Technical Issues in Performing PET Studies in Pediatric Patients*

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The purpose of this review is to familiarize the reader with aspects of PET that are important to its performance in pediatric patients. Recognition of differences in applying PET technology to children than to adults should result in higher quality scans in pediatric patients. The reader should be able to recognize key differences in performing PET scans in pediatric patients and to recall basic indications for PET scanning in children. High-quality PET imaging of pediatric patients is challenging and requires consideration of issues common to pediatric nuclear medicine but uncommon to imaging of adult patients. These include intravenous access, sedation, fasting, consent, and clearance of activity from the urinary tract. This article focuses on technical differences involved in pediatric PET compared with adult PET and serves as a guide to enhance the quality of scans and to ensure the safety and comfort of pediatric patients. Upon reading this article, the reader will be familiar with the aspects of PET that pertain to pediatric patients, know how to apply PET imaging techniques to pediatric patients, and know the indications for PET scanning in children.

Key Words: pediatrics; PET; technical issues

J Nucl Med Technol 2004; 32:5–9

Great strides have been made in PET technology over the last 20 y. These have advanced its status from a time-consuming, effort-intense method of imaging available mainly at university centers to a potentially routine diagnostic tool of great utility (*1*). A brief look at the history of PET with regard to oncology provides an appreciation for today's machinery and its suitability for pediatric patients.

At its advent, the primary application of PET was brain imaging. Accordingly, the first units were head-only devices.

Whole-body devices that emerged in the mid to late 1980s were characterized by a 10-cm *z*-axis field of view and fixed ring sources. Transmission images for attenuation correction had to be obtained before injection of tracer. Furthermore, they were only marginally useful for positioning in that only very limited anatomic information could be obtained from the transmission images. Positioning was performed before injection of tracer by correlating physical findings with CT findings (*2*). Essentially, the focus of positioning involved finding the air–soft-tissue interface at the diaphragm and then estimating how far above or below the diaphragm to center the field of view. Part or all of the tumor might lie outside the field of view of the PET camera and be missed during the acquisition.

An emission–transmission scan of 2 bed positions (20 cm) with this device was time consuming, requiring approximately 90 min: 20 min for the transmission scan, 50 min after injection for uptake of ^{18}F-FDG to occur to provide acceptable tumor-to-nontumor ratios, and 20 min for emission scans (2 levels at 10 cm each, 10 min per bed position). The patient remained on the imaging table during the uptake period to avoid errors in repositioning between the transmission and emission images. This could be very difficult for an ill, hungry, or uncomfortable child. Patient tolerance, parent tolerance, and technologist tolerance for the long imaging times impeded the application of the technique. Although images could be obtained at multiple bed positions without attenuation correction, the quality of nonattenuation-corrected emission scans was variable and the whole-body imaging display initially was not widely available (*3*).

Fortunately, there has been remarkable progress in both hardware and software (*4*), which has reduced considerably the acquisition times and increased image quality. Typical machines currently feature a 15-cm *z*-axis field of view and rotating rod sources. These allow acquisition of transmission images after injection of tracer and provide a larger field of view, reducing the number of bed positions needed for imaging 60 cm from 6 to 4. Whole-body imaging has become feasible and practical. Presently, a 2-level emission–transmission scan can be acquired in about 20 min (7-min emission, 3-min transmission per bed position) on a PET-only machine or about 11 min on a PET/CT device. As a result, pediatric PET imaging is more practical and better tolerated by patients and technologists than in previous years.

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Although modern-day PET cameras are considerably more "pediatric friendly" than their predecessors, additional efforts are required to ensure safety and comfort of the patient and quality of the imaging data. Beyond the special attention that a child must receive when embarking on what is uncertain and often a frightening procedure, a set of protocols encompassing issues relevant to pediatrics should be implemented. Some issues relevant to studying adult patients also apply (*1*). What follows is a guide to performing PET in pediatric patients emphasizing patient consent, intravenous access, bladder catheterization, and sedation.

PROCEDURE

Consent

Initially, pediatric PET studies at our institution were performed under research grants awarded by the National Institutes of Health and the University of Michigan Clinical Research Center. Additionally, ^{18}F-FDG was administered as an investigational agent under a Food and Drug Administration (FDA) Investigational New Drug. Institutional Review Board (IRB)–approved consent forms were required. IRB regulations are even more complex when children are the patients involved in research studies since they are a vulnerable population. In contrast with adult studies, wherein the procedure is explained directly to the patient and the documentation is read and signed by the patient, the pediatric patient is unlikely to understand the study and cannot give informed consent. Therefore, effective communication with parents or guardians is essential before the procedure. It is advisable to have the referring physician introduce the need for the PET scan to the parents or guardians. It is the parents or guardians who read the consent documentation and require clarification and explanation in lay terms. Since the parents may or may not be available at the actual time of the PET scan, and may or may not accompany the child to the test, consent is usually obtained the day before the procedure. The technologist along with the parents can then explain the procedure to the child in terms more appropriate to the child's age and medical experiences.

With the advent of clinical PET and widespread use of ^{18}F-FDG under FDA approval, IRB-mandated consent forms are no longer required. Nonetheless, we routinely explain the procedure in detail to the parents or guardian and to the child according to his or her degree of comprehension. At our institution, parents must still sign an acknowledgment of financial responsibility for the PET scan if not covered by insurance. Fortunately, insurance coverage for PET scans in children with neoplastic diseases has not been problematic in Michigan.

Intravenous Access

Good intravenous access is essential to the performance of the study. PET technologists are usually different personnel from pediatric nuclear medicine technologists and have limited experience establishing intravenous access in children. Establishing intravenous access in children, especially those whose veins are not readily apparent, can be particularly challenging and distressing. Patients and parents are intolerant of multiple attempts. On rare occasion, we have had to cancel a PET scan when intravenous access could not be rapidly established in the PET suite. Currently, we frequently use the services of our colleagues in pediatric nuclear medicine, pediatric oncology, and pediatric anesthesiology to secure intravenous access, especially in younger children. Hospitalized patients will usually have an indwelling intravenous line. This line can be tested and, if acceptable, used for tracer administration.

Intravenous access is best established well before the patient is transported to the PET suite. In children requiring anesthesia, access can be established shortly after the induction of anesthesia as veins dilate, and pain is no longer an issue. The child is spared the pain of venipuncture and the parents and technologists are spared the accompanying screaming and anxiety. This approach is best for patients receiving tracers for which imaging is begun soon after injection, such as ^{11}C-hydroxyephedrine (*5*). For patients receiving ^{18}F-FDG, this would add at least 45 min to the anesthesia time as the child remains sedated, while the uptake of ^{18}F-FDG occurs.

A central line is present in most patients who are going to receive systemic chemotherapy. This line may be used for intravenous delivery of the PET radiotracer. The technologist should ask the parent or guardian about the line and which port is preferred. Parents are usually well versed on the function of these lines. The line should be flushed well to minimize residual tracer in the line and the tube manipulated so that as much of the tubing as possible lies either outside the imaging area or to the side rather than on top of the patient. With care to flush the line, we usually encounter very little residual activity in the line and this residual activity does not interfere with image interpretation. Residual activity within the line could interfere with the quality of the study, especially if the amount of radiotracer actually injected was substantially reduced. When using lines with long tubing, consideration should be given to diluting the tracer before administration (Fig. 1). In addition, the central line tubing could be elevated with towels or other lightweight substances to lift it off the body.

Bladder Catheterization

There are several reasons why a bladder catheter may be necessary for a pediatric patient undergoing PET imaging. First, activity in a full bladder may obscure or cause reconstruction artifacts interfering with the assessment of activity in nearby structures. This is most important when thorough evaluation of the pelvis is necessary or desirable. Second, the urge to void during the study may result in patient movement or in voiding into the child's clothes or sheets, causing embarrassment and discomfort, as well as adversely affecting image quality (Fig. 2). Third, the preparation of pediatric patients for anesthesia and the anesthesia itself predispose the patient to retention of activity within the

FIGURE 1. A 17-y-old girl with newly diagnosed Hodgkin's disease. Residual activity at the injection site and in the intravenous tubing is readily seen. This can be minimized by thoroughly flushing the line after injection of the tracer and by diluting the tracer before injection.

urinary tract. Patients must have nothing by mouth for several hours before induction of anesthesia. This fluid restriction results in intravascular volume contraction and production of lower volume but concentrated urine. Additionally, anesthesia causes muscle relaxation, including the smooth muscle of the bladder. This can lead to bladder distention. Thus, we often perform bladder catheterization for children undergoing PET studies under anesthesia. Like the issues regarding venous catheterization, insertion of a bladder catheter is best performed by personnel well experienced in the insertion of urinary bladder catheters. We insert the catheter after the patient has been anesthetized to minimize patient trauma and to facilitate the procedure. On one occasion, a difficult catheterization prompted a request for assistance from our pediatric urology service. Backup from collegial pediatric services is clearly advantageous for the uncommon circumstances for which it is needed.

Once the patient is catheterized, care must be given to maintain proper positioning of the catheter and collection device. The collection device should be placed below the patient to allow for gravity drainage and away from the patient to avoid interference from the radioactive urine. Although this seems obvious, nonimaging personnel are usually unfamiliar with the amount of ^{18}F-FDG excreted through the urinary tract and its consequences on image reconstruction and interpretation. A small amount of urinary ^{18}F-FDG can contaminate a large region (Fig. 2).

Sedation or Anesthesia

The criteria for which children may need anesthesia for a PET scan are similar to those of other lengthy procedures in pediatric nuclear medicine: patients who are mentally impaired, young children who cannot cooperate or tolerate, and those who are claustrophobic. In short, any patient with characteristics that may interrupt or disrupt the PET scan should be considered for sedation or anesthesia.

The preferred approach to sedation varies among institutions and departments. Sedation or anesthesia is delivered in accordance with institutional guidelines and those published by the American Academy of Pediatrics (*6,7*). Sedation may be suitable for some patients. In those cases, placement of intravenous access and bladder catheters should be performed before sedation, as the arousal stimulus from those activities may be sufficient to disrupt or terminate the sedation. Qualified personnel whose sole responsibility during the scan will be to continuously monitor consciousness and cardiorespiratory function must be present throughout the entire procedure.

PET/CT Imaging

PET/CT devices are now commercially available (*8*). These PET machines are quite useful for pediatric imaging and have some advantages over state-of-the-art stand-alone PET scanners. Imaging time is reduced for at least 2 reasons: (a) the quick, spiral CT takes $<$1 min and obviates the need for transmission scans (typically 3 min per bed position); (b) the 3-dimensional mode of acquisition has allowed us to reduce the emission imaging time to 5 min per bed position. Thus, the actual camera time for a 4-level, 60-cm whole-body scan is $<$30 min. Additional considerations

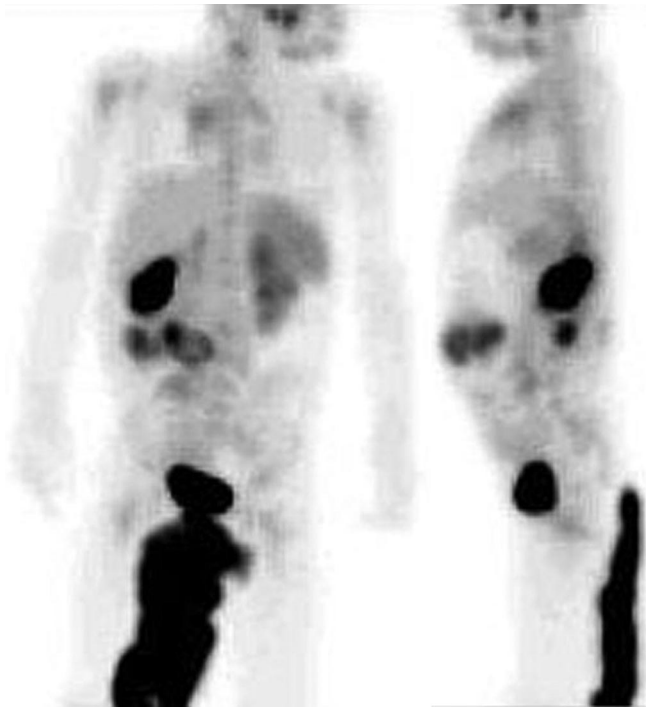

FIGURE 2. Anterior and lateral projection images of 2-y-old girl with neuroblastoma. During catheterization, the technologist noted a few drops of urine fell onto the underlying blue absorbent pad. The absorbent pad functioned well in directing the activity away from the patient.

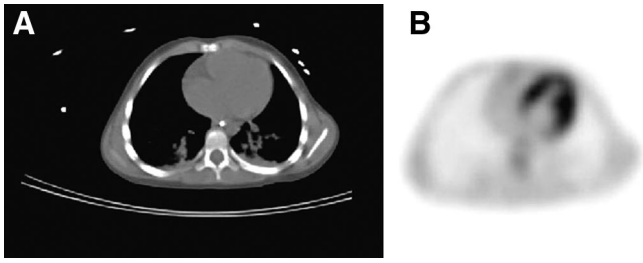

FIGURE 3. PET/CT scan of 3-y-old boy with recurrent neuroblastoma. (A) Chest CT scan shows bibasilar atelectasis. (B) Corresponding PET image shows no abnormal ^{18}F-FDG accumulation in areas of atelectatic lungs.

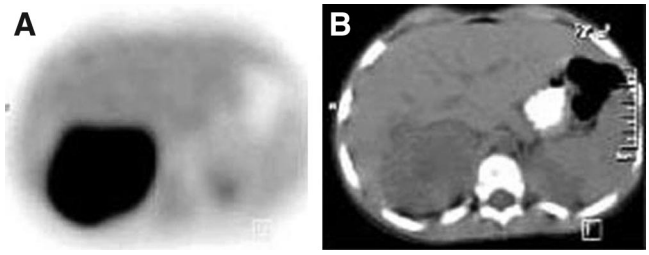

FIGURE 5. Transverse image from PET scan (A) and corresponding CT scan (B) of 3-y-old boy with neuroblastoma shows markedly increased uptake in right adrenal mass, the primary site of the patient's neuroblastoma.

depend on the principal purpose of the CT scan. As our institution has multiple state-of-the-art dedicated CT scanners and only one clinical PET scanner, we consider that the primary use of the CT scan is for attenuation correction, secondarily for anatomic localization, and thus we try to limit the diagnostic complexity of the CT scan. At some institutions, however, PET/CT machines are used to perform diagnostic CT scans along with the PET scans. Thoracic PET CT scans are done with free breathing. In intubated patients, this may result in atelectasis, which impairs the quality of the CT scan but has minimal, if any, effect on the PET component (Fig. 3). An oral contrast agent may be administered to better identify the bowel, which assists interpretation of the PET scan in helping to distinguish benign uptake in the gastrointestinal tract from abnormal uptake in adjacent soft tissues. We have not encountered artifacts from oral contrast agents that substantially complicate the interpretation of the study (*9*). An intravenous contrast agent is useful to outline the major vessels. However, this considerably complicates the acquisition, as different contrast protocols may be in order for the CT scans of the neck versus the chest versus the abdomen. We do not routinely administer an intravenous contrast agent but can when requested by the referring physician and when we believe that it will aid the interpretation of the PET scan. Although complicated CT protocols can be accomplished on the PET CT machine, we believe our patients are better served by having complex CT scans performed on dedicated CT scanners with full-time CT personnel.

Caloric Intake

Patients should not eat or drink caloric-laden beverages for at least 4 h before injection. The purpose of fasting is to reduce the circulating insulin levels, which rise after a meal and drive glucose and FDG into muscles, and to reduce circulating blood glucose levels. Hyperglycemia can result in poor uptake of FDG into tissues as the elevated blood glucose competes with FDG for transport into cells. In patients undergoing anesthesia, the fasting requirements for anesthesia are often more stringent than those required for PET alone and thus take precedence.

Indications for PET Scanning in Children

As of this writing, PET scanning in children is not supported by the Center for Medicare Services (CMS) except as their conditions coincide with reimbursed conditions in adults. Efforts are underway to secure financial support for

FIGURE 4. Anterior projection image of ^{18}F-FDG PET scan of a 17-y-old boy with newly diagnosed non-Hodgkin's lymphoma. A large mediastinal mass is evident.

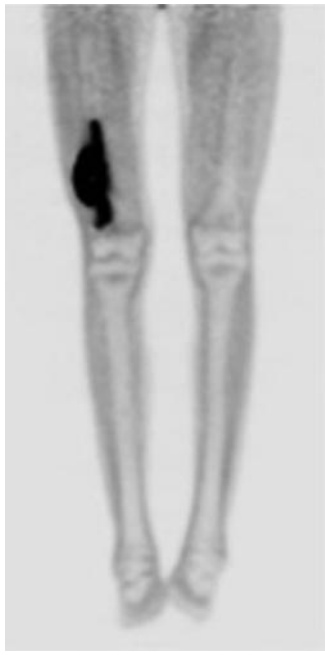

FIGURE 6. Anterior projection image of 17-y-old girl with osteosarcoma in right distal femur.

PET scanning in children with malignant diseases. We have found PET scanning to be useful for the following indications: (a) the distinction of benign from malignant neoplasms; (b) staging of the malignancy; (c) determination of the response to therapy; and (d) distinguishing scar from residual neoplasm in children who have completed therapy (*2,10,11*). The tumors we most commonly encounter are neuroblastoma, lymphoma, and soft-tissue sarcoma (Figs. 4–6). PET scanning can be quite useful in the evaluation of uncommon tumors, such as the peripheral nerve sheath tumor, and hepatoblastomas, which have not yet been well characterized with regard to FDG uptake and retention.

CONCLUSION

The use of PET to study pediatric conditions is becoming more common. The PET technique has considerable promise for expanding our knowledge about the pathophysiology of pediatric disease, especially oncologic disease. CMS coverage for pediatric oncology may be soon considered. We anticipate that the application of PET in pediatrics will continue to expand.

In summary, with particular attention to detail, high-quality functional images that provide valuable clinical information for the management of pediatric patients with malignancies can be obtained using PET. Pediatric-specific issues should be anticipated and addressed in the planning of the studies to maximize the utility of the technique in this challenging group of patients.

ACKNOWLEDGMENTS

The authors thank Jill Rothley, CNMT; Andrew Weeden, CNMT; Paul Kison, CNMT; Edward McKenna, CNMT; Shana Huber, CNMT; Stan Wegrzyn, CNMT; Lahti Lahti, CNMT; Lindsey Murray, CNMT; and Elizabeth Wynn, CNMT, for expertise in the preparation for and performance of PET scans in our pediatric patients. The authors thank Carol Kruise for assistance in the preparation of this manuscript. This work was supported by National Cancer Institute grants R01 CA54217 and M01-RR00042 from the Clinical Research Center of the University of Michigan.

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