Positron emission tomography (PET) is the imaging modality of choice for multiple pediatric neurologic and oncologic indications.\textsuperscript{1,2} In current practice, fludeoxyglucose F 18 (FDG) PET is performed in conjunction with computed tomography (CT); performed together, these techniques offer both attenuation correction and precise anatomic localization. MRI paired with PET offers several potential advantages over CT, including superior soft-tissue contrast, particularly when compared to low-dose, noncontrast “attenuation correction” CT scans. MRI also allows for a wide variety of complementary sequences, such as diffusion-weighted imaging (DWI) sequences.\textsuperscript{2} Perhaps the most important advantage of PET/MRI in the pediatric population is the potential radiation dose savings, which is particularly significant in a cumulative context.

In the past, postprocessing software allowed for fusion of the anatomic detail provided by MRI with the physiologic information provided by PET. Multiple technical challenges are inherent in the implementation of an integrated PET/MRI system.\textsuperscript{2} The PET detectors must be compatible with a strong magnetic field, and the MRI hardware must account for the PET detectors and perform more involved attenuation correction than is needed for PET/CT.\textsuperscript{2}

In 2006, the first commercial PET/MRI insert was introduced (Siemens BrainPET, Erlangen, Germany). However, the insert design effectively reduced the gantry opening to 35 cm, limiting the use of this insert to neurological applications.\textsuperscript{3} Since 2010, three large imaging hardware vendors have introduced various PET/MRI implementations, including sequential and synchronous systems. Sequential systems include the Ingenuity TF (Philips, Cleveland, Ohio) and the initial trimo-dality PET/CT + MR Discovery system (GE, Chicago, Illinois). Synchronous PET/MRI systems include the Biograph mMR (Siemens, Erlangen, Germany) and the Signa PET/MR system (GE, Chicago, Illinois).

### Sequential Vs. Synchronous PET/MRI Systems

In a sequential system, the PET examination is performed first, either in the same room as the MRI examination or in a different room. The patient is then introduced into the MRI gantry, and MRI scans are performed. The physical separation of the PET and MRI scanners offers advantages in terms of technical compatibility and cost. Disadvantages include the nonsynchronous nature of the imaging data and the potential for longer scan times.\textsuperscript{4}

In a synchronous system, the PET and MRI data are obtained at the same time. A single gantry contains the PET detectors, which are located between the body and the gradient coils of the MRI system. This approach offers the advantages of truly synchronous data, a smaller scanner footprint, and the potential for shorter scan times.\textsuperscript{4} The primary disadvantage of this approach is the technical challenge of assuring mutual technical compatibility of the system’s components.

### PET/MRI Technique

In both sequential and synchronous implementations, MRI is used to generate sequences to account for attenuation correction. In the Philips implementation, a 3-segment model
is used (air, lung, soft tissue). In the Siemens implementation, a 4-segment DIXON model is used (air, lung, fat, soft tissue). These sequences are then used to create an approximation of a mu map (Figure 1).\(^2\) For both commercial PET/MRI whole body scanners, standard uptake values (SUVs) of target lesions are generally similar between PET/CT and PET/MRI.\(^5\) However, neither technique accounts for the increased attenuation of bone, which may lead to significant underestimation of activity in or adjacent to bone (up to 11.2% ± 5.4%).\(^5\) Atlas-based attenuation correction has been proposed as a solution to retrospectively add bone attenuation information to PET/MRI. However, this approach is not effective when patient anatomy deviates from normal standards (eg, because of large tumors, treatment effects, or anatomic variants).\(^10\)

**Table 1. PET/MRI Epilepsy Protocol**

<table>
<thead>
<tr>
<th>Axial T1 images substituted for fluid attenuated inversion recovery (FLAIR) images in patients &lt; 2 years old.</th>
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<tbody>
<tr>
<td>DIXON attenuation images</td>
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<tr>
<td>Coronal T2 images</td>
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<td>Axial/coronal FLAIR images</td>
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<td>Sagittal/coronal T1 images</td>
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<td>Coronal MPRage images</td>
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<td>+/- axial/coronal postcontrast images</td>
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**Table 2. PET/MRI Body/Oncology Protocol**

| DIXON attenuation images |
| Axial/coronal T2 single shot (HASTE [half fourier single-shot turbo spin-echo]) images |
| Axial T1 images |
| +/- DW images |
| +/- fat-saturated images |
| +/- postcontrast images |

*FIGURE 1. DIXON sequences. Coronal in- (A) and out-of-phase (B) MR images are used to create a virtual mu map (C) that accounts for air, lung, fat, and soft tissue (4-segment model). This virtual mu map is then used for MR-based attenuation correction.*
After attenuation correction data are obtained, additional sequences can be obtained per the local protocol. Our examinations are performed by technologists dual-certified in MRI and nuclear medicine, and thus familiar with the technical considerations of both modalities. Example protocols from our institution are included for illustration.

For seizures, we perform our routine epilepsy protocol of the head (Table 1). For oncologic indications, imaging of the neck and torso (“eyes to thighs”) or from head to toe (whole body) can be performed (Table 2). At our institution, we obtain fast T1- and T2-weighted images in the axial and coronal planes; additional images are obtained on a case-by-case basis at the discretion of the interpreting radiologist. Potential additional sequences include fat-saturated and DWI sequences.

Information obtained from postcontrast imaging using gadolinium-based compounds is thought to be largely concordant with physiological PET information. This was demonstrated in a recent pediatric review by Klenk et al that showed no significant difference in diagnostic accuracy for unenhanced and enhanced PET/MR images (with a possible exception for the evaluation of focal liver lesions). At our institution, we obtain postcontrast imaging on a
case-by-case basis at the discretion of the ordering physician in consultation with the interpreting radiologist.

Additional full diagnostic imaging of a specified body part can also be performed. Although this adds to examination time, it can be useful in the locoregional staging of certain tumors.

**Indications for PET/MRI**

Given the recent introduction of PET/MRI, much of the data regarding effectiveness are extrapolated from the PET/CT or adult literature. The three broad categories of potential indications for pediatric PET/MRI are: neurologic, oncologic, and other/inflammatory processes.

**Neurologic indications**

The main neurologic indication for pediatric PET/MRI is seizure localization. As with PET/CT, PET/MRI is presumed to be obtained in an interictal state. This can be confirmed by performing intraprocedure electroencephalography (EEG), although this is not routinely performed at our institution. In the interictal state, the seizure focus should be hypometabolic relative to the normal brain parenchyma.

A variety of seizure foci can be detected by PET/MRI. Such foci can be the result of prior ischemic insult (Figures 2 and 3), cortical malformation/dysplasia (Figures 4 and 5), or mesial temporal sclerosis (Figure 6). Other incidental findings can also be more readily appreciated by the combined information provided by PET/MRI (Figures 7 and 8).

In a cohort study of 45 predominantly pediatric patients with cortical dysplasia (age range: 5 months to 55 years), PET/MRI software coregistration data were correlated with surgical
findings. The PET/MRI coregistration was found to add value to 33% of cases with nonconcordant EEG and neuroimaging findings. PET/MRI was particularly useful in cases of subtle Palmini type I lesions initially interpreted as normal on structural imaging scans. These patients required fewer invasive tests (such as use of intracranial electrodes) for identifying the seizure focus compared to an older cohort. An additional advantage was that the technique allowed for more precise surgical planning, as the borders of the cortical lesion could be more clearly identified, reducing the risk of an incomplete resection. It is assumed that these advantages can be extrapolated to PET/MRI scans performed either sequentially or simultaneously, although data for this extrapolation are lacking.

**Oncologic indications**

Oncologic applications for PET/MRI include lymphoma/leukemia and a variety of rarer indications; specific diagnoses for the 26 pediatric oncologic clinical cases seen at our institution over the last two years are shown in Figure 9. A recent literature review of more than 2300 published PET/MRI cases demonstrated that PET/MRI is clinically feasible and performs as well as PET/CT in most cancer types. However, PET/MRI was limited in cases of lung nodule assessment.

An early trial showed that fewer FDG-negative nodules were detected by PET/MRI than by low-dose PET/CT when only attenuation correction MRI sequences were used for anatomic localization. However, there was no significant difference between modalities on a patient-based evaluation. A subsequent study by Rauscher et al found that the detection of small (<10 mm) FDG-negative lung nodules was limited with MRI despite the use of additional fast respiratory-gated, contrast-enhanced, T1-weighted sequences. Another study using respiratory-gated T1
imaging showed that MRI had higher overall sensitivity for lung nodule detection than standalone PET (70.3% vs. 61.6%; P = .002) but significantly lower sensitivity than that of the reference standard (CT). However, improved MRI sensitivity was seen in nodules > 5 mm (88.6%) and FDG-avid nodules (95.6%). Most recently, Sawicki et al showed that the performance of PET/MRI in detecting lung lesions > 10 mm is comparable to that of PET/CT. However, the overall detection rate of PET/MRI was found to be inferior to that of PET/CT because of the limited detectability of < 10 mm on MRI. The clinical relevance of this decreased sensitivity is not well-known. A recent follow-up study showed that most lung nodules missed by MRI (78.6%) were benign; however, there were many undetected metastases, with one patient being upstaged from stage I to stage IV disease on the basis of a nodule not seen on MRI. Given the apparent decreased sensitivity of PET/MRI in this regard, we obtain an additional CT scan of the chest in malignancies that commonly metastasize to the lungs (eg, sarcomas).

Research in specific oncologic applications of PET/MRI is still scarce, and many of these early trials are limited by small numbers of participants, precluding generalization of results. Additionally, the better-studied malignancies were those of the head and neck and gastrointestinal and genitourinary systems, malignancies largely seen in older adult populations. Studies of PET/MRI for pediatric oncologic indications are even scarcer. An early case series described 15 pediatric patients who underwent 21 clinical multisequence PET/MRI studies. Seven of the patients were evaluated for lymphoma; the remainder were evaluated for a variety of rarer malignancies, including neuroblastoma, primitive neuroectodermal tumor, Ewing sarcoma, soft-tissue sarcoma, acute myeloid leukemia with extramedullary manifestation, and metastatic germ cell tumor of the testis. Although this study did not compare the sensitivity or accuracy of PET/MRI and PET/CT for disease detection, the researchers demonstrated the technical feasibility of clinical PET/MRI in the pediatric setting. They also reported a potential radiation dose reduction of up to 80% with the use of PET-MRI.

Another pediatric-specific study included 18 patients undergoing 20 multisequence PET/MRI studies. Seven of the 20 studies were performed in patients with lymphoma; the remaining 13 were performed in patients with adrenocortical carcinoma, neuroblastoma, neurofibromatosis I, pancreatic carcinoma, hepatocellular carcinoma,
thyroid carcinoma, germ cell tumor of the testis, alveolar soft part sarcoma, osteosarcoma, and colon carcinoma. A total of 17 studies were performed for initial staging, and three were performed for follow-up. Similar SUVs were found for PET/MRI and PET/CT, with more significant deviation of SUV values in bone marrow. Correlation between the modalities in SUV values was also only moderate ($r = 0.32$) for lung parenchyma. On PET/CT, 62 areas of focal uptake were detected overall; 61 of these areas were also detected with PET/MRI. PET/MRI did not depict a single lung lesion with focal FDG uptake. In one patient, an artificial false-positive focus of pulmonary uptake was noted on PET/MRI.

**FIGURE 10.** Hodgkin lymphoma in a 15-year-old boy presenting with chest pain. Presenting chest x-ray (A) showed a large anterior mediastinal mass concerning for lymphoma. Initial staging was performed by PET/MRI. Coronal HASTE image (B) demonstrates large anterior mediastinal mass. Fused PET/HASTE coronal images (C and D) demonstrate hypermetabolic anterior mediastinal mass and hypermetabolic upper abdominal lymphadenopathy. Axial fused PET/HASTE images (E and F) demonstrate hypermetabolic anterior mediastinal mass and upper abdominal mesenteric lymphadenopathy. Axial fused PET/T1 image (G) demonstrates extensive lower cervical and paraspinal activity corresponding to fat signal on MR sequence and representing brown fat activity.
Additional findings were detected with PET/MRI in four patients; these findings included two cases of malignant bone marrow infiltration, one case of renal infiltration of non-Hodgkin lymphoma, and one case of a soft-tissue metastasis. Increased detection of infiltrative disease was thought to be due to conspicuous signal abnormality appreciated on MRI. On the other hand, multiple lung metastases detected by PET/CT in two patients with sarcoma were only partly seen on PET/MRI. However, no change in diagnosis resulted from this discrepancy on a per-patient basis. The authors concluded that dedicated CT of the chest may still be necessary. PET/MRI was associated with a radiation dose savings of up to 73%.

Only a few studies have assessed the use of PET/MRI in patients with lymphoma or leukemia. Figures 10-12 contain illustrative PET/MRI cases of lymphoma. In a small prospective study of 28 adult patients (mean age, 53.6 years; range, 30-85 years) with lymphoma, sequential PET/MRI was found to be equivalent to PET/CT. PET/MRI and PET/CT were equivalent in identifying all 51 FDG-avid nodal groups, whereas DWI alone identified only 32 nodal groups. PET/MRI and PET/CT were concordant in all but 1 patient (agreement of 96.4%); the disease in this patient was upstaged after PET/MRI because of bone marrow involvement not seen on CT.

In a more recent prospective trial of 25 pediatric patients with lymphoma,
FIGURE 12. A 7-year-old boy presented with a thigh mass diagnosed as Burkitt lymphoma. Initial staging by PET/CT demonstrates aggressive bulky hypermetabolic mass centered on the left femur (A). Subsequent biopsy showed Burkitt lymphoma. Post-therapy PET/MRI (B) shows a complete metabolic response. Dedicated contrast-enhanced MRI of the left femur was performed in addition to the whole-body scan. Coronal T1 (C), STIR (D), and postcontrast images (E) demonstrate interval resolution of large soft-tissue mass. Although there was persistent signal abnormality within the femur, no corresponding increased uptake can be seen on the fused PET/STIR coronal image (F), and the signal abnormality was attributed to treatment-related bone infarction. All follow-up imaging involved PET/MRI rather than whole-body CT or PET/CT.

who underwent 40 sequential PET/CT and PET/MRI examinations, the modalities demonstrated substantial agreement.\textsuperscript{17} Sensitivity for disease detection was almost identical (92\% for PET/MRI vs. 95\% for PET/CT), with a single low-avidity left hilar lymph node not well-appreciated on PET/MRI. SUV values were also strongly correlated between PET/CT and PET/MRI (\textrho > 0.72), although PET/MRI showed systematically lower SUV measurements. The authors concluded that SUV values between the two modalities should not be directly compared to assess for disease response. In this study, PET/MRI offered an average 45\% radiation dose reduction.

Even less literature is available for the use of PET/MRI in patients with nonlymphomatous indications. Figures 13-16 illustrate PET/MRI cases of rhabdomyosarcomas and neurofibromas. The few studies performed have assessed the use of PET/MRI in various rare pediatric malignancies.\textsuperscript{18} A significant disadvantage of PET/MRI in this setting is the relatively common occurrence of lung metastases. Given the previously described limitation of this modality regarding the detection of pulmonary nodules, continued dedicated evaluation of the lungs by CT is recommended. This is the practice at our institution, although it does partially negate the dose savings of PET/MRI in this setting.

Neurofibromatosis type I represents one such condition in which PET/MRI may prove useful (Figures 15, 16). Detecting the degeneration of a neurofibroma to a malignant peripheral nerve
Sheath tumor is clinically challenging. Sudden growth is suspicious, but often the physical examination is unreliable in these patients. Additionally, the number of lesions makes clinical surveillance challenging. Investigators have described some MRI imaging characteristics associated with malignant degeneration, such as intraslesional lobulation or intrinsic internal high T1 signal. FDG PET is often used in this patient population to better define suspicious lesions that warrant resection. Correlation with $^{11}$C-methionine, another marker of cell metabolism, may further increase specificity. One study used delayed imaging at 4 hours after FDG injection to define malignant lesions, with an SUV cutoff of 3.5; PET demonstrated a sensitivity of 97% and a specificity of 87%. Using the combined findings of PET and MRI could potentially further increase the specificity for this difficult clinical diagnosis.

**Inflammatory indications**

PET/MRI can also be used in patients with infectious or inflammatory conditions (Figure 17). PET/CT has a high sensitivity for diagnosing fever of unknown origin and inflammation of unknown origin. Therefore, PET/MRI could be considered as an alternative when standard diagnostic tests such as laboratory data, abdominal ultrasound,
FIGURE 15. A 17-year-old boy with neurofibromatosis on surveillance. Coronal (A) and axial (B) T2 fat-saturated images show extensive plexiform neurofibromas of the neck, abdomen, pelvis, and along the peripheral nerves. A dominant upper abdominal lesion encases the celiac/superior mesenteric axis and displaces the upper abdominal viscera. Fused coronal PET/HASTE (C) and axial T2 fat-saturated (D) images demonstrate no significant uptake that would raise concern about malignant degeneration.

FIGURE 16. An 18-year-old man with neurofibromatosis and smaller peripheral lesions. Fused coronal (A) and axial (B) PET/HASTE images demonstrate a dominant lesion lateral to the proximal fibula. It demonstrated increased uptake, with an SUV of 3.3. PET/MRI in this context may help clinicians select which lesions to biopsy/resect.
FIGURE 17. A 2-year-old girl with a history of acute lymphoid leukemia and subsequent infection. The patient developed a scalp lesion with a biopsy revealing leukemic recurrence. After excisional biopsy, the patient underwent PET/MRI (A), which demonstrated activity at the site of the resection but no distal malignant disease. While the patient was immunosuppressed from therapy, she developed a fever. CT through the chest (B) and abdomen (C) at this time demonstrated diffuse innumerable nodular pulmonary opacities, as well as punctate hypodensities throughout the liver and spleen, respectively; these lesions were suggestive of fungal infection, and blood cultures confirmed the presence of a Candida species. After antifungal treatment, follow-up PET/MRI was performed to evaluate for response before a bone marrow transplant. Fused coronal PET/HASTE images demonstrate foci of uptake in the thoracic spine and around the knees (D, E), consistent with persistent fungal disease. Fused axial PET/T2 FS images (F-H) demonstrate decreased but persistent lung and liver fungal disease. Bony uptake in the thoracic spine and around the knees (I) and ankles, also consistent with fungal disease, was better appreciated by PET/MRI than CT.
and chest radiography cannot provide a diagnosis.

Another possible application of PET/MRI is in patients with inflammatory bowel disease. In these patients, PET can highlight and quantify the inflammation, especially in parts of the bowel inaccessible to endoscopy.\(^1\)

**Conclusion**

PET/MRI is a promising new modality with potential applications in multiple pediatric conditions. This modality combines the excellent soft-tissue contrast of MRI with the complementary physiologic information supplied by PET. Its most immediate application may be for seizure imaging; studies of software coregistration have proven its value in this setting. PET/MRI may also be useful for disease staging and assessing treatment response in a variety of pediatric malignancies. However, the low sensitivity of PET/MRI in the detection of small lung nodules has not yet been fully addressed. This limitation of PET/MRI necessitates the use of additional dedicated CT scans of the chest in patients with malignancies that have a propensity to metastasize to the lungs. Larger prospective systematic trials are needed to validate the performance of PET/MRI relative to the performance of PET/CT and also to evaluate the potential usefulness of this modality for various specific pediatric indications.

**References**