PET Imaging: An Overview and Instrumentation

Farhad Daghighian, Ronald Sumida, and Michael E. Phelps

Division of Nuclear Medicine and Biophysics, Department of Radiological Sciences; and Laboratory of Nuclear Medicine, Laboratories of Biomedical and Environmental Sciences (DOE), UCLA School of Medicine, Los Angeles, California*

This is the first article of a four-part series on positron emission tomography (PET). Upon completing the article, the reader should be able to: (1) comprehend the basic principles of PET; (2) explain various technical aspects; and (3) identify radiopharmaceuticals used in PET imaging.

Positron emission tomography (PET) is a rapidly growing technique within nuclear medicine. A radiopharmaceutical labeled with a positron emitting isotope is administered intravenously or by inhalation to the patient, and the PET scanner images the distribution of that radiopharmaceutical. It is the only imaging modality capable of providing quantitative information about *biochemical* and *physiologic* processes (*1–3*). Other techniques like magnetic resonance imaging (MRI) and x-ray computerized tomography (CT) generally image the *anatomy* or the *structure* of the body.

Positron emission tomography imaging has some unique features, which can be summarized as follows:

1. The effect of gamma ray attenuation in tissue is removed from the PET image in an exact way, thereby making the image an accurate measurement of the local radioisotope concentration (*1–3*).
2. There are no collimators in front of the PET detectors; therefore the efficiency of PET is much higher than that of single-photon emission computed tomography (SPECT). (In the gamma camera more than 99% of the emitted gamma rays are absorbed or scattered by the collimators.)
3. Most of the organic chemicals found in the body are made of carbon, oxygen, nitrogen, and hydrogen. The first three of these elements have isotopes which emit positrons, ^{11}C ($t_{1/2}$ = 20 min), ^{15}O ($t_{1/2}$ = 2 min), and ^{13}N ($t_{1/2}$ = 10 min). Fluorine-18 (^{18}F) ($t_{1/2}$ = 109 min), a positron emitting isotope, can be substituted for hydrogen in many chemical compounds. None of the above elements have any isotope which emits a gamma ray suitable for imaging with a gamma camera. Hence, one of the advantages of PET over SPECT is that it deals with isotopes of those elements that are the building blocks of biomolecules.

BRIEF HISTORY AND FUTURE OUTLOOK OF PET

Positron imaging began with the two-dimensional sodium iodide detector-based scanning devices developed in the late 1950s and 1960s by Wrenn et al. (*4*) and Brownell et al. (*5*). Burham and Brownell also developed a dual-headed multidetector camera that provided a limited form of "focal plane" tomography (*6*). Robertson and Niel took a different approach and used a "blurring tomography" with a circular array of sodium iodide detectors (*7*). This latter approach was the positron version of the device Kuhl and Edwards developed for single-photon emitting radioisotopes (*8*).

A turning point in medical imaging was reached when Hounsfield and Cormack developed x-ray computed tomography, for which they shared the Nobel prize in 1978. Earlier positron imaging devices did not employ the principle of computed tomography.

The first true positron computed tomography device was developed in 1974 by Phelps, Hoffman, Ter-Pogosian and colleagues (*9*). This work was the beginning of a rapid advance in the principles and techniques of PET. For example, Brownell et al. (*10*) and Muehllehner et al. (*11*) developed rotating multicrystal and dual-head Anger camera PET systems, respectively. Cho et al. (*12*), Derenzo et al. (*13*), Bohm et al. (*14*), Tanaka et al. (*15*), and others developed the early circular versions of PET scanners. Allemand et al. introduced the first time-of-flight PET system (*16*). Many other academic and comercially-based investigators subsequently contributed to the development of PET. Research PET centers were established throughout North America, Europe, and Asia during the late 1970s and 1980s. This not only increased biologic research with PET, but also increased research into developing new labeled compounds, tracer kinetic assay methods, and improving PET scanners. The mid-1980s were the

* Operated for the U.S. Department of Energy by the University of California under contract #DE-AC03-76-SF00012.

For reprints contact: Farhad Daghighian PhD, Dept. of Medical Physics, Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY 10021.

beginning of the growth in technology to miniaturize and simplify cyclotrons specifically for PET. In addition, automated chemical synthesis techniques for simplifying the routine production of labeled compounds were initiated and integrated into the cyclotron technology.

The principles of PET used to measure and image biologic processes in the living human subject are sound and their value undeniable. The use of PET to perform biochemical examinations of patients for clinical management has now become the motivation to develop a continuing evolution of solutions to the practicalities of its use.

WHAT ARE THE CLINICAL USES OF PET?

Although PET has been a powerful research tool in medicine, it has been shown to be a unique and critical diagnostic modality for clinical use. This is because it provides unique *physiologic* and *biochemical* information about the brain, heart, and the rest of the body. The origin of disease is fundamentally biochemical in nature. Therefore, to obtain the most accurate diagnoses and most effective treatment, it is desirable to know the biochemical status of the organ or organ system in question.

The most common uses of PET in clinical studies are measurement of the metabolic rate of glucose in different locations of the brain and the heart. These studies can:

1. Help the clinician to pinpoint the location of epileptic foci in seizure disorder patients (*3*).
2. Identify different forms of dementia and degenerative diseases (i.e., Alzheimer's, Parkinson's or Huntington's diseases).
3. Identify the pathology of brain tumors and access the viability of the brain tissue and evaluate the viability of the myocardium in patients with cardiac disease (*17–20*).

Blood flow to different locations of the brain is quantitated by PET using ^{15}O-labeled water (*3*), and in the heart by ^{13}N-labeled ammonia or ^{82}Rb (*20*). Cerebral blood flow measurements combined with measurement of the cerebral metabolic rate of oxygen is an indicator of the physiologic time course, and metabolic consequences of, and recovery from stroke (*3*). Myocardial blood flow measurements combined with the information about the glucose metabolic rate aids the clinician in identifying whether the patient has viable myocardium, which would benefit from revascularization (*20*). Some examples of PET clinical applications are summarized in Table 1. There are, however, many others that are discussed in the literature.

An example of how metabolic information acquired by PET is an aid to the clinician is shown in Figure 1. The CT, PET, and SPECT scans of a patient with biopsy-proven high-grade brain tumor is presented. The CT scan, performed after the injection of a contrast agent, indicates a disruption of the blood brain barrier (BBB) that can be caused by the tumor, radiation necroses or edema (*3*), the specifics of which can not be differentiated by CT or MRI (*3*). (The patient received a full course of radiation therapy prior to these scans.) The PET scan is performed 40 min after the injection of ^{18}F-labeled fluorodeoxyglucose (FDG), which is an analog of glucose. The SPECT image is acquired after the injection of ^{201}Tl.

In the PET image, the concentration of FDG is high in the outer layer of the tumor (the dark semicircle around the tumor). This specifically indicates the presence of active tumor cells since high grade tumor cells use more glucose (*21*). The tissue at the center of the tumor is dead and, therefore, does not metabolize glucose. In the CT scan, the bright ring around the tumor only suggests that the BBB is disrupted but not whether there is an active tumor. The SPECT image shows an area of increased uptake of ^{201}Tl, yet provides little information about state of the tumor and the surrounding tissues. The information acquired by PET in this case is important in the future treatment of the patient. Many other examples of how PET and its physiologic and metabolic

TABLE 1. Examples of Clinical PET Procedures

Procedure	Clinical Use
$^{13}NH_3$ or ^{82}Rb	1. Rest/Stress detection of coronary artery disease.
$^{13}NH_3$ or ^{82}Rb plus FDG*	1. Determination of cardiac tissue viability for selecting patients for revascularization. 2. Differentiation of iodiopathic from ischemic cardiomyopathies: Viable ischemic cardiomyopathies → revascularization; iodiopathic cardiomyopathies → transplant.
FDG	1. Detection, grading degree of malignancy, post-treatment determination of reoccurrence and treatment efficacy in tumors (cerebral and systemic). 2. Differential diagnosis of Alzheimer's, multiple infarct dementia and chronic depression. 3. Localization of seizure focus in adult and pediatric epilepsy for surgical resection. 4. Differential diagnosis of Huntington's Disease. 5. Characterization of cerebral damage and function on cerebral palsy.
$^{15}O_2$ and $H_2{}^{15}O$	1. Characterization of hemodynamic and metabolic deficits, tissue viability, and therapeutic efficacy in cerebral vascular diseases (e.g., stroke).
^{18}F-L-DOPA	1. Detection of movement disorders and characterization of dopamine deficiencies.
^{18}F	1. Bone scans, detection and monitoring of therapy in degenerative bone disease.

* ^{18}F-labeled fluorodeoxyglucose.

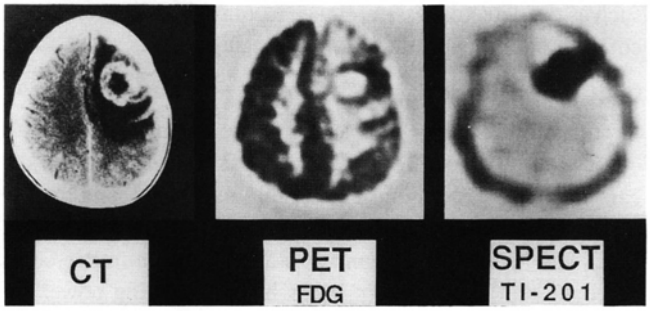

FIG. 1. X-ray CT, PET, and SPECT images of the brain of a patient post surgery and post-radiation treatment for a high grade brain tumor. The PET image provides unique metabolic information demonstrating reoccurrence of the tumor, as well as its effect on the surrounding tissue. (Courtesy of Randall Hawkins, MD)

information are helpful in diagnoses and prognoses of diseases will be discussed in future articles of this educational series.

PHYSICAL PRINCIPLES

Positrons

A positron is the anti-particle of an electron. It has the same mass as an electron except its electric charge is positive instead of negative. Positrons (or positive beta particles) are naturally emitted by many isotopes. According to the laws of modern physics, when a positron collides with an electron, there is a chance that they both annihilate, and two gamma rays are created simultaneously. The energy of each of these gamma rays is 511 keV. To conserve momentum, these two gamma rays travel in opposite directions (*22*). The detectors in a PET scanner are tuned to accept *coincident* detection of these two gamma rays.

The positron is emitted from the nucleus of those isotopes which have an excess number of protons compared to the number of neutrons. What occurs inside the nucleus is that one of its protons decays to a neutron along with ejection of a positron and a neutrino; therefore, the nucleus decays to a more stable isotope. The emitted positron will lose its initial kinetic energy by many scatterings with the electrons and nuclei in the surrounding medium (Fig. 2). Eventually, it will collide with one of the many electrons in the medium and spontaneous annihilation takes place:

$$e^+ + e^- \rightarrow \text{Gamma} + \text{Gamma}.$$

All these events are so fast that for all practical purposes the emission and annihilation of the positron can be considered simultaneous. However, the positron has traveled some distance from the place it was emitted. This distance in tissue is typically a couple of millimeters and depends on the energy of the emitted positron. Hence, we can say that the positron annihilates at the same time and at almost the same position as it is emitted by the isotope; and that the *PET scanner finds this position.*

To develop a conceptual understanding of PET imaging consider the following example:

Suppose that we have two gamma cameras *with no collimators* facing each other and in between them, at the center, a phantom is placed (Fig. 3). This phantom is filled with some positron emitting radioisotope. The energy windows of the cameras are set around 511 keV and the electronic logics of the two cameras area connected to each other such that a true count is registered only if a count in one camera is in *coincidence* with another count in the other camera (by coincidence we mean time difference of less than a 15-billionth of a second). This event would be the signal of a positron emission and subsequent annihilation to two opposite 511 keV gamma rays. The two detection points on each camera are registered in the computer, and we know that a positron was emitted at a point on the line joining these two points (i.e., the line of coincidence or response). A computer keeps track of all these lines and registers them in its memory. After accumulating data for a few minutes, both cameras are rotated to another angle and data collection is continued in the same fashion. When both

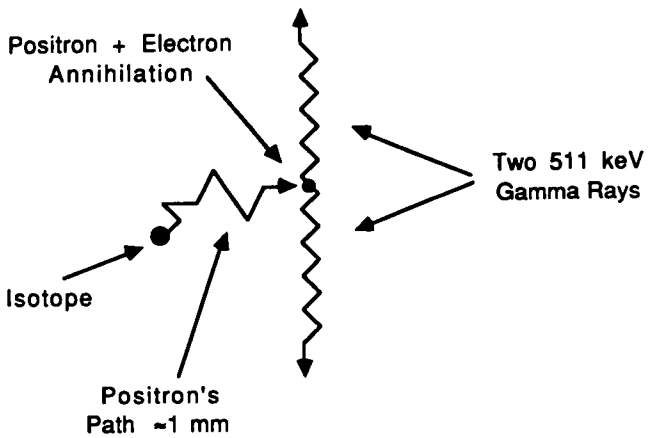

FIG. 2. A positron is emitted from the isotope, travels in a zig-zag path through matter, due to collisions, losing its velocity and finally binds to an electron with which it annihilates creating two 511-keV gamma rays.

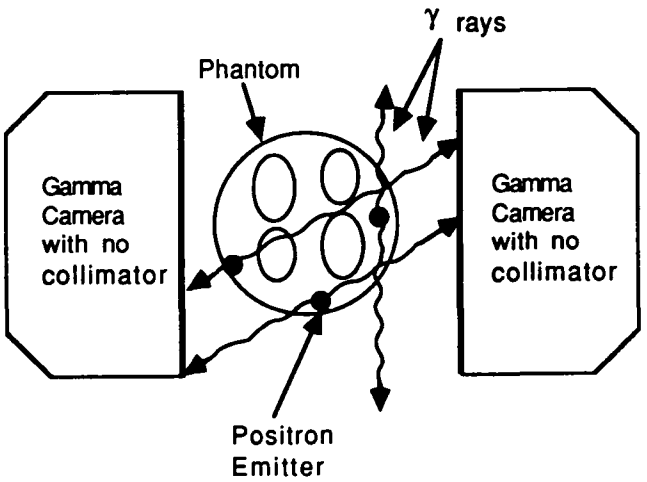

FIG. 3. Two gamma cameras with no collimators are used to illustrate the principle of coincident detection of two 511-keV gamma rays. These gamma rays are created by annihilation of the positrons. The phantom in the center is filled with a positron emitting isotope.

cameras have completed 180° of rotation, a collection of these lines of responses, which are stored in the memory are then used to generate a tomographic image of the phantom (as in SPECT). Notice that the extra information of the coincident counting of gamma rays in both cameras removed the need for collimators. This constitutes one of the advantages of PET over SPECT, i.e. its high sensitivity. The collimators on gamma cameras absorb 99% of the gamma rays, making them very inefficient; therefore, a large portion of the dose given to a patient is not used for imaging. For example, when you perform a flood image on a gamma camera without a collimator, the number of counts is typically 200 times more than when the collimator is in place.

This example illustrated the basic principles of PET scanning, but no PET scanner looks like this. A modern PET scanner (Fig. 4) is made of individual detectors arranged next to each other on a ring. Each detector faces many other detectors in the semicircle in front of it. More than a million detector pair coincidence combinations are simultaneously collecting data in a modern PET scanner. A commercial PET scanner, which is operated by a mini-computer, is shown in Figure 5.

TECHNICAL ASPECTS

Now that we have a basic understanding of the physics involved in PET, we will discuss the more technical aspects such as the detector system, image reconstruction, attenuation correction, and two-dimensional imaging.

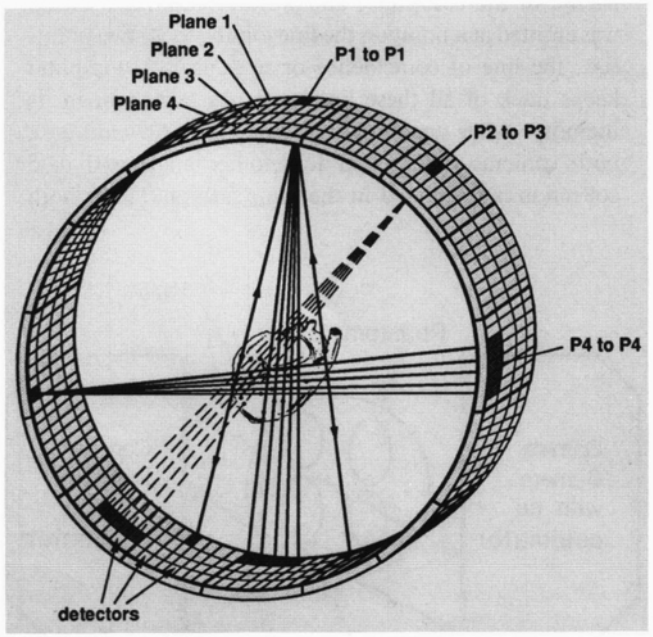

FIG. 4. A simplified drawing of the detectors in a modern PET scanner. Four rings, or planes, of detectors are shown with a few of the lines of response representing the paths of outgoing gamma rays. The direct plane images are created by coincident detection of gamma rays between each detector and all the detectors in the semicircle in front of it in the same plane (e.g., P1 to P1). The "cross plane images" are reconstructed by the lines of response of detectors of one plane with those of an adjacent plane (e.g., P2 to P3).

Detector Systems

Today, all existing PET scanners use scintillation crystals coupled to photomultiplier tubes (PMTs) for detection of the gamma rays. Most companies building PET scanners use Bismuth Germanate Oxide (BGO) crystals as the scintillator. BGO has higher density and average atomic number compared to NaI(Tl), therefore it has higher stopping power for the 511 keV gamma rays. Because of this fact, smaller individual detector elements can be used; therefore, better image resolution can be achieved. To have fewer PMTs, the BGO detectors are arranged in modular detector systems or detector blocks (Fig. 6).

As an example, one of these detector modules consists of a block of BGO detectors (~5 × 5 × 3 cm) with cuts of different depths, coupled to four PMTs. These cuts divide the face of the block to 32 independent detectors. When a gamma ray hits one of these detectors it generates scintillation light which will be guided and distributed to the PMTs. From the ratio of the light detected by each PMT, the detector is identified. For example, if detector 1 detects one gamma ray the scintillation light will be recorded only by PMT A, but if detector 2 is hit by the gamma ray, 90% of the light goes to PMT A and 10% to PMT B, because of the depth of the crystal's cut. For detector 3, PMT A receives 30% and PMT B 70% of the scintillation light and so on. There is a circuit for each block that identifies which detector has received the gamma ray by looking at the ratio of the signals from different PMTs. This is the same type of position logic used in the Anger camera, which solves the problem of packing too many PMTs close together and reduces the number of the PMTs that are required. These blocks are arranged in a circular array to form the detection system of a PET scanner. To further increase efficiency and organ coverage, additional circular arrays of blocks can be added. Each row of detector elements in the circumferential array form a single image plane, while the number of rows defines the number of image planes. In addition, detectors in row 1 are connected in coincidence with detectors in row 2 so that an image plane in between rows 1 and 2 are formed. The image plane formed from detectors of each row is usually called the "direct plane" and the plane formed from coincidence of detectors of two adjacent rows is called the "cross plane" image (Fig. 4). The use of cross planes increases efficiency and sampling in the axial direction. Thus, a tomograph with two rings of block arrays would have eight direct and seven cross planes, for a total of 15 simultaneous image planes.

Image Reconstruction

The basic principles of tomographic image reconstruction from projections of an object is common to x-ray CT, MRI, SPECT, and PET. The detectors collect a series of lines of responses, as explained above, and from them a profile of counts versus distance is produced for each angle. These profiles are equivalent to the projection images collected from different angles (similar to SPECT). The task of tomographic

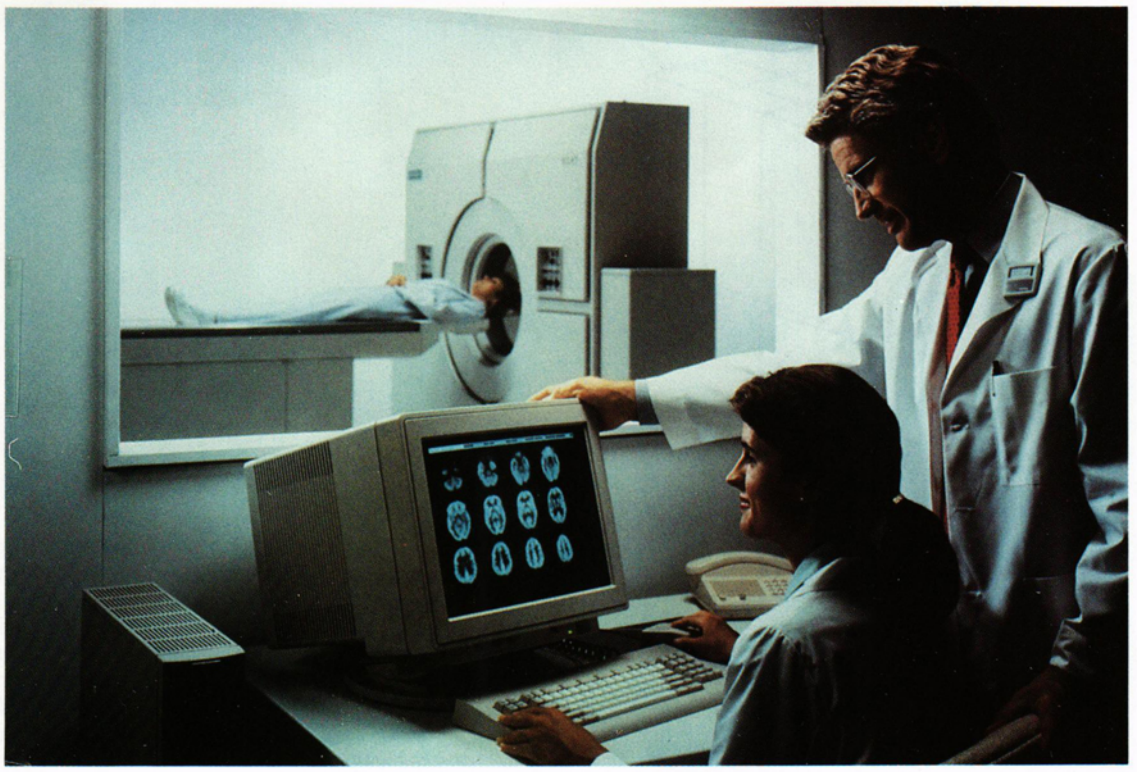

FIG. 5. A modern PET scanner. A mini-computer with menu-driven software controls the system and performs the image reconstruction and processing tasks. (Courtesy of Siemens Corporation.)

image reconstruction is to produce a tomographic, or slice, image from these measured count profiles or projection images. To illustrate, consider the scan profiles for the simple case of a point of activity within an object (Fig. 7). Each profile maps the location of the source in the direction parallel to the scan profile, however, the source can lie at any depth along the line perpendicular to that profile. A first approximation for the source distribution can be obtained by projecting the data from each scan profile back across the entire image grid. This operation is known as *backprojection*. If the backprojections of scan profiles at different angles are then added together (linear superposition), an approximation of the original radioactivity distribution results. This operation is called linear superposition of backprojections (LSBP). There is an inherent blurring in this technique, which is removed by performing a filtering operation on the projections or scan profiles. This filtering is a mathematical operation done in the image reconstruction software. Usually, there are different choices for the shape and parameters of the filter which effect the image resolution. The entire reconstruction process is known as linear superposition of filtered backprojections (LSFBP) (*23*).

Attenuation Correction

The images produced by PET do not only show the distribution of the radioactive material in the body but also they contain the effect of gamma ray attenuation caused by the surrounding tissue and bone (*1*). Gamma rays originated from deeper regions are attenuated more. The magnitude of attenuation depends on the attenuation coefficient of the tissue and the thickness of the tissue transversed. Since the tissue is nonhomogeneous, this coefficient varies in different locations. Therefore assuming a constant attenuation coefficient makes the attenuation correction of the image inaccurate.

In PET scanning, correcting the emission image for the attenuation effects can be done in an exact manner because two back-to-back gamma rays are involved. Therefore, by measuring the total attenuation along the line that these gamma rays travel (i.e., lines of response) the attenuation effect can be corrected from the emission image. The following steps are taken in a measured attenuation correction procedure:

1. A source of 511 keV gamma radiation (e.g., a ring filled with 15 mCi of ^{68}Ge is placed in the patient gantry, without the patient, and a "blank scan" is collected for 30 min. This will be used as a reference later.
2. Before administering any radioactivity, a "transmission scan" is acquired for 15 min by placing the patient in the scanner while the external source (e.g., the ring source) is still there. The gamma rays pass through the patient's body and are detected by the PET detectors therefore providing exact information about the photon attenuation across each "line of response" (i.e., lines joining facing detectors). During the transmission scan, the patient was in place but during the blank scan there

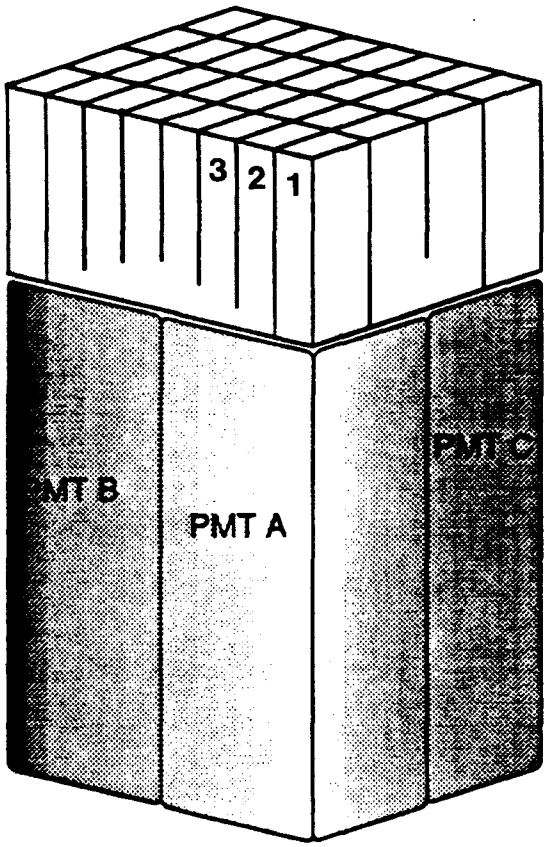

FIG. 6. The block detector module, used in many modern PET scanners, consists of a block of BGO scintillating crystal with cuts of different depths acting as light guides. This crystal is optically connected to four PMTs.

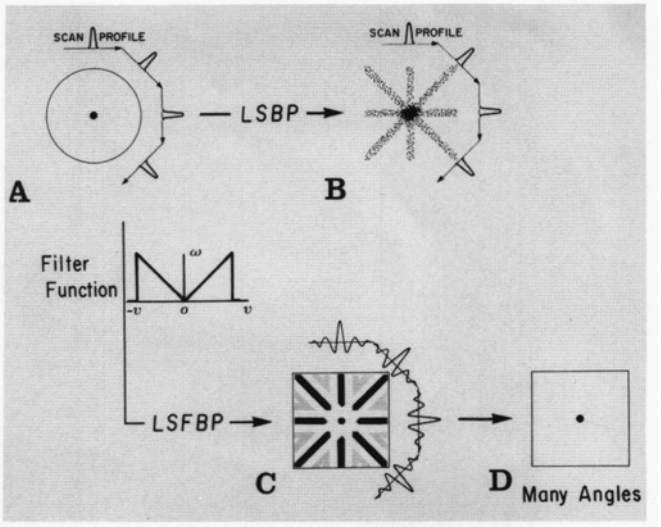

FIG. 7. Steps involved in blurring and computed tomography. (A) Linear scan profiles at different angles around an object containing a single point source. (B) Blurring tomography of LSBP. (C) Computed tomography approach in which LSFBP is employed. Scan profiles are passed through a ramp filter that produces filtered scan profiles with positive and negative components. The negative components of filtered profiles subtract the blurring noise seen in B. With a few angles, the noise is only partially removed. (D) When many angular projections are employed, all blurring is removed to produce the correct image of the point source.

was no patient; therefore, the ratio of these two counts for each line of response will give a map of the tissue attenuation.

3. The external source is removed and the radioactivity is administered to the patient, and the emission scan is started at the desired time. Software in the PET scanner's computer uses the data of the transmission scan which contains the attenuation information for each line of response. Using the blank scan as a reference, the software then corrects the emission scan to generate the "attenuation-corrected image."

Two-Dimensional Imaging

In addition to tomographic imaging, PET scanners also efficiently perform two-dimensional (2-D) imaging. This scan mode serves several purposes. The first is to provide a "scout" examination for patient setup or selecting regions to be examined in detail with the tomographic mode. The second is to provide standard whole-body images. If a patient is simply placed on the bed and moved through the tomograph, 2-D images are simultaneously collected at many different angular views through a full 180-degree angle around the patient. No tomographic reconstruction is performed. These 2-D images can be presented individually, in a step-wise sequence, or in a cine format. Examples of a few angles from a ^{18}F bone scan are shown in Figure 8.

The 2-D imaging mode provides a way for the biologic PET tracer to be used to identify lesions throughout the whole body. Once the lesions are identified, analytical tomographic assays can be performed to characterize the lesion in more detail.

RADIOLABELED COMPOUND PRODUCTION FOR PET

Over 500 compounds have been labeled with ^{15}O, ^{13}N, ^{11}C, and ^{18}F for use in PET imaging. These compounds range from simple labeled molecules such as $H_2{}^{15}O$, $C^{15}O$, and $^{15}O_2$ to many forms of sugars, amino acids, fatty acids, carboxylic acids, alcohols, numerous substrates, analogs and drugs. These positron emitting isotopes are produced in cyclotrons. Today, there are self-shielded medical cyclotrons available commercially, which can be operated with a personal computer (Fig. 9). The self-contained and automated production of labeled compounds with a cyclotron is now designed to produce repeated doses as needed for patient studies. The ^{18}F-labeled compounds ($T_{½}$ = 109 min) are made in large batches and stored for studies throughout the day or shipped, thus making patient doses available throughout the day. For producing ^{15}O-, ^{11}C-, and ^{13}N-labeled compounds, the cyclotron should be in close proximity of the scanner because of the short half-lives of these compounds. There are other clinically useful positron emitting isotopes that are generator-produced, such as ^{68}Ga and ^{82}Rb, which is an analog of thallium.

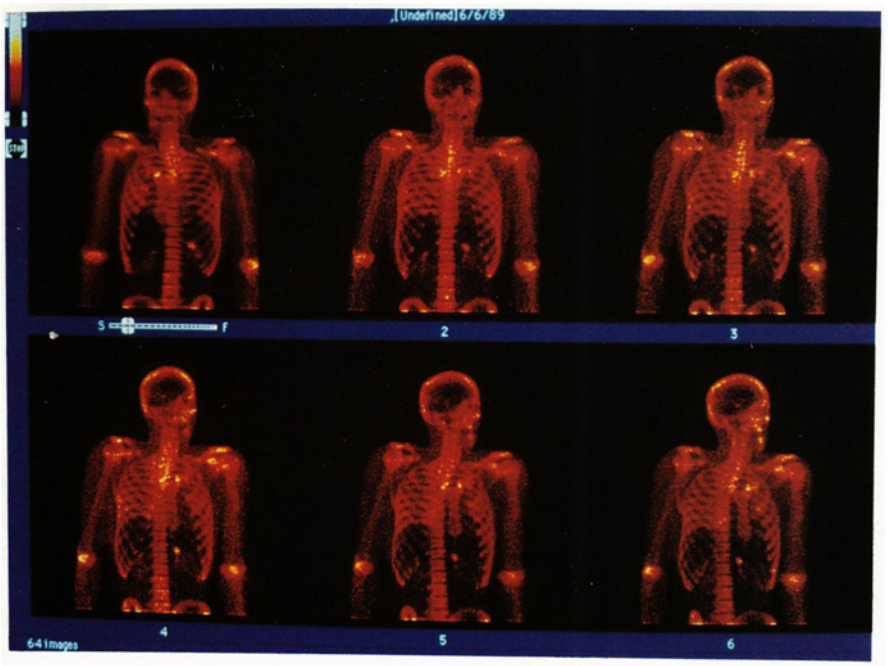

FIG. 8. Two-dimensional bone scan of a normal subject after injection of ^{18}F. Sixty-four angular 2-D images are simultaneously collected. Only selected examples at a few angles are shown. (Courtesy of Thomas M. Guerrero, UCLA School of Medicine.)

How Does the Cyclotron Work?

If an energetic proton (the nucleus of a hydrogen atom) collides with a heavier nucleus, there is some possibility that a different nucleus may be created. The cyclotron is the device that accelerates protons to the high energies needed for these nuclear reactions. For example, ^{18}F is generated by bombarding ^{18}O, a commercially available stable isotope of oxygen, with protons which are accelerated to around 10 MeV energy:

$$\text{Energetic Proton} + {}^{18}O \rightarrow {}^{18}F + \text{Neutron}.$$

The basic principle used in the cyclotron is the fact that a charged particle gains velocity, and therefore energy, when attracted to an oppositely charged metal. This opposite charge is supplied by a high voltage supply. If the particle circles around and crosses this region of high voltage repeatedly, it would gain more energy each time. A magnet is used in the cyclotron to make the path of the charged particle circular. Cyclotrons accelerate both negative and positive particles. For a negative ion, the cyclotron works as follows: the cyclotron classically consists of a pair of hollow, semicircular metal electrodes called "D" electrodes because of their semicircular shapes (Fig. 10). The Ds are positioned between the poles of an electromagnet. The Ds are separated from one another by a narrow gap. During the operation, protons are generated in bursts by ionizing hydrogen gas in the ion source at the center

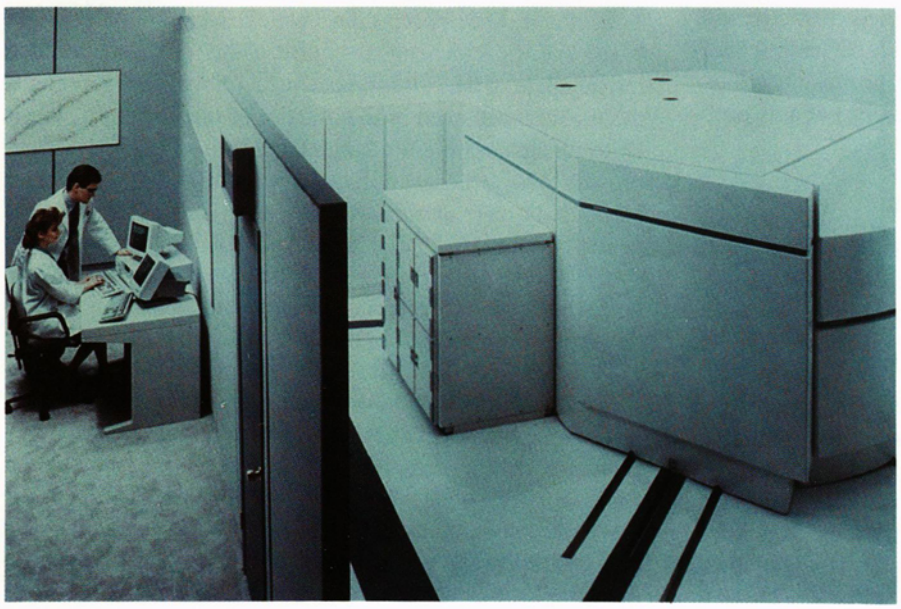

FIG. 9. A self-shielded negative-ion cyclotron. The cyclotron is located inside the shields. The rectangular cabinet on the left of the shield contains the automated chemical synthetic systems for producing labeled compounds. The cyclotron and chemical synthesis are controlled by a personal computer station shown to the left. (Courtesy of Siemens Corporation.)

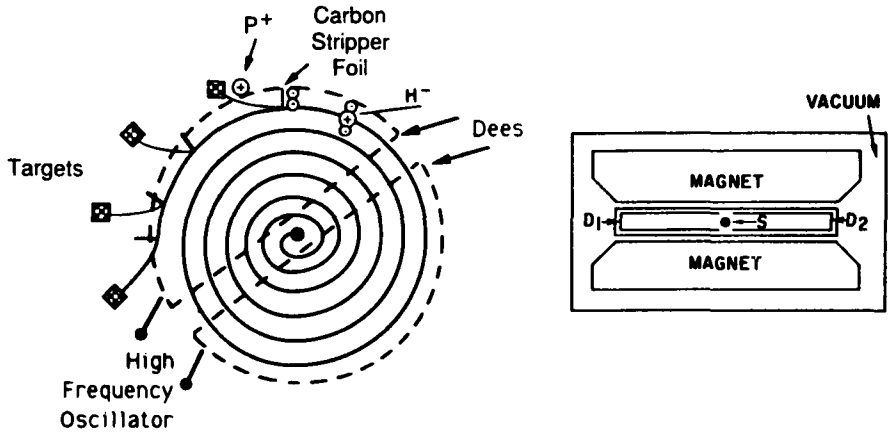

FIG. 10. Principle of the negative ion cyclotron. The ion source, S, produces negatively charged protons by the addition of an extra electron to hydrogen. Extraction of the beam out of the cyclotron occurs by an electron stripping reaction using a thin carbon foil. The resulting positive ion spirals in the opposite direction and out of the cyclotron. Simultaneous extraction of beams occurs with multiple stripping foils that remove a part of the beam along its negative ion pathway.

of the machine, and a high voltage is generated by a high-frequency oscillator (e.g., 200 kV, 5 MHz) is applied across the Ds. The negatively charged hydrogen ions are directed into the gap and immediately accelerated toward the positively charged D by the electric field generated by the applied voltage. Inside the D, there is no electric field, but because the ions are in a magnetic field they follow a circular path around to the opposite side of the D. The AC voltage across the D is such that the ions arrive at the gap just as the voltage across the D reaches its maximum value in the opposite direction (i.e., the opposite D is now positive). The negative hydrogen ions are accelerated across the gap, gaining ~200 keV of energy in the process, and then continue on a circular path within the opposite D. Each time they cross the gap they gain energy and velocity, and, therefore, they follow a spiraling path of increasing radius. The Ds are contained in a vacuum tank so the accelerated ions do not lose their extra electrons by colliding with gas particles in the machine. The particle beam is extracted by stripping the two electrons off H^- and converting it to H^+ with a thin (i.e., 20 μm) carbon foil. Since the charge of the particle is reversed, the magnetic field causes the H^+ to orbit out of the cyclotron. The extracted beam can be guided by simply tilting and rotating the carbon foil. Multiple simultaneous beams can be uniquely extracted with a negative ion cyclotron, thus allowing multiple labeled compounds to be produced simultaneously or to make necessary adjustments due to the normal scheduling or patients problems.

PRACTICAL NOTES

The user's interaction with a modern PET scanner and cyclotron has been simplified by menu-driven software and mini-computer systems. There are, however, a few practical notes which should be mentioned to prevent possible errors.

1. *Patient movement* will cause a loss of resolution and create an error in the process of measured attenuation correction. The patient should not move between the "transmission scan" and the "emission scan." It is important to make the patient as comfortable as possible by explaining the procedure in detail to the patient to ease anxiety and by placing pillows under the knees to relieve pressure off the back. Heart patients' arms should be supported to prevent movement. Brain patients should be placed in a head holder and be reminded not to move.
2. *Injection of the dose* into the patient's arm should be completed by a flush of normal saline to prevent image artifacts caused by residue of radioactivity at the injection site.
3. *Radiation safety* issues are slightly different from those involved in work with lower-energy radionulides (e.g., ^{99m}Tc, 140 keV). The 511-keV gamma rays, which are the byproduct of all positron emitting isotopes, are more penetrating than 140 keV gamma rays emitted by ^{99m}Tc, therefore new thicker syringe shields, holders, and vial containers must be developed. Table top shields with additional lead bricks will eliminate exposure to the personnel. Because of the short half-life of the positron emitters, radioactive contamination issues are reduced.

CONCLUSION

Human disease is biochemical in nature. The most effective treatment provides a biochemical solution to the problem. Thus, the most important diagnostic description of a patient is the specific biochemical nature of his medical problem. Independent of PET, this biochemical information represents the most critical need in the practice of medicine, whether it be to understand the fundamental nature of human disease, provide diagnostic examinations with high sensitivity and particularly high specificity, or to select and monitor therapeutic corrections. PET is a modality that uses the classical tracer-kinetic principle, novel instrument technology, and biochemical knowledge and principles to provide access to this critical information in the human body.

The transition of PET from research to clinical practice has been marked by the evolution of new technologies to provide its intrinsic bioassay capabilities in a format and cost appropriate for clinical care. Academic programs throughout the world are continually developing new labeled compounds, new procedures, and new uses of PET. Commercial and academic programs are producing solutions that are lowering the complexity and cost of the clinical versions of the tech-

nology. Since there are over 500 labeled biologically-active compounds as well as over 80 academic PET research centers and over 20 commercial companies (including the large medical imaging companies), these factors represent a tremendous resource to continually expand the use of the important principles embodied in PET through simplifying what is required to do it.

ACKNOWLEDGMENTS

The authors thank L. Griswold for illustrations. This work was supported by the Department of Energy Contract DEFC-03-87-ER60615.

REFERENCES

1. Phelps ME, Mazziotta JC, Schelbert HR, eds. *Positron emission tomography and autoradiography: Principles and applications for the brain and heart.* New York: Raven Press; 1986.

2. Reivich M, Alavi A. *Positron emission tomography.* New York: Alan R. Liss, Inc.; 1985.

3. Mazziotta JC, Gilman S, eds. *Contemporary neurology series: Neuroimaging.* Philadelphia, PA: FA Davis Co; in press.

4. Wrenn FR, Good MI, Handler P. The use of positron emitting radioisotopes for localization of brain tumors. *Science* 1951;113:525–527.

5. Brownell Gl, Sweet HW. Localization of brain tumors with positron emitters. *Nucleonics* 1953;11:40–45.

6. Burnham CA, Brownell GL. A multicrystal positron camera. *IEEE Trans Nucl Sci* 1972;NS-19:201–205.

7. Robertson JS, Niell AM. Use of a digital computer in the development of a positron scanning procedure. *Proceedings from Fourth IBM Medical Symposium.* 1962, pp 77–103.

8. Kuhl DE, Edwards RQ. Cylindrical and section radioisotope scanning of the liver and brain. *Radiology* 1964;83:926–936.

9. Phelps ME, Hoffman EJ, Mullani NA, Ter-Pogossian MM. Applications of annihilation coincidence to transaxial reconstruction tomography. *J Nucl Med* 1975;16:210–224.

10. Brownell GL, Burnham CA, Chesler DA, Correia JA, Correll JA, Hoop B, Parker JA, Subramanyan R. Transverse section imaging of radionuclide distributions in the heart, lung and brain. In: Ter-Pogossian MM, Phelps ME, Brownell GL, eds. *Reconstruction tomography in diagnostic radiology and nuclear medicine.* Baltimore: University Park Press; 1977:293–307.

11. Muehllehner, G, Buschin, MP, and Dudek JH. Performance parameters of a positron imaging camera, *IEEE Trans Nucl Sci* Ns-23:528–537, 1976.

12. Cho ZH, Cohen MB, Singh M, Eriksson L, Chan J, MacDonald N, Spolter L. Performance and evaluation of the circular ring transverse axial positron camera (CRTAPC). *IEEE Trans Nucl Sci.* 1977; NS-24:530–543.

13. Derenzo SE, Budinger TF, Cahoon JL, Huesman RH, Jackson HG. High resolution computed tomography of positron emitters. *IEEE Trans Nucl Sci* 1977; NS-24:544–558.

14. Bohm C, Eriksson L, Bergstrom M, Litton J, Sundman R: A computer assisted ring detector positron camera system for reconstruction tomography of the brain. *IEEE Trans Nucl Sci* 1978;NS-25:624–637.

15. Tanaka E, Nohara N, Yamamoto M, Dannals RF, Douglass KH, Links JM, Kuhar MJ. Positology—the search for suitable detector arrangements for a positron ECT with continuous rotation. *IEEE Trans Nucl Sci* 1978;NS-26.

16. Allemand R, Gresset C, Vacher J. Potential advantages of a cesium fluoride scintillator for a time-of-flight positron camera. *J Nucl Med* 1980;21:153–155.

17. Larson SM. *Positron emission tomography in oncology and allied diseases: Principle and practice of oncology updates, Volume 3.* Philadelphia: Lippincott; 1989:1–12.

18. Hawkins RA, Phelps ME. Applications of positron emission tomography (PET) in tumor management. In: Withers HR, Peters LJ, eds. *Innovations in radiation oncology.* New York: Springer-Verlag; 1988:209–220.

19. Hawkins RA, Phelps ME. PET in clinical oncology. *Cancer Metastasis Rev* 1988;7:119–142.

20. Brunken RC, Schelbert HR. Positron emission tomography in clinical cardiology. *Cardiol Clin* 1989;7:607–629.

21. Di Chiro G, Brooks RA. PET FDG of untreated and treated cerebral gliomas [Letter]. *J Nucl Med* 1988;29:421.

22. Frauenfelder H, Henley EM. *Introduction to nuclear and particle physics: Background and symmetries.* Reading, MA: W.A. Benjamin; 1975:156–65.

23. Brooks RA, DiChiro G. Theory of image reconstruction in computed tomography. *Radiology* 1975;117:561–572.