INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES
[ISSN: 0975-4725; CODEN(USA): IJPS00]
Journal Homepage: https://www.ijpsjournal.com

OPEN ACCESS

Review Article

The Role Of Pet Scan In Diagnosis, Staging And Management Of Cancer

Kalyani P. Sangle, Ashwini Bhivasane, Dr. Gajanan Sanap

Late Bhagirathi Yashwantrao Pathrikar College of Pharmacy, Pathri Phulambri Chh. Sambhajinagar 431111

ARTICLE INFO

Published: 19 Dec. 2024

Keywords:

Positron Emission Tomography (PET), Cyclotrons, PET Radiotracer Ultrasonography, FDG.

DOI:

10.5281/zenodo.14524264

ABSTRACT

Nowadays, PET scans are a crucial part of the diagnostic and staging process for cancer, providing information about the prognosis based on response. This paper aims to provide a thorough analysis of the utility of PET in the locoregional and distant staging of non-small cell lung cancer (NSCLC), as well as to highlight some of the more recent uses and highlight any possible implications for patient care. When evaluating an ambiguous solitary pulmonary nodule or mass, computed tomography (CT) is not as accurate as PET in differentiating between benign and malignant lesions, so PET is the gold standard in this regard. Since PET is far more reliable than CT in assessing the progression of metastases to locoregional lymph nodes, many patients with negative mediastinal PET scans may be spared invasive surgical staging. In cases where invasive surgical staging is required for patients with positive mediastinal PET scans, false-positive results resulting from inflammatory nodes or granulomatous diseases may still exist. PET is a helpful addition to traditional imaging in the hunt for metastatic spread. This could be from the exclusion of malignancy in lesions that are unclear on routine imaging, or it could be the discovery of unanticipated metastatic lesions. PET does not, however, now take the place of traditional imaging. Currently, large-scale randomized trials are being conducted to investigate whether PET staging can genuinely make lung cancer appear better.

INTRODUCTION

The majority of commercial versions of PET scanners today reach very good morphologic resolution, ranging from 6 to 8 mm. It can identify changes at the nanomolar level and has a high sensitivity to detect a regional rise or decrease in a tracer's concentration. PET/CT hybrid scanners enable the simultaneous acquisition of CT and PET images in a single investigation, allowing for their separate or combined visualization. As a result, the same pictures can contain information about the anatomy from CT and the function or metabolism of PET.[1] Numerous materials, including endogenous compounds, can be used as PET tracers to visualize and evaluate a wide range of metabolic events inside cells.

***Corresponding Author:** Kalyani P. Sangle

Address: *Late Bhagirathi Yashwantrao Pathrikar College of Pharmacy, Pathri Phulambri Chh. Sambhajinagar 431111*

Email ✉: kalyanisangle2@gmail.com

Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Sarcoidosis is a multisystemic illness that affects several organ systems and is characterized by cellular immune activity and the development of noncaseating granulomas. Consistent clinical characteristics and histological evidence of non-caseating epithelioid cell granulomas are typically used to make the diagnosis. Sarcoidosis's clinical course is incredibly unpredictable.[2]Through the noninvasive diagnostic imaging technique known as Positron Emission Tomography (PET), medical professionals can see the biological processes of the human body and learn about disease processes. PET had been thought of and used as a research tool up until recently, specifically in the study of neurophysiology. Nonetheless, during the past ten years, it has become more and more clear how useful PET is as a clinical imaging technique. PET scans have been used by medical experts in the domains of neurology, cardiology, and oncology to evaluate metabolism in relation to cancer, damaged cardiac tissue, and brain diseases.[3]

With an estimated 3 million new cases annually worldwide, lung cancer is the most common cause of cancer-related death in the Western world. Imaging methods are critical to the diagnosis, staging, and aftercare of lung cancer patients. The use of Positron Emission Tomography (PET) in lung cancer imaging has grown in importance. Variations in the structure of tissues serve as the foundation for standard imaging techniques. The improved glucose metabolism of lung cancer cells serves as the basis for PET using the glucose analogue 2-18F-fluoro-2-deoxy-D-glucose (FDG).[4]

The intake of FDG is similar to that of glucose, but upon phosphorylation by hexokinase, it becomes metabolically trapped and accumulates within the cancer cell. Increased uptake of the positron-emitting radiopharmaceutical FDG is seen in malignant tumors. PET imaging can show this enhanced FDG uptake in tumors. When determining the difference between benign and malignant lung nodules, FDG PET has a far greater accuracy rate than other imaging modalities.[5]

PET has a 96% sensitivity and a 77% specificity in identifying cancerous nodules. In terms of staging mediastinal nodal involvement, PET is also more accurate than computed tomography (CT) (89% sensitivity, 94% specificity). PET can reliably distinguish between scar tissue and a recurrent tumor due to the limited absorption of FDG in scar tissue. Preliminary research indicates that PET may have a bright future in assessing treatment response. 18F-FDG PET imaging has gained acceptance as a useful diagnostic imaging tool for cancer patients since the Health Care Financing Administration (HCFA) authorized Medicare to reimburse for 18F-FDG PET imaging for specific indications in 1998 and the American Food and Drug Administration (FDA) approved 18F-FDG as a safe and effective radiopharmaceutical for oncologic applications in 1997. But the primary challenge with PET is that it does not have an anatomical reference frame.[6]

History of pet scan:

The narrative of positron emission tomography's (PET) creation and advancement is rooted in the inventiveness of experimental and theoretical physicists, biologists, chemists, and physicians—people who did not initially anticipate the significant advantages the new technology would offer. Historically, military-oriented research has been essential to medical advancements. In addition to PET, some notable instances include the discovery of the element iodine, the creation of penicillin and other medicines, blood transfusion and blood type, ultrasonography, and computers. Sadly, in the case of PET, the public's enduring belief that radiation is dangerous and should be avoided at all costs continues to stand in the way of the advancement of atomic energy's benign applications. P. Dirac, a theoretical physicist, proposed the possibility of positive electrons, or positrons, based on Einstein's theory of relativity and the quantum mechanical equations.[7]]He gave an example of how the square root of the square of the particles' momentum and rest energy, plus or negative, determines the energy of subatomic particles. Thus, it is possible for subatomic particles to be positive or negative.[8]

The accuracy of Dirac's prediction was demonstrated in 1932 by experimental physicist C.D. Anderson of the California Institute of Technology, who observed that cosmic rays contain particles with the mass of electrons but travel along a path in a strong magnetic field that suggests they have a positive charge.[9] These particles were dubbed "positrons," or positive electrons, by him.

Artificial Radioactivity And Cyclotrons:

In 1934, Curie and Joliot noticed that positrons continued to be released from targets that had been bombarded with alpha particles from radium or polonium for a while after the bombardment had stopped.[10] This was the first indication that it was possible to create artificial radioactive atoms.

The idea of accelerating particles between two D-shaped magnets, or a cyclotron, was conceived four years earlier in Berkeley, California, by Ernest Lawrence et al. The goal was to produce protons and deuterons with increasingly higher energy so that they could bombard elements and learn more about the nature of the atomic nucleus .[11] Their original cyclotron contained 4 inch cyclotron magnets; the magnets in their later machines were 10, 37, and 60 inches in diameter.

Biologists, physiologists, and doctors came to Berkeley in the 1930s, realizing the significance of the new radioelements in implementing the tracer principle—first proposed by Hevesy utilizing naturally occurring ring radiotracers. A "medical cyclotron" was the term given by Lawrence, Livingston, et al. in 1938 to their fourth cyclotron (Fig 1)

Fig.1. S. Livingston and e. Lawrence with the medical cyclotron developed in the late 1930s at the university of california in berkeley.

The cyclotron is placed on a back burner by the reactor: Copenhagen-born physicist Niels Bohr came to Princeton University in 1939 to see Einstein. He learned of O. Hahn and F. Strassmann's experiments, which were published in Naturwissenschaflen in January 1939, shortly before he left Denmark.[12]

Three aspects of atomic energy have always been closely related to one another: nuclear weapons, nuclear power, and nuclear medicine. The invention of the nuclear reactor by Fermi et al. at the University of Chicago produced large amounts of tritium, phosphorus-32, carbon-14, and other radionuclides, which in turn led to the development of modern biochemistry. It would take thirty years for doctors' interest in cyclotrons to resurface in biomedical research due to their wish to quantify in vivo regional biochemistry.

Carbon is the fundamental element of organic chemistry, and the only carbon radionuclide that emits photons is carbon-11, which can only be produced in a cyclotron.

The "biological" elements—carbon, fluorine, nitrogen, and oxygen—returned to the focus of the nuclear medicine community with the advent of "competitive" imaging techniques like computed tomography (CT) and magnetic resonance imaging (MRI).

In Vivo Biochemistry: Since the 1940s, when nuclear medicine first emerged, measurements of radiotracers' external distribution within the body have been made. Initially, to assist determine if a thyroid nodule was benign or cancerous, handheld Geiger-Muller counters were moved methodically in a grid pattern to assess the rate of uptake of radioactive iodine by the thyroid gland In 1950, Benedict Cassen of UCLA invented what was referred to be a "scanner" by automating the movement of the detector across the thyroid region and substituting newly developed thallium-activated sodium iodide crystals for the GM detector. Nuclear pictures of the liver, spleen, and lungs were rapidly created using this apparatus. Molecular imaging in vivo was created.

Positron Imaging: Kety and Schmidt first applied the Fick principle to quantify cerebral blood flow in 1948 using the nonradioactive tracer nitrous oxide.[13] Later, in order to make the measurements easier, they substituted krypton-79 for nitrous gas, and the numbers they obtained for cerebral blood flow were nearly equal to those obtained with nitrous oxide. Lassen and Munck modified the nitrous oxide method using krypton-85 and utilized xenon-133 instead of krypton-133 in 1961 to measure the quantitatively the regional cerebral blood flow in humans using many small single crystal radiation detectors. "It may be predicted that these component structures' rates of blood flow would differ greatly and vary independently of one another, given that their functional activities vary independently of one another.[14]

Consequently, he focused his research on measuring the blood flow to distinct tiny cerebral areas in cat brains using autoradiography and I-131 tagged trifluoroiodomethane. A multidetector system for localizing brain tumors using positron-emitting radionuclides, copper-64 and arsenic-75, was disclosed by Brownell and Sweet in 1953. The apparatus seen in Figure 2 was built by Yamamoto et al. at Brookhaven National Laboratory (BNL) in 1966 in order to quantify regional cerebral blood flow using positron emitting radiotracers. The device was taken to the Montreal Neurological Institute where the detectors were arranged in a single plane around the patient's head following initial research on it at BNL. The filtered back projection approach, which was to be effective in computed tomography (CT) of conventional x-ray imaging and subsequently used to PET imaging, was not discovered by these investigators despite their attempts at many reconstruction techniques.

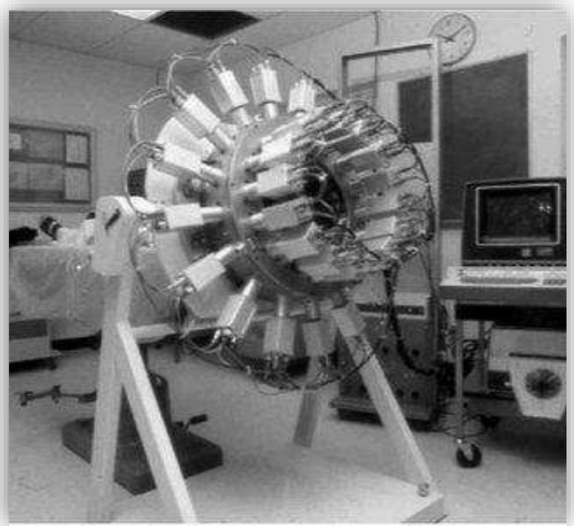


Fig.2: Yamamoto, Robertson, et al.'s original concept for the Brookhaven National Laboratory's instrument to study positron emitting radiotracers in the brain. It had not yet been thought of to arrange a circular array of detectors in a single plane.

Tomography: In 1968, Kuhl and Edwards developed a machine to create these kinds of images and proposed the idea of reconstructing source distributions in conventional nuclear imaging by superimposing many cross sections of transverse axial scans (Fig 3).[15] The reconstruction technique was extremely basic, and Hounsfield's invention of transverse axial tomography for radiography sped forward the development of PET. [15],[16]

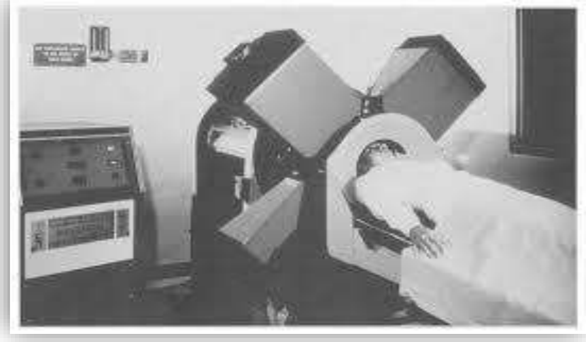


Fig.3: shows the Mark IV tomographic scanner that Kuhl et al. from the University of Pennsylvania constructed to analyze radiotracers that generate single photons. An key advancement was placing the detectors in a ring around the patient's head.

A PET device using the filtered back projection reconstruction method was described by Ter-Pogossian, Phelps, and Hoffman in 1975 (Fig 4).[17, 18]

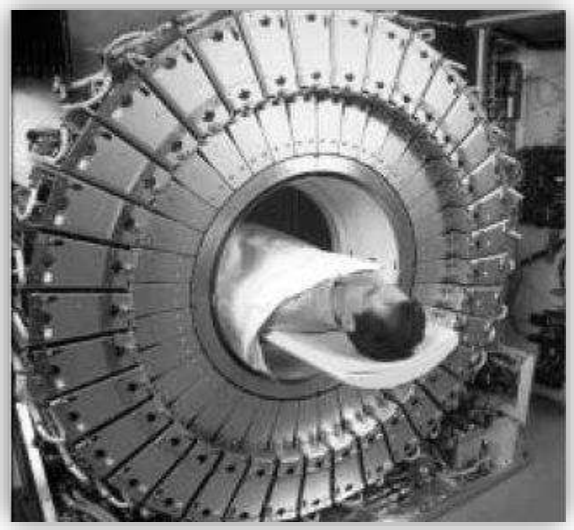


Fig.4: shows the author being evaluated in the initial PEI-T scanner at Washington University in Saint Louis by Ter-Pogossian et al. Carbon-11 carbon monoxide was the tracer.

In order to investigate the oxygenation of tumors, TerPogossian and Powers (1958) at Washington University in St. Louis, MO, used oxygen-15 (half-life 21/2 minutes) generated by the cyclotron constructed in the physics department in the early 1940s to study mice with mammary adenocarcinomas in the mid-1950s. They used autoradiography to map the location of the injected oxygen-15(Fig5).

Fig.5: Michel Ter-Pogossian with the cyclotron at Washington University.

The FDG Story: Langstrom stated: "Carbon-ll fulfills Claude Bernard's dream of a tracer for examining physiological processes in complex living systems." Sokoloff et al. published a famous publication in 1977, ten years after the technology's inception, outlining the carbon-14 deoxy-glucose method for measuring local cerebral glucose use.[19] Prior to this work, the cerebral arteriovenous difference in glucose levels and blood flow measurements in living individuals could be used to calculate the average rate of glucose usage in the brain overall. This was made feasible by the Kety-Schmidt method for measuring cerebral blood flow.

Ido and associates had developed this tracer. [19]

The creation of this tracer, modeling its application to identify cerebral glucose usage on a regional scale, and measuring cerebral blood flow on a regional scale using oxygen-15 water led to the development of functional mapping of the human brain. The last paper in the PET series will go into great detail about the clinical use of FDG in the fields of cardiology, neurology, and oncology.

2-fluoro-2-deoxy-D-glucose “FDG”

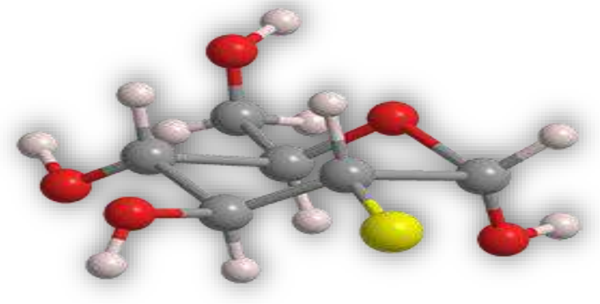


Fig.6: A Chemical Sketch of FDG

FDG competes with the body's glucose for admission into cells to participate in intracellular metabolism because of its glucose orientation. FDG, however, does not continue in the cell's metabolic process like glucose does; instead, it stops at the phosphorylation stage and stays within the cell, where it is found and seen during the PET technique. Because cancer cells proliferate and expand more quickly than normal cells, they survive on a greater rate of metabolism. As a result, during an FDG-PET scan technique, most cancer cells absorb more glucose-based FDG than normal cells [approximately 20 times more, according to some sources]. As a result, on a PET scan, the cancer-ridden regions of aberrant [increased] metabolic activity show up as "hot spots" or intensely lit regions. On a PET scan, abnormal metabolic activity that appears as "hot spots" may also be a sign of brain or cardiac problems (Figure 7).[3],[20],[8],

Nuclear Oncology: Over the past ten years, a number of studies using specialized PET scanners and fluorine-18 labeled deoxyglucose (18F-FDG) have demonstrated how measuring the accumulation of 18F-FDG by malignant lesions can aid in the resolution of several issues pertaining to the treatment of cancer patients. [8],[21] It has been discovered that, in comparison to normal tissue, several forms of cancer exhibit enhanced anaerobic breakdown of glycogen to glucose as an energy source. Hexokinase HKII is frequently elevated, which improves the glycolytic process and converts glucose to lactate instead of carbon dioxide and water.

Molecular Coincidence Detection (MCD): When Gerd Mueller and his engineering team at ADAC Laboratories modified a single photon emission tomography (SPECT) scanner in 1994 to perform coincidence imaging of the 511 keV photons emitted by decay of positron-emitting radiotracers, such as 18F-FDG, without a lead collimator, it opened up a new avenue for imaging FDG accumulation by neoplasms.[22] "Molecular Coincidence Detection" (MCD) was the term given to the procedure. This development provided a completely new method for 18F-FDG imaging in cancer patients' care, initially to assess the possibility of curative surgery. The growing accessibility of commercially generated 18F-FDG was another aspect that enabled the increased application of 18F-FDG investigations in cancer patient treatment.

PET: Proton-rich, cyclotron-produced radioisotopes that decay to their ground state by either grabbing an electron and turning the excess proton into a neutron (111Indium) or producing positrons, which are positively charged beta particles (e.g., 18Fluorine). When positron decay occurs, the newly formed ß+ particle nearly instantly annihilates and interacts with a free electron (e–), producing two gamma rays with an energy of 0.511 MeV each. PET is made possible by the fact that these gamma rays are 180° apart and travel in different directions. PET employs the same filtered back projection reconstruction methods as CT.When compared to other nuclear medicine imaging methods, one distinctive characteristic of PET is its ability to adjust pictures for gamma ray tissue attenuation.

Principle: Using the annihilation photons released by positron emitters known as radiotracers, positron emission tomography (PET) is a tomographic technique that calculates the three-dimensional distribution of radioactivity. PET enables the quantitative, non-invasive evaluation of biological and functional processes. The glucose analogue FDG is currently the most widely used tracer. The amount of glucose used determines the amount of FDG buildup in tissue. Most malignancies have increased glucose intake, which is partly caused by elevated hexokinase activity and over-expression of the GLUT-1 glucose transporters. Owing to the kinetics of FDG, sufficient static pictures are often obtained 60 minutes following injection.

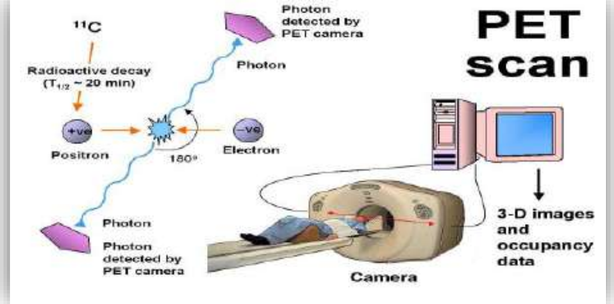
It is acknowledged, although, that the absorption period varies greatly, with some tumors not exhibiting a plateau in FDG concentration for as long as 4-6 hours [23]. Variable uptake is probably connected to the biological characteristics of particular tumors, as shown in most prostate carcinomas as well as various subtypes of malignant lymphoma, carcinoids, renal, thyroid, and broncho-alveolar carcinomas. This biological heterogeneity's cause and prognostic significance are not always evident. Nonetheless, FDG PET is generally a sensitive imaging technique for cancer therapy response assessment, staging, restaging, and detection [24],[25]

Computed tomography (CT), as opposed to PET, creates tomographic pictures using an x-ray beam. High anatomical resolution visualization of morphological and anatomical structures is possible with CT. The utilisation of CT-derived anatomical and morphological data can enhance the accuracy of FDG PET-detected lesion location, extent, and characterization.[26] In ordinary clinical practice, FDG PET and CT are well-established imaging modalities that have undergone substantial validation. PET/CT is becoming increasingly important for imaging in oncology. Simultaneously, there is a growing recognition that the quantitative characteristics of PET could significantly influence clinical practice and oncology studies.

How Pet Work: In order to study and visualize human physiology, positron emission tomography, or PET, is a nuclear medicine scanning technique that uses electronic detection of short-lived positron-emitting radiopharmaceuticals, which are substances that contain a carrier molecule, like glucose, and a positron-emitting radioactive isotope that labels or tags the carrier molecule. While patients are comfortable, conscious, and awake during the PET scanning process, doctors and researchers may measure in detail how the human brain and other organs function. Three-dimensional images of the body's distribution of a radiopharmaceutical supplied by IV are produced by the PET scanner or camera. The images make it possible to track and assess physiological functions such cerebral blood flow, oxygen and glucose metabolism, and metabolism.

In order to comprehend PET, we first look at what happens from a physics perspective during a PET scan and how the PET scanner or camera records, processes, and interprets those events. Next, we examine the PET scan process from the viewpoint of the patient, including everything the patient witnesses, feels, and learns about behind the scenes. Details on the scan's creation process and the disparities between the representations of healthy and unhealthy tissue are covered by that viewpoint.Lastly, we go over the main radiopharmaceuticals used in PET, their synthesis, and their particular suitability for oncology, cardiology, and neurology clinical applications. The main challenges (i.e., equipment cost, setting up a PET system, insurance reimbursement) that many believe stand in the way of PET's widespread use as a clinical treatment are outlined in the second section. [27]SSS

Technical Consideration



The Pet Scan Procedure: The patient first has a blood glucose test and a preliminary evaluation of their medical history before receiving an IV injection of a positron-emitting radiopharmaceutical that was recently synthesized from a positron-emitting radioisotope produced using a cyclotron. The moderately radioactive radiopharmaceutical diffuses throughout the body through the blood stream and builds up in the organ or system under evaluation in less than an hour while the patient relaxes. There is very little radiation exposure—in fact, less radiation exposure than there is from many x-ray procedures. The specific radiopharmaceutical is selected according to how well-suited it is for a given organ or bodily system. Depending on the radiopharmaceutical, different times are needed for distribution and accumulation.

The patient is comfortably positioned on a narrow table known as a scanning bed that moves slowly through the PET scanner or gamma camera by the PET technologist, a skilled medical professional with specialized education in radiation protection, radiopharmaceuticals, and nuclear medicine techniques. This is done after allowing for the appropriate time for the distribution and accumulation of the radiopharmaceutical. The processes of coincident imaging and detection occur while the scanner bed moves, producing a sequence of tiny slices of the organ or bodily system under evaluation. The slices are then rebuilt into a three-dimensional picture that shows where the radiopharmaceutical is located and concentrated in that particular physiological system or organ. Making the patient as comfortable as possible is essential since, depending on the technique, the patient must stay still and silent for the duration of the scanning process (which can be anywhere from 30 to 2 hours) in order to produce high-quality photos at the conclusion of the process. When patients are getting PET scans of the head, specific precautions, such as the use of special cushions to hold the head in place or a mask with openings for the eyes, nose, and mouth that is linked to the scanning bed, may be utilized to keep the head still.

The PET scanner has thousands, or perhaps 12,000, of detectors with unique scintillation crystals inside of them. When gamma rays strike these crystals, they form electrical signals. As the gamma radiation from the collision, contact, and annihilation of the radiopharmaceutical's released positrons with the patient's body electrons is detected by the scintillation crystals, an emission scan is produced. The photos' varying hues and luminosities correspond to various physiological function levels. When a glucose-based radiopharmaceutical is used in oncologic studies, the background area of the image will represent healthy tissue, while the foreground will be much brighter due to the cancerous tissue's absorption of more radiopharmaceutical than the normal tissue. This is because most cancerous tissue has an innate tendency to metabolize glucose more than normal tissue—up to 20 times more.[28]

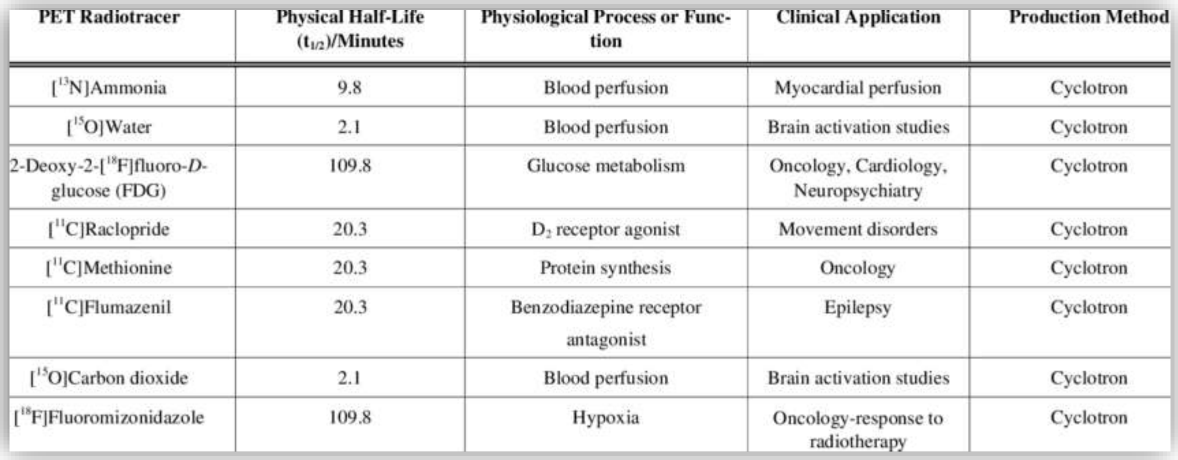
Patients are advised to pee following the operation since radiopharmaceuticals generally tend to collect in the bladder. Furthermore, patients are advised to ensure that the radiopharmaceutical is removed from their systems as soon as possible by drinking a lot of liquids throughout the rest of the day and urinating often. Because of the short half-life of the radioisotope component in radiopharmaceuticals, the majority of the radiation usually goes away in the first four to eight hours after the injection.[29] PET scans are typically carried out as outpatient treatments. The PET technologist processes and records the scan data after the procedure. A nuclear medicine specialist then evaluates and interprets the obtained images. Lastly, the doctor who requested the PET study receives a report straight from the physician based on his or her results.

The stages involved in a PET scan technique are as follows:

- The radiopharmaceutical is brought from an off-site location to the imaging site, or it is synthesized on site from a positron-emitting radioisotope produced by a cyclotron.
- The PET technician gives the patient the radiopharmaceutical intravenously (IV) and gives the drug time to spread throughout the body. The patient's electrons (e-) and the radiopharmaceutical's positrons (e+) collide as the patient slowly passes through the scanner on a scanning bed.
- The collisions cause annihilation and the release of gamma rays, which are then detected by detectors in the PET scanner outside the patient's body.
- The gamma rays that are coincident are identified by the scanner electronics, which then pair them into coincident events.
- The doctor who ordered the PET study receives information from a radiologist after they have analyzed and interpreted the images.

Pet Scan Modes: There are various ways to derive PET scans. The whole-body static mode, which is essentially a snapshot of the patient's physiology, is one often used mode. A different mode that depicts the uptake of radiopharmaceuticals over time is a more dynamic and active mode. Additional modes include the three-dimensional volume-imaging mode, which is well-known for its capacity to enhance image quality and shorten scan times, and the gated mode, which mimics the cardiac cycle in a sequence of images.

Radiopharmaceutical In Pet: Radiopharmaceuticals are needed for the PET imaging procedure in addition to a computer and PET scanner. A positron-emitting radio isotope that identifies the carrier molecule and a carrier molecule that contains a natural substrate, such glucose, make up the majority of radiopharmaceuticals. The PET scanner can identify, record, and image the products of positron emission and collision with electrons inside the body as gamma radiation detected outside the body because the carrier molecule and the positron-emitting radioisotope are bound to each other.[30] A cyclotron is used to produce the majority of the radioisotopes used in PET radiopharmaceuticals (Table).



PET Radiotracer	Physical Half-Life ($t_{1/2}$)/Minutes	Physiological Process or Function	Clinical Application	Production Method
[^{13}N]Ammonia	9.8	Blood perfusion	Myocardial perfusion	Cyclotron
[^{15}O]Water	2.1	Blood perfusion	Brain activation studies	Cyclotron
2-Deoxy-2-[^{18}F]fluoro-*D*-glucose (FDG)	109.8	Glucose metabolism	Oncology, Cardiology, Neuropsychiatry	Cyclotron
[^{11}C]Raclopride	20.3	D_2 receptor agonist	Movement disorders	Cyclotron
[^{11}C]Methionine	20.3	Protein synthesis	Oncology	Cyclotron
[^{11}C]Flumazenil	20.3	Benzodiazepine receptor antagonist	Epilepsy	Cyclotron
[^{15}O]Carbon dioxide	2.1	Blood perfusion	Brain activation studies	Cyclotron
[^{18}F]Fluoromizonidazole	109.8	Hypoxia	Oncology-response to radiotherapy	Cyclotron

PET radioisotopes fall into three groups according to the bodily functions they measure. Radioisotopes like Fluorine 18 that are used to monitor broad metabolic parameters like protein synthesis and glucose uptake fall under the first group. First-class radioisotopes enter cells after exiting the circulation. On the other hand, Oxygen-15 and the other radioisotopes in the second category are stable in the bloodstream for the whole duration of the study, which makes them suitable for monitoring blood flow. Radioisotopes in the third category, including Carbon-11, measure and distinguish biological receptors.

Fluorine-18, Nitrogen-13, Oxygen-15, and Carbon-11 are the four PET radioisotopes that are most frequently utilized; their half-lives are 109.8 minutes, 9.96 minutes, 2.03 minutes, and 20.3 minutes, respectively. PET radiopharmaceuticals are typically prepared one dosage at a time and given to the patient a few minutes later.[31],[32] At certain establishments, the complete procedure—producing the radiosotope or positron-emitting element in the cyclotron and converting it into a radiopharmaceutical in the biosynthesis unit—is carried out in the cylcotron laboratory and is entirely automated. Afterwards, a special pneumatic tube system is used to transfer the radiopharmacical to the on-site PET scanning laboratory when a patient there needs a dose.[33]

Imperatives To The Growth Of PET Use:

Early detection and intervention, elimination of other more invasive procedures, pre-operative evaluation, identification of distant metastases, substitution of several tests, and the capacity to monitor therapeutic efficacy are only a few of its many benefits. Unfortunately, a number of obstacles have surpassed these benefits and kept PET from being extensively employed. The main obstacles have been the disagreement over insurance reimbursement for PET services, the difficulty of setting up a PET system, and the high expense of specialized PET equipment.

Pet's Clinical Applications:

Pet In Cardiovascular Disease:

PET in cardiovascular disorders Several authors have shown that areas of the heart that are significantly hypoperfused can absorb FDG. The existence of an ischemic yet viable myocardium is indicated by the flow-metabolism dissociation pattern. Currently, myocardial viability may be diagnosed by PET-measured FDG uptake, which is the gold standard. Finding out a patient's myocardial viability before they have coronary surgery is the primary use of FDG-PET in cardiovascular pathology. According to Schwaiger M and Hicks R (1991), patients will receive medical treatment or be placed on a transplant waiting list if PET results show no cardiac viability.[32] Cardiologists employed ammonia111 tagged with 13N and 82Rb created by generators as stand-in markers for cardiac blood flow early in the development of PET applications. [34],[35] This resulted in a very modest injection volume of PET tracer; however, this constraint was substantially alleviated with the advent of LSO-based devices. For a thorough examination of PET in cardiology, see [36],[37]

PET In Central Nervous System (Cns) Diseases: It is acknowledged that the most accurate in vivo imaging technique for assessing both regional and global cerebral metabolism is FDG-PET. In September 2004, the HCFA and Medicare in the United States established that FDG PET can be used to differentiate between front-temporal dementia and Alzheimer's dementia in patients with moderate cognitive impairment. One such known suitable use of FDG-PET is the examination of individuals with partial epilepsy who are not responding to medicinal therapies prior to surgery. The epileptogenous focus is identified by FDG-PET as a hypometabolic focused area in the cerebral cortex during the interictal phase.[38]

PET In Cancer: FDG PET is primarily used for cancer patient diagnosis, staging, therapy monitoring, and prognosis. PET results have a direct clinical impact on patient care. FDG-PET can show the tumor cells' aberrant increase in glucose consumption that they display in vitro. Without phosphatase, tumor cells aggressively retain FDG-6 P metabolically. When there is a noticeable difference between the uptake of tumor cells and that of healthy cells, PET has a high sensitivity for identification. The absorption of FDG, high cellularity, and cellular proliferation are all associated with the degree of malignancy. Less aggressive tumors absorb less FDG, but in order to grow faster yet, the most aggressive tumors must take in more glucose.

The use of FDG-PET can be beneficial in a number of clinical scenarios. These include confirming the diagnosis of a benign lesion or malignancy in processes that other techniques have detected, but which require difficult or impossible histological confirmation; determining the extent of a known tumor before treatment staging; distinguishing neoplastic tissue from fibrotic residual masses following surgery, chemotherapy, and/or radiation therapy; locating a tumor recurrency suspected by clinical analysis and/or an increase in tumor markers; conducting a new study of extension following re-staging based on recurrence diagnosis; assessing the early therapeutic effects; and searching for the primary tumor in a patient with metastatic disease of unknown origin or para-neoplastic syndrome. Furthermore, PET can be used to define the radiation volume during radiotherapy planning and to assist needle aspiration or biopsy. FDG-PET also has the drawback of potentially producing false-positive results for infections and non-malignant diseases such as granulomas, TB, histoplasmosis, aspergyllosis, etc., which can exhibit FDG uptake akin to that of malignant tumors.[39]

Uses of PET Scanner For Patients With Cancers:

(1)Finding the main locations of cancer;

(2) differentiating between benign and malignant lesions;

(3) grading a lesion's degree of malignancy;

(4) staging the disease's progression; and

(5) determining whether lesions observed on CT or MRI are cancerous

(6) Treatment planning;

(7) Treatment response monitoring;

(8) Recurrent disease detection.

Fdg-Pet In Oncology:

This section describes the use of PET in various types of tumors. Brain tumors: When it comes to distinguishing between radionecrosis and high-grade tumor-like recurrence, FDG-PET is more specific than CT and MRI. MRI is a more accurate tool than FDG-PET for the detection of brain metastases since these metastases are usually small in size and positioned in the cortical-subcortical area, making FDG-PET less useful for this purpose.

This led to the creation of statistical parametric mapping (SPM), which has emerged as one of the most important analytical techniques for locating changes in specific regions in brain function images.[40] The human neuroscience uncovered by PET-based brain activation studies of cerebral blood flow served as a catalyst for the development of the BOLD fMRIbrain activation technique.[41] PET imaging of the brain is currently being used to study Alzheimer's disease, with a focus on leveraging the range of biomarkers developed for amyloid and tau imaging. [42]

Tumors of the head and neck: CT and MRI are the best methods for identifying local invasion of a basic tumor of these tissues, however FDG-PET is more practical and accurate in identifying metastases and lymph nodes.

Lung Cancer: The established FDG-PET indication is used to differentiate solitary lung nodules when CT is unable to identify them. It has been noted that some granulomas, such those related to tuberculosis, can result in falsely positive results. If a PET test comes back positive, cancer must be ruled out. When there is non-FDG-uptake in a radiological nodule larger than 1 cm in diameter, one should be proactive because this indicates benignancy with a high negative predictive value for malignancy. The investigation of mediastinal staging in non-small cell lung cancer (NSCLC) is another indicator. Forty percent of NSCLC patients had their therapeutic regimens changed as a result of PET, which finds a greater extension of the cancer in many patients who were earlier considered surgical candidates.

Presurgical staging of the esophagus: FDG-PET is advised for gastrointestinal cancers. Another accepted basis for the clinical, analytical, and/or radiological suspicion of colorectal cancer recurrence is identifying the site and performing a re-staging to evaluate the potential for radical surgery. It is beneficial for patients with colorectal cancer who have already had surgery and also develop liver metastases since, in the event that PET detects extra-hepatic sickness, a new procedure must be avoided.

Breast cancer: FDG-PET is currently recognized as the method of choice for detecting and staging recurrent and/or metastatic illness in order to choose the most appropriate course of action. Regarding the identification of small bone metastases, especially those located in the medullar area, FDG-PET seems to be a more practical and reliable technique than bone scintigraphy. FDG-PET is used in non-surgical multisystemic recurrence patients as well as those with locally advanced primitive tumors to evaluate treatment response prior to surgery. Genitourinary tract tumor: Due to the frequent excretion of FDG in the urine, these tumors are challenging to diagnose. In addition, the distinct histology of urinary cancers does not cause higher FDG uptake. This is accurate in the case of prostate cancer. It has been observed that other tracers, such as coline-C11 or acetate-C11, offer better sensitivity and specificity in patients with recurrent or metastatic prostate gland cancer.

ADVANTAGES OF PET SCANNER:

Reduction in Imaging Time: One of the main advantages of total-body scanning is that it takes less time to complete the imaging process. Some authors have calculated that this imaging method can shorten imaging times by a factor of 24[63]. This means that a study that takes 12 minutes to complete in multiple bed positions can be completed in less than 30 seconds in a single bed position with comparable image quality, and the entire scan only takes 5 minutes. Additionally, imaging pediatric patients or patients with pain or claustrophobia becomes much simpler and more comfortable. [43]

Extended Acquisition Delay: The ability to obtain studies at much later time points after tracer injection improves the contrast between the tumoral lesion and background tissue. Some authors, like Price et al., have even observed that the contrast between the tumor and background tissue increases by about four times if the interval between FDG administration is increased [44]. This phenomenon can be explained by a number of factors, including greater distribution of radiotracer on delayed images, greater accumulation in the tumor, renal excretion, and greater washout from normal tissue Consequently, images obtained with a longer delay may reveal additional information about the extent of disease and allow visualization of smaller or less tracer-avid lesions not seen on previous imaging. [45]

Drug Development: Animal models are still used in many labs today for pharmacokinetic and pharmacodynamic research, although they have significant drawbacks. To counter this, innovative therapeutic drugs have been introduced to humans by micro-dosing procedures that use highly sensitive imaging instruments (such PET and single-photon emission computed tomography, or SPECT) [46],[47]. At the end of the day, microdosing speeds up the decision-making process by rapidly eliminating inefficient compounds from the drug pipeline and including humans before phase I trials.[48] Very modest dosages of a radionucleotide-labeled compound are given to perform these trials in order to ascertain the plasma pharmacokinetics. To ascertain the drug's effects when using such subpharmacological dosages in phase 0/micro-dose trials, sensitive analytical instruments like PET are needed. Total-body PET scanning provides simultaneous imaging of the entire body, making it possible to track changes in a drug's distribution throughout the body and get insight into how an agent can concentrate in tissues over time. Therefore, before beginning costly clinical trials, clinicians can evaluate the pharmacokinetics and pharmacodynamics of novel therapeutic medicines in all bodily organs, providing crucial information [49],[50]

Tracking Therapies Based on Cells and Nanoparticles: In the realm of cancer, new treatment approaches including cell-based therapies (such as adoptive immunotherapy and stem-cell therapy) have garnered a lot of interest lately. A dependable and highly sensitive evaluation technique, like total-body PET technology, is required to ascertain the in vivo distribution and biological destiny of injected compounds in order to expedite the development of these nanoparticle-mediated therapeutics

Additionally, these cell-tracking techniques provide a unique chance to see immune cell trafficking, which could clarify the process underlying the inconsistent results associated with cancer immunotherapy [51]

Multi-Tracer PET Research (Injectable Cocktail): Although FDG-PET/CT technology is essential for imaging some malignancies, because some cancers have varying rates of glucose metabolism, FDG cannot be used to detect certain malignant lesions. The new cocktail injection technique, which combines two radiopharmaceuticals before a single PET collection, has been devised to get around this restriction [52] Similar to this, alternative cocktail formulae have been proposed for various cancer types, such as F-fluoroestradiol (FES)/FDG for hormone-dependent (estrogen receptor (ER)-positive) breast cancers or 68Ga-DOTATOC/FDG to image neuroendocrine tumors.[53]

CONCLUSION:

PET is a fascinating nuclear medicine technology that uses non-invasive diagnostic imaging procedures to assess the physiological and chemical alterations linked to the human body's metabolic activities. The physics-based processes involved in injecting a patient with a radiopharmaceutical that contains a positron-emitting radioisotope are the basis for several imaging techniques. The culmination of the physics-based exercises is electromagnetic energy, which is picked up and monitored by sophisticated PET scanners or cameras. A PET technologist uses the electromagnetic energy's detection and tracking as data to create diagnostic images, which a radiologist then analyzes, interprets, and reports to the referring physician.

Image quality for patient investigations has significantly improved since the 1970s thanks to technological advancements in PET equipment. Despite being perceived as rather expensive at first, these developments have ultimately turned out to be cost-effective by creating new clinical uses. There is no reason to think that these developments won't go as far as previously imagined. Physicists, engineers, and the business community must accept the significant technical hurdles that will accompany this advancement. The potential of hitherto unheard-of uses of PET-based molecular imaging in clinical research and healthcare must serve as the impetus for these initiatives.

REFERENCES

1. Phelps ME. Positron emission tomography provides molecular imaging of biological processes. Proc Natl Acad Sci U S A. 2000;97(16):9226-9233. doi:10.1073/pnas.97.16.9226
2. Fontana JR. CLINICIAN ' S CORNER Sarcoidosis and Therapeutics. 2011;305(4):391-399.
3. Martlew D. History and Development of Glass. Windows. 2018;(810):121-157. doi:10.4324/9781315793832-4
4. Schrevens L, Lorent N, Dooms C, Vansteenkiste J. The Role of PET Scan in Diagnosis, Staging, and Management of Non-Small Cell Lung Cancer. Oncologist. 2004;9(6):633-643. doi:10.1634/theoncologist.9-6-633
5. Coates G. Emerging role of PET in the diagnosis and staging of lung cancer. Can Respir J. 1999;6(2):145-152. doi:10.1155/1999/717104
6. Stark MM. Fundamental Principles. Clin Forensic Med A Physician's Guid Fourth Ed. Published online 2020:23-61. doi:10.1007/978-3-030-29462-5_2
7. MILES J. Toward A Theory O F Style and Change . J Aesthet Art Crit. 1963;22(1):63-68. doi:10.1111/1540_6245.jaac22.1.0063
8. Wagner HN. A brief history of positron emission tomography (PET). Semin Nucl Med. 1998;28(3):213-220. doi:10.1016/S0001-2998(98)80027-5
9. Series S. 1932 gl,. 1932;325.
10. Curie I. 放射性元素的人工生产-法国Joliot and Curie-1934. Published online 1934:201-202.
11. Lawrence EO, Livingston MS. The production of high speed protons without the use of high voltages [3]. Phys Rev. 1931;38(4):834. doi:10.1103/PhysRev.38.834
12. HAIt'N U. STRASSMANN : Nachweis der Entstehung aktiver Bariumisotope aus Uran u. Thormm. 89 ~.
13. Oxide THEN, Of D. the Nitrous Oxide Method for the Quantitative. 1947;(1):476-483.
14. Sokoloff L, Reivich M, Kennedy C, et al. the [14C]Deoxyglucose Method for the Measurement of Local Cerebral Glucose Utilization: Theory, Procedure, and Normal Values in the Conscious and Anesthetized Albino Rat. J Neurochem. 1977;28(5):897-916. doi:10.1111/j.1471-4159.1977.tb10649.x
15. Kuhl DE, Edwards RQ. Reorganizing data from transverse section scans of the brain using digital processing. Radiology. 1968;91(5):975-983. doi:10.1148/91.5.975
16. Or A, At T. United States Patent (19). 1973;(19).
17. Ter Pogossian MM, Phelps ME, Hoffman andMullani EJNA. A positron emission transaxial tomograph for nuclear imaging (PETT). Radiology. 1975;114(1):89-98. doi:10.1148/114.1.89
18. Phelps ME, Hoffman E, Ter-pogossian MM. Calculation of Positron Range and Its on the Fundamental Limit of Peffect of Positron on Spatial Resolution. J Nucl Med. 1975;16(7):649-652.
19. Ido T, Wan CN, Casella V, et al. Labeled 2-Deoxy-D-Glucose Analogs. 18F-Labeled 2-Deoxy-2-Fluoro-D-Glucose, 2-Deoxy-2-Fluoro-D-Mannose and 4C-2-Deoxy-2-Fluoro-D-Glucose. J Label Compd Radiopharm. 1977;1(2):175-183.
20. Moses WW. Trends in PET imaging. Nucl Instruments Methods Phys Res Sect A Accel Spectrometers, Detect Assoc Equip.

2001;471(1-2):209-214. doi:10.1016/S0168-9002(01)00969-X

21. Straussand LG, Conti PS. Strauss91- PET clinical oncol. Published online 1991:623-648.
22. Nellemann P, Hines H, Braymer W, Muehllehner G, Geagan M. Performance characteristics of a dual head SPECT scanner with PET capability. IEEE Nucl Sci Symp Med Imaging Conf. 1995;3:1751-1755. doi:10.1109/nssmic.1995.501924
23. Lowe VJ, Delong DM, Hoffman JM, Coleman RE, Unwerrity E. Optimum Scanning Protocol for FDG-PET.pdf. J Nucl Med. 1995;36:883-887.
24. Fletcher JW, Djulbegovic B, Soares HP, et al. Recommendations on the use of 18F-FDG PET in oncology. J Nucl Med. 2008;49(3):480-508. doi:10.2967/jnumed.107.047787
25. Weber WA. Use of PET for Monitoring Cancer Therapy and for Predicting Outcome Continuing Education. J Nucl Med. Published online 2005:983-995.
26. Boellaard R, O’Doherty MJ, Weber WA, et al. FDG PET and PET/CT: EANM procedure guidelines for tumour PET imaging: Version 1.0. Eur J Nucl Med Mol Imaging. 2010;37(1):181-200. doi:10.1007/s00259-009-1297-4
27. Aher TR, Mokle BA, Sanap GS. Review: Introduction To 3D Bioprinting. World J Pharm Res. 2015;12(5):724-740. doi:10.20959/wjpr20235-27592
28. Townsend DW, Ieee SM, Beyer T, et al. A combined PET / CT scanner for clinical oncology The SMART scanner : a combined PETET tomograph for clinical oncologys. 2000;(January).
29. Dorle MD, Bhivasane A, Sanap GS. REVIEW : CUTANEOUS MUCORMYCOSIS. 2023;12(7):57-69. doi:10.20959/wjpr20237-27831
30. Sanap GS, Mohanta GP. Design and evaluation of miconazole nitrate loaded nanostructured lipid carriers (NLC) for improving the antifungal therapy. J Appl Pharm Sci. 2013;3(1):46-54. doi:10.7324/JAPS.2013.30109
31. Nutt R, Karp JS. Is LSO the future of PET? Eur J Nucl Med. 2002;29(11):1523-1528. doi:10.1007/s00259-002-0987-y
32. Schwaiger M, Hicks R. The clinical role of metabolic imaging of the heart by positron emission tomography. J Nucl Med. 1991;32(4):565-578.
33. Gaidhani, K. A., Harwalkar, M., Bhambere, D., & Nirgude PS. World Journal of Pharmaceutical research FORMULATION. SJIF J. 2021;2(5):1685-1703. doi:10.20959/wjpr202317-29690
34. Budinger TF, Yano Y, Hoop B, Hospital MG. @:?: i : Lr @@,@.:@:;: 1974;i(5):429-431.
35. Selwyn AP, Allan RM, L’Abbate A, et al. Relation between regional myocardial uptake of rubidium-82 and perfusion: Absolute reduction of cation uptake in ischemia. Am J Cardiol. 1982;50(1):112-121. doi:10.1016/0002-9149(82)90016-9
36. Bengel FM, Higuchi T, Javadi MS, Lautamäki R. Cardiac Positron Emission Tomography. J Am Coll Cardiol. 2009;54(1):1-15. doi:10.1016/j.jacc.2009.02.065
37. Saxena S, Pramod BJ, Dayananda BC, Nagaraju K. Design, architecture and application of nanorobotics in oncology. Indian J Cancer. 2015;52(2):236-241. doi:10.4103/0019-509X.175805
38. Newberg A, Alavi A, Reivich M. Determination of regional cerebral function with FDG-PET imaging in neuropsychiatric disorders. Semin Nucl Med. 2002;32(1):13-34. doi:10.1053/snuc.2002.29276

39. Lomeña F, Soler M. BRAZILIAN ARCHIVES OF BIOLOGY AND TECHNOLOGY Clinical Application of Pet. Brazilian Arch Biol Technol. 2005;48(October):179-183.
40. Friston KJ, Holmes AP, Worsley JP, Frith CD, Frackowiak RS. Statistical parametric maps in functional imaging: a general linear approach. Hum Brain Mapp. 1995;2(081):189-210.
41. Kwong KK, Belliveau JW, Chesler DA, et al. Dynamic magnetic resonance imaging of human brain activity during primary sensory stimulation. Proc Natl Acad Sci U S A. 1992;89(12):5675-5679. doi:10.1073/pnas.89.12.5675
42. Brier MR, Gordon B, Friedrichsen K, et al. Alzheimer ' s disease. 2017;8(338). doi:10.1126/scitranslmed.aaf2362.Tau
43. Nardo L, Schmall JP, Werner T, Malogolowkin M, Badawi RD, Alavi A. Potential Roles of Total Body PET / CT in Pediatric Imaging. 2021;15(3):271-279. doi:10.1016/j.cpet.2020.03.009.Potential
44. Price PM, Badawi RD, Cherry SR, Jones T. Ultra staging to unmask the prescribing of adjuvant therapy in cancer patients: The future opportunity to image micrometastases using total-body 18F-FDG PET scanning. J Nucl Med. 2014;55(4):696-697. doi:10.2967/jnumed.113.133892
45. Ref,No.66.pdf.
46. Lappin G, Noveck R, Burt T. Microdosing and drug development: Past, present and future. Expert Opin Drug Metab Toxicol. 2013;9(7):817-834. doi:10.1517/17425255.2013.786042
47. Bergstrom M. The use of microdosing in the development of small organic and protein therapeutics. J Nucl Med. 2017;58(8):1188-1195. doi:10.2967/jnumed.116.188037
48. Jekunen AP, Pauwels EKJ, Kairemo KJA. Microdosing in early lead discovery. Bioanalysis. 2010;2(3):421-428. doi:10.4155/bio.09.189
49. Cherry SR, Jones T, Karp JS, Qi J, Moses WW, Badawi RD. Total-body PET: Maximizing sensitivity to create new opportunities for clinical research and patient care. J Nucl Med. 2018;59(1):3-12. doi:10.2967/jnumed.116.184028
50. Burt T, John CS, Ruckle JL, Vuong LT. Phase-0/microdosing studies using PET, AMS, and LC-MS/MS: a range of study methodologies and conduct considerations. Accelerating development of novel pharmaceuticals through safe testing in humans–a practical guide. Expert Opin Drug Deliv. 2017;14(5):657-672. doi:10.1080/17425247.2016.1227786
51. Akins EJ, Dubey P. Noninvasive imaging of cell-mediated therapy for treatment of cancer. J Nucl Med. 2008;49(SUPPL.6):180-195. doi:10.2967/jnumed.107.045971
52. Iagaru A, Mittra E, Yaghoubi SS, et al. Novel strategy for a cocktail 18F-fluoride and 18F-FDG PET/CT scan for evaluation of malignancy: Results of the pilot-phase study. J Nucl Med. 2009;50(4):501-505. doi:10.2967/jnumed.108.058339
53. Barrio M, Czernin J, Fanti S, et al. The impact of somatostatin receptor-directed PET/CT on the management of patients with neuroendocrine tumor: A systematic review and meta-analysis. J Nucl Med. 2017;58(5):756-761. doi:10.2967/jnumed.116.185587

HOW TO CITE: Kalyani P.Sangle, The Role Of Pet Scan In Diagnosis, Staging And Management Of Cancer, Int. J. of Pharm. Sci., 2024, Vol 2, Issue 12, 2469-2475. https://doi.org/10.5281/zenodo.14524264