarco VP; Murawski AM et al. (2014). "Imaging Enterobacteriaceae infection in vivo with 18F-fluorodeoxysorbitol positron emission tomography". *Science Translational Medicine* **6** (259). doi:10.1126/scitranslmed.3009815 (https://dx.doi.org/10.1126%2Fscitranslmed.3009815). PMID 25338757 (https://www.ncbi.nlm.nih.gov/pubmed/25338757).
46. "Tracing biological pathways | Harvard Gazette" (http://news.harvard.edu/gazette/story/2011/11/tracing-biological-pathways/). News.harvard.edu. Retrieved 2012-08-13.
47. Rat Conscious Animal PET (http://www.chemistry.bnl.gov/ratcap/gallery.html)
48. Oi N; Iwaya T; Itoh M; Yamaguchi K et al. (2003). "FDG-PET imaging of lower extremity muscular activity during level walking". *J Orthop Sci* **8** (1): 55–61. doi:10.1007/s007760300009 (https://dx.doi.org/10.1007%2Fs007760300009). PMID 12560887 (https://www.ncbi.nlm.nih.gov/pubmed/12560887).
49. Kelloff GJ; Hoffman JM; Johnson B; Scher HI et al. (Apr 2005). "Progress and promise of FDG-PET imaging for cancer patient management and oncologic drug development". *Clin. Cancer Res.* **11** (8): 2785–808. doi:10.1158/1078-0432.CCR-04-2626 (https://dx.doi.org/10.1158%2F1078-0432.CCR-04-2626). PMID 15837727 (https://www.ncbi.nlm.nih.gov/pubmed/15837727).
50. Background Radiation in Denver (http://isis-online.org/risk/tab7), Institute for Science and International Security
51. Managing Patient Does (https://web.archive.org/web/20051015024328/http://www.icrp.org/downloadDoc.asp document=docs/ICRP_87_CT_s.pps), ICRP, 30 October 2009.
52. de Jong PA; Tiddens HA; Lequin MH; Robinson TE et al. (May 2008). "Estimation of the radiation dose from CT in cystic fibrosis". *Chest* **133** (5): 1289–91; author6 reply 1290–1. doi:10.1378/chest.07-2840 (https://dx.doi.org/10.1378%2Fchest.07-2840). PMID 18460535 (https://www.ncbi.nlm.nih.gov/pubmed/18460535).
53. Chapter 9 Occupational Exposure to Radiation (http://www.iaea.org/Publications/Booklets/RadPeopleEnv/pdf/chapter_9.pdf), IAEA
54. Information for Radiation Workers (http://www.nrc.gov/about-nrc/radiation/health-effects/info.html#dose) , Nuclear Regulatory Commission
55. Brix G; Lechel U; Glatting G; Ziegler SI et al. (April 2005). "Radiation exposure of patients undergoing whole-body dual-modality 18F-FDG PET/CT examinations". *J. Nucl. Med.* **46** (4): 608–13. PMID 15809483 (https://www.ncbi.nlm.nih.gov/pubmed/15809483).
56. Ontario PET Steering Committee (August 31, 2008), *PET SCAN PRIMER, A Guide to the Implementation of Positron Emission Tomography Imaging in Ontario, Executive Summary* (https://www.cancercare.on.ca/common/pages/UserFile.aspx?fileId=13626), pp. iii

External links

- PET Images (http://rad.usuhs.edu/medpix/master.php3?mode=image_finder&action=search&srchstr=&srch_type=all&labels=&details=2&no_filter=2&plane_id=&capt_id=-4&filter_m=modality&filter_o=&acr_pre=8 Search MedPix(r)
- Seeing is believing: In vivo functional real-time imaging of transplanted islets using positron emission tomography (PET) (a protocol) (http://www.natureprotocols.com/2006/12/21/seeing_is_believing_in_vivo_fu_1.php), Nature Protocols, from Nature Medicine 12, 1423–1428 (2006).
- The nuclear medicine and molecular medicine podcast (http://nuccast.com)—Podcast
- Positron Emission Particle Tracking (http://www.np.ph.bham.ac.uk/pic/pept.htm) (PEPT)—engineering analysis tool based on PET that is able to track single particles in 3D within mixing systems or fluidised beds. Developed at the University of Birmingham, UK.
- CMS coverage of PET scans (http://www.hematologytimes.com/ht/p_article.do?id=948)
- PET-CT atlas Harvard Medical School (http://www.med.harvard.edu/JPNM/chetan/)
- National Isotope Development Center (http://isotopes.gov/)—U.S. government source of radionuclides including those for PET—production, research, development, distribution, and information