Radiopharmaceuticals in PET Imaging

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Objective: PET isotopes are being used more commonly in nuclear medicine. This paper introduces the nuclear medicine technologist to the use of PET imaging. The major focus of this article is on the isotopes that are used in this modality and how they differ from traditional isotopes. The nuclear medicine technologist will become familiar with PET isotopes by reading about PET history, the production and availability of PET isotopes, and the use of this modality in a traditional hospital setting.

Key Words: positron emission tomography; fluorodeoxyglucose; coincidence detection; attenuation correction; radiation safety

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The use of PET imaging as a diagnostic tool has become increasingly popular due, in part, to innovations and availability of products and equipment. Once just a research tool, this modality has become a useful adjunct in the work-up and diagnosis of many diseases. The availability of PET isotopes for the general hospital setting may prove to be the catalyst to increasing the use of this beneficial tool. There are many areas which the nuclear medicine community will need to become familiar with before beginning full-scale use of these products. This paper briefly presents the historical development of PET imaging and products, from early development through the present.

This paper focuses on the various isotopes that are used for PET imaging and how they differ from traditional isotopes. The article discusses the expanded role that nuclear medicine technologists and their departments will be required to play in the transition to in-house PET imaging. This paper briefly addresses radiation safety, instrumentation and equipment, and waste handling. Finally, there is a discussion of the future role of PET and how the nuclear medicine community is adapting to meet this challenge.

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HISTORY

The use of positron-emitting isotopes dates back to the late 1950s and early 1960s and to the work of Wrenn, Brownell and colleagues, while the art of CT was developed in 1978 by Hounsfield and Cormack (*1*). The combination of these two broad areas in 1974 was the beginning of the science of PET. Research centers were established throughout the world in the late 1970s and early 1980s and led to the broad incentive for developing positron-emitting radiopharmaceuticals for use in medicine. As PET radiopharmaceuticals became more numerous and complex, so did the equipment and technology used for imaging these agents.

The use of PET imaging previously was limited to institutions that could financially support an in-house cyclotron. Although advancements in technology have reduced the size of cyclotrons, the units still require dedicated space and frequently range in price from $1 to $2 million. In addition, a dedicated PET scanner can fall into the $1.5 to $3 million price range (*2*). An institution also will need to consider the cost of the laboratory equipment that is necessary to monitor, compound and perform quality assurance testing on each product that is made, as well as the cost of routine and unexpected maintenance and the actual operating costs. Originally, these costs were likely to be incorporated into a research budget. Thus, many PET centers are located in a research-driven institute, such as a university or other large teaching hospital. However, with the growing interest and proven benefits of PET imaging in certain clinical situations, recent developments have been aimed at providing PET-labeled compounds to a wider variety of customers, allowing smaller institutions the opportunity to be involved in this advanced imaging technology.

In recent years the use of conventional imaging equipment, such as dual-head SPECT cameras, has been proposed for imaging PET isotopes as well. By modifying existing cameras to allow for coincidence detecting and transmission scanning, institutions will be able to use their current equipment for this advanced purpose, eliminating the financial burden of purchasing a dedicated PET scanner.

In response to this increase in imaging capabilities, unit dose PET suppliers are becoming more common, especially in large

metropolitan areas with many hospitals in close proximity. These outside suppliers provide smaller hospitals with the ability to use PET imaging for patient care where in the past they were financially unable to do so. These off-site vendors have cyclotrons in which they produce the isotopes and chemically synthesize the final product for distribution. The vendor can produce multiple doses with each production run and supply the desired isotope in unit dose form to surrounding hospitals (*3*). Each production of the isotope must undergo thorough quality control testing to assure the chemical purity of the final product. Unlike a traditional nuclear pharmacy, in which most tests can be done by rapid thin-layer chromatography, PET isotopes require a more complex testing procedure.

The short half-life of PET-labeled products prohibits manufacture on a large scale. These products can be produced only on an as-needed basis. Since this process is not regulated by usual manufacturing guidelines, testing of the final products generally will undergo many more quality assurance tests than seen with conventional products. Tests such as high-pressure liquid chromatography, gas chromatography, sterility testing, pyrogen testing and pH determination are generally performed on each shipment for administration to a patient (*4–6*). Although the half-life of many of the isotopes used in PET imaging is not satisfactory for long-distance or extended-time delivery, agents with somewhat longer half-lives can be used to overcome these limitations.

PET VERSUS TRADITIONAL ISOTOPES

Positron-emitting isotopes have decay properties that differ from those of conventional nuclear medicine isotopes. In conventional imaging, the radioactive material decays with a distinct half-life and the emission of gamma photons, beta particles or a combination of both, each with an energy emission that is characteristic of that particular isotope. Some isotopes are monoenergenic, such as ^{99m}Tc with one 140-keV gamma photon, or there may be two or more characteristic gamma rays which are used for imaging.

Gamma-emitting isotopes are used to label tracers that are specific for a certain organ or organ system within the body. After administration to the patient, the radioactive tracer will localize in the desired organ and emit gamma photons. These photons travel through the tissues of the body and they are detected by an external gamma camera.

Radioactive decay by traditional isotopes is a random process with photon emissions in any possible direction from the source nucleus. Positron emission differs from the decay of traditional isotopes, yet has certain similarities to traditional imaging. PET isotopes decay not by the release of gamma photons directly, but by the emission of a positron. PET isotopes have a neutron-poor nucleus, or simply have an excess number of protons. To reach a more stable form, the nucleus will convert an excess proton into a neutron and a positron. The basic positron decay scheme is shown in Figure 1. The neutron is a neutral particle within the nucleus. A positron is equivalent in size and mass to an electron, but it has a positive

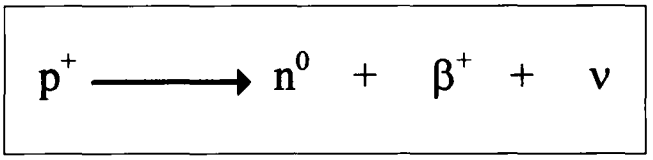

FIGURE 1. Positron decay. Excess protons within the nucleus are converted to a neutron, a positron and a neutrino. p+ = excess proton within the nucleus; n^0 = neutron (with no charge); β^+ = positron (with positive charge); ν = neutrino (to maintain overall mass; no charge).

instead of negative charge. The conversion to a neutron and the release of the positron imparts stability to the original nucleus. The positron carries a strong positive charge and, once it is released from the atomic nucleus, will interact with an electron. Positrons will travel only a few millimeters after release from the nucleus. The interaction with the negatively charged electron, termed an annihilation reaction, occurs rapidly due to the abundance of electrons in matter.

Once the positron and electron react, they immediately convert their energy into two 511-keV gamma photons which are released at approximately a 180° angle from one another. This interaction can be seen in Figure 2. As a result of this reaction and the resulting 511-keV gamma photons which are produced, detection of the positron emitter within the body can be performed using an external detector such as a PET scanner or, more recently, a converted gamma camera.

The use of 511-keV photons makes imaging more challenging. Traditional gamma cameras are unable to adequately image these high-energy photons. The high energy causes a large percentage of the photons to penetrate through the sodium iodide crystal of most gamma cameras without interacting with the crystal. Since interaction is necessary for the camera to recognize the photon emission, the resulting images lack sufficient resolution and quality. In addition, the time for scintillations to occur within the sodium iodide crystal (>800 nsec) prohibits accurate detection when counting rates are very high, as they are with PET isotopes. PET cameras have been developed with a different crystal, bismuth germanate oxide (BGO), that allows detection of the 511-keV photons. BGO can stop a larger percentage of high-energy photons, but lacks

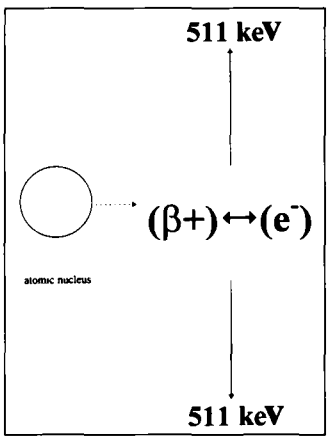

FIGURE 2. Positron annihilation reaction. After release from the nucleus, the positively charged positron interacts with a negatively charged electron in the environment. The interaction produces two 511-keV photons, released at approximately a 180° angle from one another.

TABLE 1
Positron-Emitting Radiopharmaceuticals

Cyclotron-produced isotope	Physical half-life		
Oxygen-15	2 min		
Nitrogen-13	10 min		
Carbon-11	20 min		
Fluorine-18	110 min		
Generator-produced parent isotope	**Physical half-life**	**Daughter isotope**	**Physical half-life**
Strontium-82	25 days	Rubidium-82	75 sec
Zinc-62	9.3 hr	Copper-62	10 min
Germanium-68	288 days	Gallium-68	68 min

the resolution to detect lower photon energies from traditional isotopes (*7*). PET scanners also take advantage of the fact that the 511-keV photons are given off simultaneously at approximately a 180° angle. In PET cameras there is a ring of detectors that surrounds the patient, instead of the rotating single detectors, which are often used for SPECT. Each detector is connected electronically to multiple detectors within the detector ring. The connection between each pair of detectors is termed a coincidence circuit. When an annihilation reaction occurs, the two photons that are given off are detected by the ring of detectors outside of the patient. If photon interaction occurs at both detectors in a particular coincidence circuit, the interaction is determined to be a true annihilation reaction, and the interaction is recorded. If there is no matching interaction at the opposite detector, or if the interaction does not occur within a set time limit, the interaction is not recorded. Since there will be a multitude of interactions occurring at the same time, this method of detection accurately localizes the isotope within the patient's body.

PET imaging eliminates the need for the lead collimators used in traditional imaging by requiring the dual interaction of opposing detectors. Lead collimators on traditional gamma cameras attempt to accurately localize an internal radioactive source by detecting photons that are emitted from the patient in a perpendicular line to the camera. Any interactions that are not emitted directly towards the camera are blocked by the lead of the collimator.

The use of conventional imaging equipment for imaging PET isotopes greatly enhances the use of these isotopes in a nuclear medicine department. The growing use of conventional SPECT cameras has greatly enhanced the ability of smaller institutions to use PET imaging. Several camera companies have developed modifications for SPECT cameras which allow imaging of the high-energy 511-keV photons. These new camera adaptations incorporate thicker crystals to increase sensitivity for higher energy photons while allowing imaging of conventional isotopes with minimal changes in the intrinsic resolution of the camera. Coincident photon detection capabilities and the ability to perform transmission scanning also are available to the customer.

Software upgrades allow rapid and accurate reconstruction of the large amount of data obtained during a PET scan into viewable images. The resolution obtained with a modified SPECT camera is almost as good as that of a dedicated PET scanner, however, the images are still inferior to images from a PET scanner. This is due to the lower counting rate of the modified SPECT camera. PET cameras can process more than 5 million photons per second, while modified SPECT cameras only can handle approximately 1 million photons per second. This difference may limit the types of studies that can be done. However, the images obtained likely will be sufficient for many applications. A modified SPECT camera also can be used for other applications during the day, avoiding the downtime that would occur if the camera was a dedicated PET device. It is important to realize that it will take time and dedication to introduce PET technology as an imaging option to nuclear medicine department staff.

RADIOPHARMACEUTICALS AND THEIR USES

In many disease states, the functional capability of affected tissue changes long before there is any alteration in the anatomy. PET isotopes are incorporated into substances such as sugars, proteins, water and other biologically active compounds that have specific localization patterns in the body. The most commonly used PET isotopes and their half-lives are listed in Table 1.

Radiopharmaceuticals that are used for PET imaging can be produced by either a cyclotron, or by parent/daughter generator systems similar to the $^{99}Mo/^{99m}Tc$ generator. The cyclotron production method is the source for most of the commonly used isotopes, while generator systems, with the exception of one commercially available product, are limited to research status at this time. The cyclotron method of isotope production involves proton bombardment of a predetermined target or starting material. Bombardment of the target forces the interaction of the proton and a heavier nucleus from the

target. This interaction causes the formation of an entirely different nucleus with new properties. For this reaction to occur, the photon must have sufficient energy to interact with the target. The cyclotron accelerates the proton. As a charged particle (in this case, the proton) gains velocity, the energy of this particle is increased also. When the increase in energy is sufficiently high, the photon is introduced to the target material. All of these reactions take place inside the cyclotron. In many cases, once the cyclotron is loaded with the correct target material and any additional material needed for synthesis, the end product can be produced in an automated synthetic module with little human manipulation. When more complex labeling is needed, these newly formed isotopes can be incorporated into a wide variety of compounds through chemical manipulation outside the cyclotron.

PET-based generator systems behave similarly to the ^{99}Mo/^{99m}Tc generator system. A radioactive parent isotope is loaded onto a fixed column. Passing a liquid, such as saline, over this column removes any of the daughter isotope that has been produced. These isotopes are positron emitters. As with all PET isotopes, the short physical half-life may pose a problem in preparing the radiopharmaceutical for patient administration. The commercially available ^{82}Sr/^{82}Rb generator (CardioGen®; Bracco Diagnostics, Princeton, NJ), with an ultrashort half-life of 75 sec, can be set up to infuse directly from the generator column into the patient's arm (*8*).

CYCLOTRON-PRODUCED PRODUCTS

There are four main isotopes used in PET imaging that are produced with a cyclotron: ^{15}O, ^{11}C, ^{13}N and ^{18}F. Oxygen-15 has a 2 min half-life, limiting its use to sites where there is an in-house cyclotron. Oxygen-15 has several clinically important uses. It can be used to study cerebral oxygen metabolism. The patient breathes in the gas and the consumption of oxygen by the brain can be mapped.

Further manipulation of ^{15}O at high temperatures outside the cyclotron produces ^{15}O carbon monoxide. When administered by inhalation, like nonradioactive carbon monoxide, the radioactive form will bind with great affinity to hemoglobin in the blood. This allows imaging of the blood pool within the body.

Another ^{15}O-labeled product is ^{15}O water. It is produced using ^{15}O and hydrogen at high temperatures outside the cyclotron. Oxygen-15 water is a freely diffusible tracer. The ability of a tracer to be freely diffusible allows accurate assessment of blood flow to a designated tissue. The regional counting rate within the tissue will be directly proportional to the quantity of blood that is flowing through the tissue at the time. Oxygen-15 water is used to determine perfusion of both the myocardium and the brain. Oxygen-15 water imaging must be completed immediately before major changes in tissue concentration occur. Unfortunately, at very high blood flow rates, especially in the brain, the extraction of ^{15}O water from the brain is less than the absolute blood flow. This will underestimate slightly the actual blood perfusion to the tissue, however, this difference is not extremely significant. In addition, the short T½ of ^{15}O allows performing subsequent scans, such as metabolic studies, in a short period of time (*9*).

Since ^{15}O water is diffusible, blood-pool concentrations do not decrease enough to be able to differentiate myocardial tissue from the blood pool which is traversing through the atria and ventricles of the heart. To correct for this, two scans must be done. One scan images the perfusion of the heart (^{15}O water) and the other images the amount of blood within the ventricles. This can be done with a blood-pool study, such as ^{15}O carbon monoxide. Using a computer to digitally remove the image obtained with the ^{15}O carbon monoxide from the image of the ^{15}O water, an image of the perfusion of the heart can be generated. This protocol requires the patient to undergo two studies with no movement between them to accurately align the images obtained. This problem can be eliminated by using ^{13}N-ammonia.

Nitrogen-13, with a T½ of 10 min, is synthesized most often into N-ammonia. Like ^{15}O water, it is used to study myocardial blood flow due to a high extraction on first pass through the heart. Nitrogen-13-ammonia behaves as a highly diffusible tracer, similar to ^{201}Tl. Like ^{201}Tl, ^{13}N-ammonia is transported into the myocardial cells by a carrier-mediated transport mechanism (*10*). Once ^{13}N-ammonia is taken into the myocardial tissue, however, it is incorporated into amino acids within the cells and effectively trapped within the tissue. This allows imaging of myocardial perfusion for a longer period of time since the tracer does not diffuse back out of the heart. Nitrogen-13-labeled ammonia is currently used in institutions with an on-site production facility.

Carbon-11, with a 20-min half-life, also can be used as a blood-pool tracer, in the form of ^{11}C carbon monoxide. The longer half-life of ^{11}C, compared with ^{15}O carbon monoxide, makes it less likely to be used. Carbon-11 is used frequently in labeling compounds that have certain pharmacologic and/or biologic functions within the body. Research using radiolabeled amines, such as ^{11}C-spiperone, can be used to map dopamine receptors in the brain. Spiperone, a pharmacologic agent with affinity for D-2 dopamine receptors in the brain, can be used to monitor the number and functional capacity of these receptors (*11*). Dopamine receptors and transport mechanisms play an important role in diagnosing and treating many psychological diseases, such as depression, schizophrenia and other mental health disorders. The effectiveness of various drug therapies in these disorders can be better understood and lead to improved patient care through the ability to monitor the intensity and pattern of dopamine receptors in the brain.

Carbon-11-labeled fatty acids, such as palmitate, are used to monitor regional myocardial metabolism, or the functional capacity of the cells of the heart. Fatty acids are the primary source of energy for myocardial cells when the tissue is receiving adequate oxygenation. Palmitate will undergo fatty acid metabolism within the mitochondria of myocardial cells (*12*). The ability of the myocardial cells to biologically process fatty acids is dependent on their metabolic capacity. Under normal conditions, fatty acid metabolism will be the primary source of energy (40%–60%) (*10*), with glucose providing an additional 20% to 60%, depending on the whether the patient has eaten

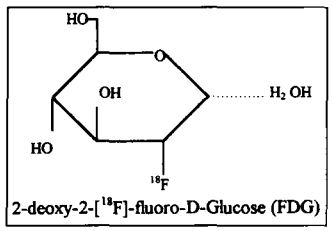

FIGURE 3. Structure of ^{18}F-FDG. This molecule is structurally similar to glucose, with a ^{18}F molecule in the number 2 position.

or not. Nonviable cells, found after the tissue has become infarcted, will not metabolize fatty acids or glucose. There is no need for these nonviable cells to have an energy source. Normally functioning cells will show fatty acid metabolism through ^{11}C-fatty acid uptake. In patients with ischemic tissue, the energy source becomes predominantly glucose, providing energy through anaerobic metabolism. Low levels of oxygen will decrease fatty acid metabolism within the cell by downregulation of enzymes required for their metabolism. The fatty acids are shunted to the body's triglyceride pool instead of into the cell mitochondria. The fatty acids are no longer able to inhibit glycolysis, so anaerobic glycolysis becomes the predominant energy source (*11*). Ischemic tissue can be differentiated from normal tissue by using a ^{11}C-fatty acid study. Ischemic tissue will have decreased uptake of the radiolabeled tracer (*10*).

When studies such as this are combined with myocardial perfusion studies, using either PET or SPECT methods, the differentiation between ischemic and infarcted tissue can be visualized. Both studies can be completed easily within the same day because of the relatively short half-life and high-energy photons of the PET isotopes (*9*). Carbon-11-labeled products are used exclusively in research settings, due to the short half-life of the isotope which prohibits shipping.

The half-lives of PET isotopes present a problem when using them in a diagnostic setting. Oxygen-15, ^{11}C and ^{13}N have a wide variety of clinical uses as presented above. Their short half-lives prohibit their use unless they are produced on-site. When produced by an in-house cyclotron, these tracers decay so quickly that only one or two patient studies can be done with each run of the cyclotron. The amount of activity that is actually produced is limited by the radiation exposure to the personnel who handle the products. Off-site PET facilities have this problem and are unable to produce, synthesize and deliver these radiotracers in a timely and cost-effective manner.

This introduces the most commonly used tracer, ^{18}F which can be incorporated into a useful sugar form (fluorodeoxyglucose [FDG]) and which has a sufficiently long half-life (110 min), making it practical for multiple patient preparations as well as for delivery to an area that can extend for miles from the site of production.

Fluorine-18 is produced by cyclotron bombardment and can be synthesized automatically into the fluorodeoxyglucose form. Fluorodeoxyglucose is a glucose analog in which a radioactive fluorine molecule is incorporated, replacing one of the usual hydroxyl (-OH) groups (Fig. 3). The body handles ^{18}F-FDG similar to how it handles an ordinary glucose molecule, taking it up in glucose-using tissues such as the brain and heart. Once inside the cell, ^{18}F-FDG proceeds through the usual metabolic pathway of glucose. Once phosphorylated, the ^{18}F molecule prevents the ^{18}F-FDG from continuing along the usual glucose metabolic pathway, and thus will be trapped inside the cell (*13*).

Fluorine-18-FDG is used for a wide variety of imaging studies. The most common areas of study are neurology, cardiology and oncology. The primary energy source for the brain is glucose. The normal metabolic activity of brain tissues has been determined. Changes in the metabolic capacity of brain tissues will be evident on the ^{18}F-FDG scan. This difference in tracer uptake can be used to diagnose various diseases or to monitor therapy in these patients. Fluorine-18-FDG is used as a diagnostic tool in epilepsy, psychologic disorders such as dementia or schizophrenia, stroke patients, Alzheimer's disease, and Parkinson's disease and in patients with brain tumors. The regional decrease in glucose use in tissues heavily affected by Alzheimer's and Parkinson's diseases can help lead researchers to better understand the physical changes that occur in certain areas of the brain in these diseases and how to formulate and evaluate therapeutic treatment options in these patients. The increased metabolism of glucose in brain tumors can help determine treatment options, such as whether sites are surgically removable. If sites are resected, residual glucose uptake can help determine if the tumor tissue was completely removed. In nonresectable tumors, glucose metabolism may be a relatively easy, noninvasive method to evaluate the benefits of nonsurgical treatments such as chemotherapy or radiation therapy, and to differentiate tumor tissue from scar tissue as a result of previous surgery or radiation. The use of PET in neurology is expanding. A great number of people are affected by some type of neurologic condition. An accurate, noninvasive method of diagnosing, treating and/or monitoring these patients would be of great benefit. PET may be this tool (*14*).

Once the myocardium becomes ischemic, there is a shift toward utilization of glucose as an energy source since the cells will be able to obtain energy through anaerobic glycolysis. Manipulation of the body's glucose levels by providing a glucose-rich state or glucose load will increase the uptake of glucose by the myocardium in relation to the usual fatty acid substrate. After an oral glucose load, ^{18}F-FDG will be trapped by viable, noninfarcted myocardial cells. The glucose load will accentuate the visual differentiation between tissues that take up glucose and those that are infarcted and do not. A perfusion study (either PET or SPECT) will differentiate normal tissues from tissues that receive lower than normal blood perfusion, however, it may be difficult and time consuming to differentiate if this decreased area of perfusion is due to ischemia or infarct and no longer viable. By combining the perfusion study with a ^{18}F-FDG study, the area in question on the perfusion scan can be compared to the ^{18}F-FDG metabolic images to see if there is viable tissue in the area in question.

The use of ^{18}F-FDG is becoming important in oncology. Glucose also has been shown to be a major energy source for tumor cells. Fluorine-18-FDG also can be used to localize metastatic lesions. Tumor cells are usually fast growing in comparison to normal cells, and thus require additional energy

to sustain their rapid growth rate. Whole-body imaging may be used to detect the spread of disease before changes are noted by other imaging modalities, thus improving patient treatment. Since ^{18}F-FDG measures the metabolic activity of a tumor, ^{18}F-FDG also shows promise in monitoring drug therapy and differentiating between active tumor and necrotic scar tissue which may be indistinguishable by other imaging modalities. When treating patients with chemotherapeutic agents or radiation therapy, standard anatomic imaging using CT or MR imaging may not be able to show the efficacy of therapy through structural changes for an extended period of time after the start of therapy. By using ^{18}F-FDG to monitor the biochemical changes in the tumor site, the effectiveness of therapy frequently can be determined. After surgical or radiation therapy, differentiation between active tumor and necrotic or scar tissue is difficult using modalities such as CT or MRI. Fluorine-18-FDG may help determine visually whether the tissue in question contains active tumor cells or necrosis. The use of ^{18}F-FDG in oncology shows great promise and will further promote the use of PET imaging.

TECHNOLOGIST CONCERNS

The use of PET isotopes in some hospitals may prove to be a challenging undertaking. The availability of PET isotopes has been enhanced by the development of commercial radiopharmacies that have dedicated sites for producing and delivering PET isotopes, most commonly ^{18}F-FDG. The acquisition of the radiopharmaceutical requires only a simple phone call and a preset delivery time. There are many other considerations when working with positron emitters that will require changes in the way that the nuclear medicine department plans, preps and images a patient.

One of the first concerns will be radiation exposure. The 511-keV photons have considerably more energy. Most lead shielding able to shield ^{99m}Tc photons is not sufficient to adequately shield these high-energy photons. Technetium-99m has a half-value layer of 0.2 mm of lead while the 511-keV photons have a half-value layer of 4.0 mm (*6*). Commercially available 511-keV shields weigh between 40 lb and 100 lb, making manipulation and transport difficult. Shielding made of tungsten, a substance that is much denser than lead, is better for blocking the high-energy photons and is ideal for PET isotopes.

Shipments of PET isotopes from an outside vendor are received similar to traditional deliveries. However, the appearance of the delivery is somewhat different. Since the amount of shielding needed would make the package too cumbersome and heavy to handle, other principles of radiation safety must be used. Usually unit dose vendors have the authority to ship White Bar I or Yellow Bar II packages. The shipment must fall under the limits of Yellow Bar II packaging, a surface reading less than 50 mR/hr and a transportation index of less than 1.0 mR/hr at 1 m. The principle of distance is incorporated into the packaging. The dose is packaged in a lead-lined container with conventional isotopes. This shielding will not be sufficient to maintain Yellow Bar II shipping standards when delivered in an ammo can or suitcase-type delivery container. This lead-lined container is placed into a larger box with packaging material that holds the dose in the center of the box. The distance between the lead-lined container and the outer surface of the box has increased, thus decreasing the radiation exposure at the surface. Although the size of the box is somewhat larger than usual, the radiation exposure for the delivery and receiving personnel is equivalent to that of other shipments to the nuclear medicine department. When accepting the package, the technologist who opens the shipping box and moves the container out of the box into a storage area and/or prepares it for patient administration will have a somewhat higher radiation exposure. Radiation exposure can be kept within acceptable levels by decreasing the amount of time that the unit dose is handled. It is expected that all personnel who handle PET isotopes likely have higher exposure reports. A study on occupational exposures that compared exposures to nuclear medicine technologists in conventional and PET settings showed that the average annual whole-body exposure for technologists in the traditional hospital setting was 180 mrem, while PET technologists had an average of 410 mrem. Although users who handle PET isotopes have a higher exposure, the exposure falls within the safety guidelines (*15*).

Administration of PET radiopharmaceuticals is similar to traditional radiopharmaceuticals. The short half-life of PET products allows for larger amounts of activity to be administered to the patient while adhering to ALARA principles. Generally 5–15 mCi ^{18}F-FDG are used. Before patient administration, the activity must be assayed. There are dedicated PET dose calibrators, however, it is acceptable to use the dose calibrator currently in the department (*4*). Depending on the model, a 511-keV button or dial setting can be set to allow rapid determination of the administered activity. Studies have shown that the whole-body exposure is increased to the individual who prepares and administers PET radiopharmaceuticals. Proper radiation safety training, as well as efficient syringe handling during administration, can help decrease this exposure (*15*).

When considering PET imaging, one must consider several factors such as camera location, restroom facilities and patient proximity to staff and other patients. A dedicated PET area should be identified to minimize patient movement, radiation exposure to others in the department and interference with other scans. Brown et al. (*16*) found that the exposure from ^{18}F-FDG is 2.7 times greater within the scanning room and 9.5 times greater in adjacent rooms as compared to exposures resulting from the use of ^{99m}Tc. PET radiopharmaceuticals should be received in an area where there is little chance for exposure to other personnel and patients. When receiving a package, it should be checked in and stored immediately. When setting up a storage area it must be well shielded to avoid increasing exposure to others who move in and out of the area. It also is important to adequately shield any surrounding rooms. It is best to identify a camera location that is as far away as possible from the other cameras. Patients who have been injected with a positron emitter, like all patients, become a

source of radiation exposure and have the potential for producing radioactive contamination (i.e., urine contamination). Patients should be given instructions to prevent contamination.

One of the best features of PET isotopes is their short half-lives which make radioactive waste much easier to handle. With a 110-min half-life, ^{18}F-FDG waste only needs to be held for approximately 18 hr to reach the 10 half-life rule of thumb for radioactive decay. Ancillary supplies, such as syringes, stopcocks and saline flushes which are decayed in storage can be disposed of the next day (*6*). This minimizes the amount of radioactive waste and reduces the storage space needed in the department. Usually radioactive material vendors accept return radioactive waste as well, allowing return of the used vial or syringe. Radioactive material spill or contamination also is easily cleaned and the area will decay quickly, usually by the next day.

The ability to update existing cameras has potential benefits and drawbacks in the department. The cost of updating traditional cameras must be considered and incorporated into the planning of the department's budget. Although not as costly as purchasing a new camera, the equipment update and software/computer additions require some planning. The needed new software will require additional training of the technologist. Daily quality control testing, which is normally done on each camera, must be expanded to account for this new technology. It is also important to review your institution's radioactive material license to assure that the facility is authorized to receive and use PET isotopes. The submission of an amendment to include positron emitters is required regardless of whether you develop a broad-scale or limited-use PET imaging facility (*4*).

THE FUTURE OF PET

Research has shown that the superior imaging capabilities of PET have a wide variety of uses. The overriding factor limiting the success of PET is a financial one. The financial burden required to purchase and operate the equipment forces the price of these studies to be extremely high. The development of outside vendors who can supply PET isotopes to a large number of customers on a unit dose basis and the adaptability of SPECT cameras for PET imaging should start to increase the use of this modality. Increased use and studies on the cost effectiveness of PET imaging in the overall care of patients should improve reimbursement. Medicare began coverage of PET scans used in diagnosing solitary pulmonary nodules and in staging lung cancer in January 1998. The Health Care Financing Administration (HCFA) plans to review cardiac and neuro-oncology applications as well (*17*). With resolution of reimbursement issues and prudent use of this diagnostic modality, PET imaging should become a viable and efficacious tool in the clinical setting.

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