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PET imaging in pediatric oncology

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Abstract High-quality PET imaging of pediatric patients is challenging and requires attention to issues commonly encountered in the practice of pediatric nuclear medicine, but uncommon to the imaging of adult patients. These include intravenous access, fasting, sedation, consent, and clearance of activity from the urinary tract. This paper discusses some technical differences involved in pediatric PET to enhance the quality of scans and assure the safety and comfort of pediatric patients.

Keywords PET imaging · Pediatric oncology

Introduction

Over the past 20 years, there has been considerable progress in PET technology, which has made pediatric PET imaging feasible and much more pediatric friendly [1]. The technology has evolved from time-consuming and effort-intense to virtually routine. Early on, the primary application of PET was brain imaging and the first units were head-only devices.

Whole-body devices became commercially available in the mid to late 1980s and had a 10-cm z-axis field of view and fixed ring sources. Transmission images for attenuation correction had to be acquired prior to injection of tracer. Furthermore, they were minimally useful for positioning in that only very limited anatomic information such as the diaphragmatic interface could be obtained from the transmission images. Patients were positioned before injection of tracer by correlating

physical findings with CT findings. For all practical purposes, positioning involved finding the air-soft tissue interface at the diaphragm, 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 this could not be appreciated until after the study had been completed and then reconstructed.

A transmission-emission scan of two bed positions (20 cm) with this device was time consuming, requiring about 90 min: 20 min for the transmission scan, 50 min post-injection for adequate uptake of FDG to occur, and 20 min for emission scans (two levels at 10 cm each, 10 min per bed position). This could be unrealistic for an ill, hungry, uncomfortable child. Patient, parent, and technologist tolerance for the long imaging times were not favorable. Although images could be obtained at multiple bed positions without attenuation correction, the quality of non-attenuation-corrected emission scans was variable, and whole-body imaging software was not widely available.

There have been considerable advances in both machinery and software. This has resulted in both impressive reductions in acquisition times as well as improvements in image quality. Currently, PET machines commonly feature a 15-cm z-axis field of view and rotating rod sources. Transmission images can be obtained following injection of tracer, and the larger field of view reduces the number of bed positions needed for imaging 60 cm from 6 to 4. ''Whole-body'' imaging has become practical. Presently, a two-level emission-transmission scan can be acquired in about 20 minutes (7-min emission, 3-min transmission per bed position). As a result, pediatric PET imaging is much better tolerated by patients and technologists than in the past.

Although modern PET cameras are more pediatric friendly than their predecessors, additional efforts are required to make the study as tolerable as possible for the patient and to ensure that the quality of the imaging data is high. Preparation of the adult patient for PET imaging has been well described [2]. A set of protocols encompassing issues unique to pediatrics is necessary. The following discussion is a guide to performing PET in pediatric patients, emphasizing patient consent, IV access, bladder catheterization, and sedation.

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. ^{18}F-FDG was administered as an investigational agent under an FDA IND (Investigational New Drug). Institutional Review Board (IRB) approved consent forms were required. Although routinely complicated, IRB regulations are even more complex when children are the patients involved in research studies since they are a ''vulnerable population.'' In contrast to studies in adult patients, where the procedure is explained directly to the patient and the documentation read and signed by the patient, the pediatric patient cannot give informed consent. Parents/guardians must grant informed consent, and it can be difficult to locate a working parent. In our institution, verbal consent can be obtained by telephone by reading the entire document to the parent/guardian with a hospital representative listening as a witness. Because FDG PET scanning is now performed mostly for clinical rather than research indications, the imaging consent form is no longer regulated by the IRB. We recommend having the patient's treating physician involved with the parents in introducing the need for the PET scan. It is the parents/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, we usually obtain consent the day prior to the procedure for research studies. 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.

IV access

Reliable intravenous access is critical to the study. PET technologists are usually different personnel from pediatric nuclear medicine technologists and have less experience establishing intravenous access in children. Establishing IV access in children, especially those whose veins are not easily seen, can be particularly problematic. Patients and parents do not tolerate multiple attempts at IV access. Rarely, we have had to cancel a PET scan when IV access could not be rapidly established in the PET suite. We frequently utilize the skills of our colleagues in pediatric nuclear medicine, pediatric oncology, and pediatric anesthesiology to secure IV access, especially in younger children. Hospitalized patients will usually have an indwelling intravenous line that can be tested and used for tracer administration, if acceptable.

Intravenous access is best established well before the patient is transported to the PET suite. In children requiring anesthesia and whose imaging will begin shortly after injection, 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 (for example,

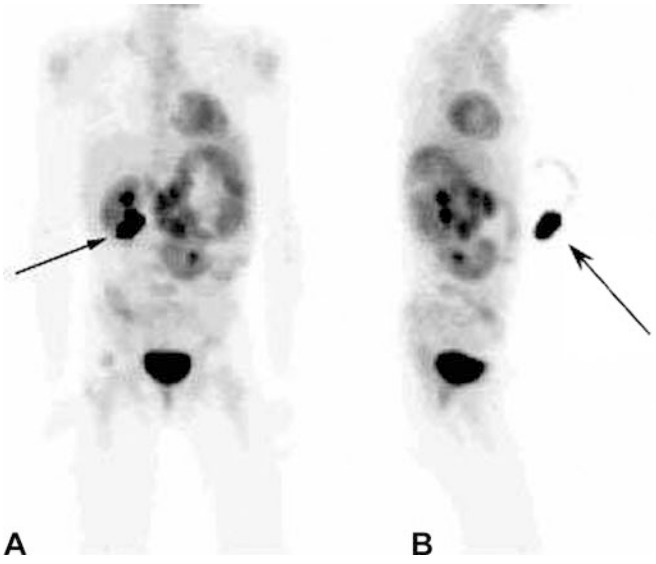

Fig. 1A, B Eight-year-old boy with neuroblastoma at presentation. **A** Anterior projection image of FDG PET scan. Activity overlying the right kidney (*arrow*) is shown to represent residual radiotracer in the injection tubing (*arrow*) on lateral projection image (**B**). The large area of uptake is the left upper quadrant at the same level as the right kidney, represents the primary tumor. The region of decreased uptake within the mass is due to central necrosis

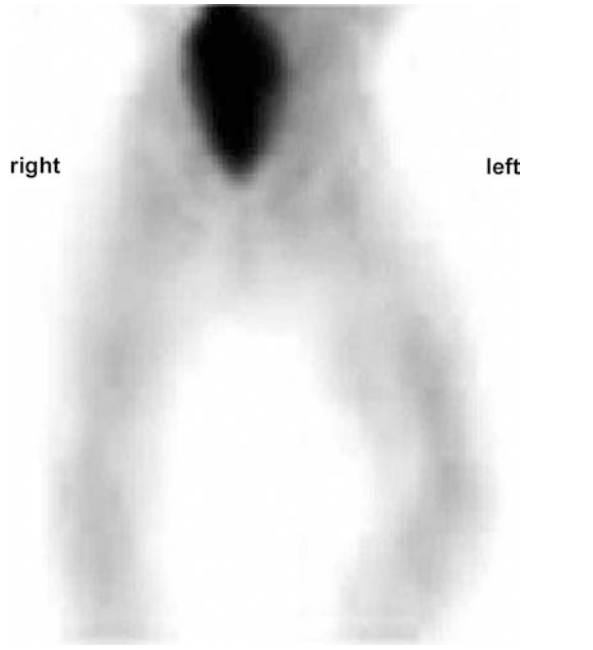

Fig. 2 Anterior projection image of FDG PET scan of 3-year-old girl with primitive neuroectodermal tumor of the sacrum. Bladder activity precludes adequate evaluation of the pelvis. The study was repeated with bladder catheterization and intravenous fluids

^{11}C-hydroxyephedrine) [3]. 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, and is impractical.

A central line is present in most patients who are going to be treated with systemic chemotherapy. This line can be used for injection of the PET radiotracer. The technologist should ask the parent or guardian about the line and which port is preferred. Parents are usually quite familiar with the function of these lines. The line should be flushed well to clear residual tracer from the line. The tubing should be manipulated so that as much of it as possible lies either outside the imaging area or to the side of the patient rather than on top (Fig. 1). 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.

Bladder catheterization

There are several reasons why bladder catheterization may be needed. First, activity in a full bladder may obscure or cause reconstruction artifacts interfering with the recognition of activity in nearby structures (Fig. 2). This aspect is particularly pertinent in small children in whom small sites of pathologic avidity may be obscured by avidity in adjacent normal structures such as a distended bladder. This is most important when thorough evaluation of the pelvis is necessary or desirable. Second, an urge to void during the study can result in patient movement or result in voiding onto the child's clothes or sheets, causing embarrassment and discomfort and adversely affecting image quality. Third, the preparation of pediatric patients for anesthesia and the anesthesia itself predispose the patient to retain activity within the urinary tract. Patients must remain npo for several hours prior to induction of anesthesia. This fluid restriction results in intravascular volume contraction and production of lower volume but concentrated urine (Fig. 3). Additionally, anesthesia causes muscle relaxation, including the smooth muscle of the bladder. This can lead to bladder distention. For these reasons, 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 experienced in the insertion of urinary bladder catheters. We usually insert the catheter after the patient has been anesthetized in order 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.

Once catheterized, care must be given to maintain proper positioning of the catheter and collection device. The collection device must be placed below the patient for gravity drainage and away from the patient to avoid

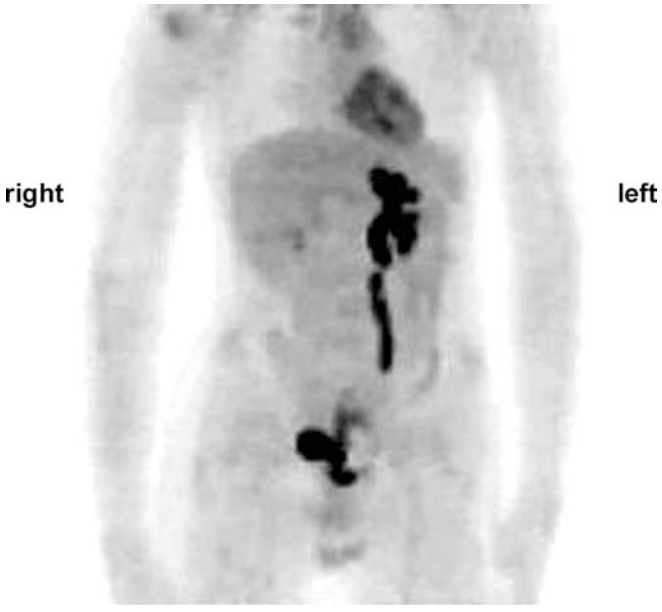

Fig. 3 Anterior projection image of 16-year-old boy with history of Wilms' tumor, status post right nephrectomy. There is considerable radioactivity in the left kidney and urinary collecting system owing to prolonged clearance of tracer

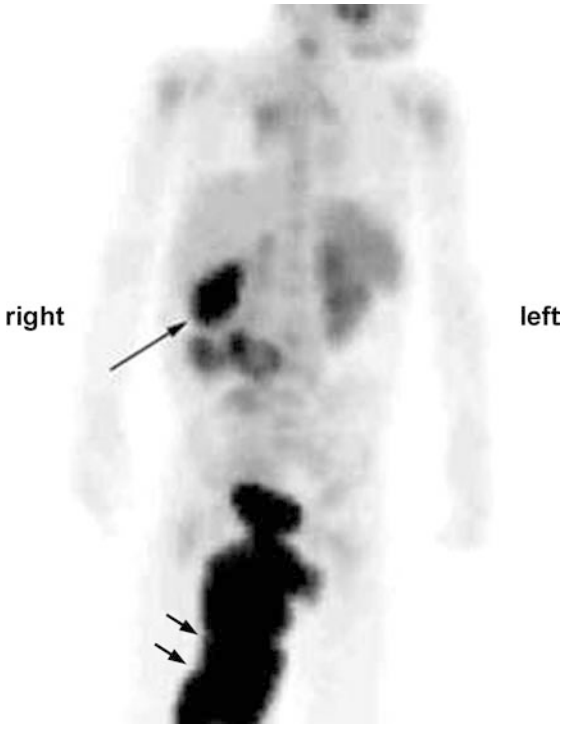

Fig. 4 Anterior projection image of 2-year-old girl with neuroblastoma (*arrow*). During catheterization, the technologist noted a few drops of urine fall onto the underlying blue absorbent pad (*short arrows*)

interference from the radioactive urine. Although this seems obvious, nonimaging personnel can be unfamiliar with the amount of FDG excreted through the urinary tract and its consequences on image reconstruction and interpretation. A small amount of urinary FDG can contaminate a large region (Fig. 4). In our experience, gravity drainage is adequate for maintaining bladder decompression. We have not found a need for continuous bladder irrigation.

Sedation/anesthesia

Children may need anesthesia for a PET scan just as for other lengthy procedures in pediatric radiology: patients who are mentally impaired, young children who cannot cooperate/tolerate, and those who are claustrophobic will probably need sedation. 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/anesthesia is delivered in accordance with institutional guidelines and those published by the American Academy of Pediatrics and American Society of Anesthesiology [4, 5]. Sedation may be suitable for some patients, although we rarely encounter patients for whom "light" sedation is adequate. In those cases, placement of intravenous access and bladder catheters should be performed prior to sedation, as the arousal stimulus from those activities may be sufficient to disrupt or terminate the sedation. In our experience, once the child is aroused and irritated, additional sedation is not likely to be effective. Qualified personnel, whose sole responsibility during the scan will be to monitor consciousness and cardiorespiratory function continuously, must be present throughout the entire procedure.

PET-CT devices are now commercially available. These PET machines are quite valuable for pediatric PET imaging and have some advantages over even state-of-the-art stand-alone PET scanners [6]. Imaging time is reduced for at least two reasons: (1) the quick, spiral CT takes less than a minute and obviates the need for transmission scans (typically 3 min per bed position); (2) the 3D mode of acquisition of emission data has allowed us to reduce the emission imaging time to 5 min per bed position. The actual camera time for a four-level, 60-cm "whole-body" scan is less than 30 min. Additional considerations depend upon 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, the primary use of the CT scan is for attenuation correction and secondarily for anatomic localization. CT scans performed for attenuation correction are obtained with reduced mA. This reduction decreases the

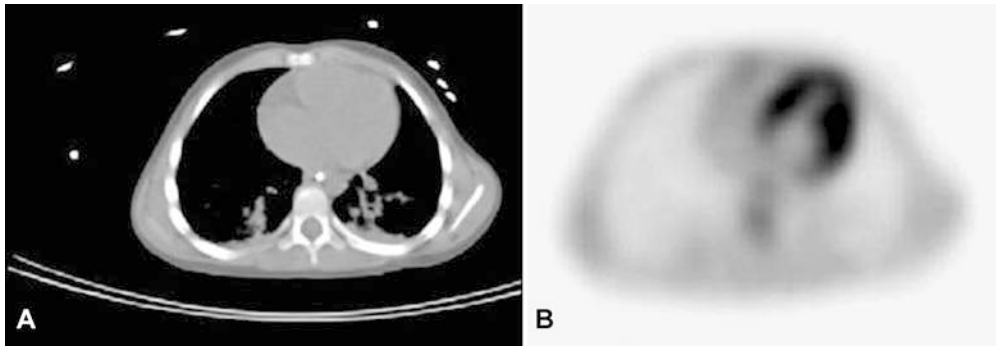

Fig. 5A, B PET-CT scan of 3-year-old boy with recurrent neuroblastoma. **A** Chest CT shows bibasilar atelectasis. **B** Corresponding PET image shows no abnormal FDG accumulation in areas of atelectatic lungs

absorbed dose to the patient without loss of image quality in the reconstructed PET images. We try to limit the "diagnostic" complexity of the CT scan to facilitate tolerance of the procedure on the part of the patients and to facilitate patient access for the medical community. Thoracic PET CT scans are done with free breathing in contrast to diagnostic chest CT examinations often being performed with the breath-hold technique. Breath-holding with PET-CT can contribute to misregistration between CT and PET data. 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. 5). Oral contrast may be given to identify the bowel better, and that assists interpretation of the PET scan by helping to distinguish benign uptake in the gastrointestinal tract from abnormal uptake in adjacent soft tissues. The choice of oral contrast agents is probably not important, and oral contrast has been shown not to interfere substantially with image interpretation [7]. Intravenous contrast may be 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 chest versus abdomen. We do not routinely administer IV contrast but can when requested by the referring physician and when we believe that will aid the interpretation of the PET scan. Although complicated CT protocols can be accomplished on the PET CT machine, patients may be better served by having complex CT scans performed on dedicated CT scanners with full-time CT personnel.

Indications for PET scanning in children

As of this writing, PET scanning in children is not supported by the Center for Medicare and Medicaid Services except as their conditions coincide with reimbursed conditions in adults. Efforts are underway to secure financial support for PET scanning in children with malignant diseases. We have found PET scanning useful for the following indications: (1) the distinction of benign from malignant neoplasms; (2) selection of the site for biopsy; (3) staging of the malignancy; (4) determination of the response to therapy; and (5) distinguishing scar from residual neoplasm in children who have completed therapy. The tumors we most commonly

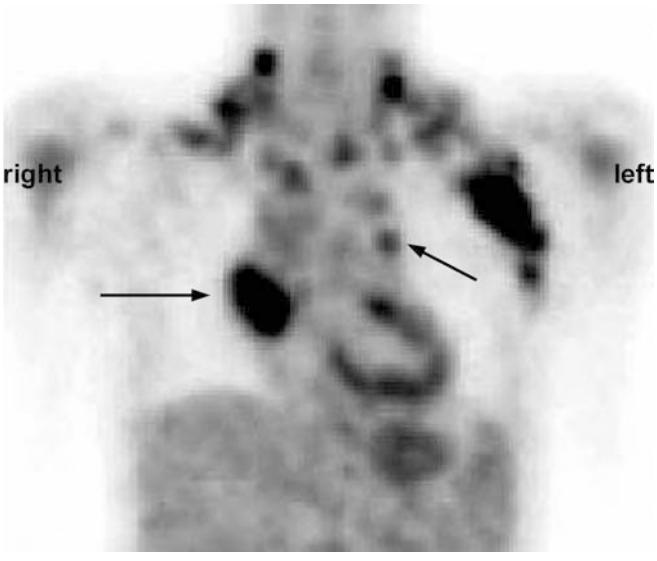

Fig. 6 Anterior projection image of FDG PET scan of a 17-year-old boy with newly diagnosed nodular sclerosing Hodgkin's disease. Multiple abnormal mediastinal and hilar nodes are evident (*arrows*)

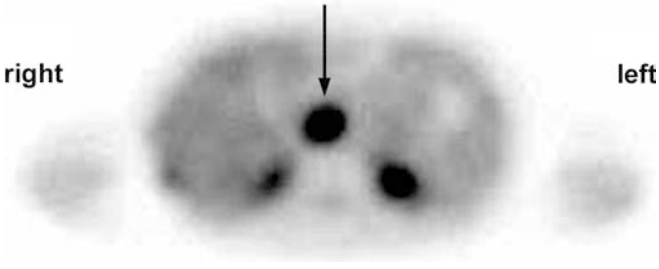

Fig. 7 Transverse image of FDG PET scan of 12-year-old girl with metastatic rhabdomyosarcoma shows intense activity in a metastasis at the liver hilum (*arrows*). Bilateral renal activity is seen inferior to the mass (*dashed arrows*)

encounter are neuroblastomas, lymphomas, and soft tissue sarcomas (Figs. 1, 6, 7) [8, 9, 10]. 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.

In 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. Tracers besides ^{18}F-FDG, may be useful in selected clinical situations. CMS coverage for pediatric oncology may be soon considered. We anticipate that the application of PET in pediatrics will continue to expand.

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. Specific issues for pediatric patients should be anticipated and addressed in order to maximize the utility of the technique in this challenging group of patients.

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