Pediatric PET/MRI: Current and Future Directions

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Pediatric PET/MRI: Current and future directions

Outline:

- Principles of PET/MRI
  - Scanners
  - Protocols
  - Radiation Exposure

- Our Experience at Washington University, MIR in St. Louis

- PET/MRI in Neuroimaging
  - Principles of neuroimaging
  - FDG
  - Amino acid agents

- Whole body PET/MRI
  - FDG
  - Gallium 68
  - Na Fluoride

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Scanners

PET/MRI Types

Sequential Scanner

Simultaneous PET/MRI

PET and MRI

Radiology: Volume 267: Number 1—April 2013
Pediatric PET/MRI: Current and future directions

Why PET/MRI?

Reduced radiation exposure

High soft tissue contrast

Multimodality imaging review

Advanced MRI techniques

- MIP
- PET Fusion
- DWI

- rCBV
- FLAIR
- FDOPA
PET/MRI in Pediatric Oncology

Clinical PET/MRI in Adults versus Pediatric

**PET/MRI in Adults**
- Technically feasible
- Comparable to existing technologies (PET/CT, MRI)
- Specific indications that benefit from PET/MRI: Work in progress
- Integration into clinical workflows
- Economic viability of clinical PET/MRI

**PET/MRI in Pediatric**
- Technically feasible but limited experience
- Limited Experience: Cannot extrapolate data from adults due to: Physiologic differences in children, Tumor biology
- Specific indications that benefit from PET/MRI: Work in progress
- Integration into clinical workflows
- Economic viability of clinical PET/MRI: Work in progress

**Work in progress**
“The number of MRI sequences have to be reduced from ‘desirable to sufficient’”

‘Fast Protocol” versus “standard protocol”

Basic Brain PET-MR Protocol

<table>
<thead>
<tr>
<th>PET</th>
<th>Dixon MPRAGE FLAIR</th>
<th>10 min</th>
</tr>
</thead>
</table>

Basic Whole Body PET-MR Protocol

<table>
<thead>
<tr>
<th>PET</th>
<th>Dixon HASTE DWI</th>
<th>4-5min</th>
</tr>
</thead>
<tbody>
<tr>
<td>PET</td>
<td>Dixon HASTE DWI</td>
<td>4-5min</td>
</tr>
<tr>
<td>PET</td>
<td>Dixon HASTE DWI</td>
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<td>PET</td>
<td>Dixon HASTE DWI</td>
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</tr>
</tbody>
</table>
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Simultaneous PET/MRI Protocol

Example generic timeline for a PET/MRI oncological “whole-body” examination

<table>
<thead>
<tr>
<th>Elapsed time [min]</th>
<th>PET exam</th>
<th>MRI exam</th>
<th>MRI details</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–2</td>
<td></td>
<td>Fast view scout</td>
<td>AC (DIXON) 19 s</td>
</tr>
<tr>
<td>3–4</td>
<td></td>
<td>Planning exam</td>
<td>T2w HASTE 42 s</td>
</tr>
<tr>
<td>5–10</td>
<td>Pos1—pelvis</td>
<td>Pos1—pelvis</td>
<td>DWI 120 s</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Auto shim/breath hold</td>
<td>T2w TRIM 150 s</td>
</tr>
<tr>
<td>11–18</td>
<td>Pos2—abdomen</td>
<td>Pos2—abdomen</td>
<td></td>
</tr>
<tr>
<td>19–20</td>
<td></td>
<td>Auto shim/breath hold</td>
<td></td>
</tr>
<tr>
<td>21–26</td>
<td>Pos3—thorax</td>
<td>Pos3—thorax</td>
<td></td>
</tr>
<tr>
<td>27–28</td>
<td></td>
<td>Auto shim/breath hold</td>
<td></td>
</tr>
<tr>
<td>29–34</td>
<td>Pos4—neck</td>
<td>Pos4—neck</td>
<td></td>
</tr>
<tr>
<td>35–36</td>
<td></td>
<td>Auto shim/breath hold</td>
<td></td>
</tr>
<tr>
<td>37–42</td>
<td>Pos5—head</td>
<td>Pos5—head</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Auto shim/breath hold</td>
<td></td>
</tr>
<tr>
<td>43</td>
<td></td>
<td>Head-to-pelvis pre-contrast</td>
<td>T1 VIBE</td>
</tr>
<tr>
<td>44–47</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>48–50</td>
<td>Liver</td>
<td></td>
<td>4× T1 VIBE</td>
</tr>
<tr>
<td>51–54</td>
<td>Head-to-pelvis post-contrast</td>
<td>T1 VIBE</td>
<td></td>
</tr>
</tbody>
</table>

Example timeline of a ‘fast protocol’ for a whole-body PET/MRI for oncological indications (length equivalent to that of a whole-body PET/CT)

<table>
<thead>
<tr>
<th>PET (min:s)</th>
<th>Anatomical region</th>
<th>MRI details</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pelvis</td>
<td>AC</td>
</tr>
<tr>
<td></td>
<td></td>
<td>HASTE (axial) DWI</td>
</tr>
<tr>
<td></td>
<td>Abdomen</td>
<td>AC</td>
</tr>
<tr>
<td></td>
<td></td>
<td>HASTE (axial) DWI</td>
</tr>
<tr>
<td></td>
<td>Thorax</td>
<td>AC</td>
</tr>
<tr>
<td></td>
<td></td>
<td>HASTE (axial) DWI</td>
</tr>
<tr>
<td></td>
<td>Head/neck</td>
<td>AC</td>
</tr>
<tr>
<td></td>
<td></td>
<td>HASTE (axial) DWI + Gd-contrast</td>
</tr>
</tbody>
</table>

Combined PET/MRI: from Status Quo to Status Go. Summary Report of the Fifth International Workshop on PET/MR Imaging; February 15–19, 2016; Tübingen, Germany
Longer acquisition time allows longer PET acquisition with lower dose and may further reduce radiation exposition.
# PET/MRI in Pediatric Oncology

## Basic Principles: Why PET/MRI?

### Reduced radiation exposure

<table>
<thead>
<tr>
<th>Publication</th>
<th>Population</th>
<th>Number of patients</th>
<th>Average reduction in dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shafer et al, 2014</td>
<td>Solid tumors and lymphoma</td>
<td>18</td>
<td>73%</td>
</tr>
<tr>
<td>Ponisio et al, 2016</td>
<td>Aggressive lymphoma</td>
<td>8</td>
<td>39%</td>
</tr>
<tr>
<td>Sher et al, 2016</td>
<td>Lymphoma</td>
<td>25</td>
<td>45%</td>
</tr>
<tr>
<td>Gatidis, 2016</td>
<td>Solid tumors</td>
<td>9</td>
<td>48%</td>
</tr>
</tbody>
</table>

### Key Points:

PET/MRI provides significant reduction in radiation dose without compromising anatomic imaging by removing the CT component of PET/CT, a key component for achieving "As Low As Reasonably Achievable" (ALARA) in pediatric patients undergoing serial examinations.
2 point Dixon sequence:

- Dixon fat- and water-weighted images were used to create an attenuation map with 4 distinct tissue-classes: background/air, fat, lungs, and soft tissue.
Attenuation map (μ-map): generated based on 2-point Dixon

Dixon fat- and water-weighted images were used to create an attenuation map with 4 distinct tissue-classes:

I. Background/air
II. Fat
III. Lungs
IV. Soft tissue
Pediatric PET/MRI: Current and future directions:
Combined PET/MRI: from Status Quo to Status Go. Summary Report of the Fifth International Workshop on PET/MR Imaging

Work being done:
 Optimization of PET/MRI protocols
 To optimized acquisition protocols and software for analysis
 The development of specific guidelines for PET/MRI investigations
 Development of a suitable evidence base for the appropriate use of PET/MRI
 Added clinical value combining multiparametric PET/MRI data with multi-scale clinical, laboratory, histopathologic

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  - Amino acid agents
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Our Experience at Washington University in St. Louis

Ponisio, Maria Rosana, MD
Washington University in St. Louis
Clinical Workflow with PET/MRI at Washington University at St. Louis

1. Physician’s office orders PET/MRI
2. PET/MRI is approved and protocolled by NM and appropriate MR service
3. CPT codes provided to ordering physician’s office for precertification of SOC PET and SOC MRI
4. MRI screening and instructions to patient over the phone
5. Radiopharmaceutical is ordered
6. PET/MRI study is performed and jointly interpreted by NM and MRI services
7. Billing is performed separately for SOC PET and for SOC MR

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- **Summary**

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Washington University in St. Louis
4 year-old with refractory seizures

**EEG:** seizure arising from the right occipito-parietal

**Prior MRI:** normal

- Drug-resistant epilepsy diagnosed at age 2 years
- Seizures occur multiple times per day, lasting about 60 seconds each, and consist of vision loss followed by eye and head deviation to the right then left side

- **PET/MRI**
PET/MRI in Pediatric Neuroimaging
4 year-old with refractory seizures

**EEG:** seizure arising from the right occipito-parietal
**Prior MRI:** normal

- **Operative note**

  NAME OF OPERATION:
  1. Stereotactic biopsy of right occipital lesion.
  2. MRI guided laser ablation of right occipital seizure foci.

- **Surgical Pathology:**

  **DIAGNOSIS:**
  BRAIN, "RIGHT OCCIPITAL LESION," BIOPSY
  - FOCAL CORTICAL DYSPLASIA, TYPE II A (SEE COMMENT)

  asf/10/7/2015 10:37
PET/MRI in Pediatric Neuroimaging
4 year-old with refractory seizures

EEG: seizure arising from the right occipito-parietal
Prior MRI: normal

A-B: FDG-PET/CT focus of decreased avidity in the right occipital lobe
C: MPRAGE with contrast shows no anatomical abnormalities

A-B: Interictal FDG cortical surface projections redemonstrates focal decreased activity in the right occipital lobe and diffuse in the right temporal lobe

A-B: stereotactic biopsy of right occipital lesion with MRI guided laser ablation of right occipital seizure foci
C-D: Follow up FDG-PETMRI shows residual focus of decreased avidity in the ablation cavity with interval resolution of the temporal hypo metabolism

FOCAL CORTICAL DYSPLASIA, TYPE IIA
FOCAL CORTICAL DYSPLASIA, TYPE IIA

Teaching Points:

- **Extratemporal** epilepsy has higher incidence in *children* and most have *normal MR imaging findings*

- FDG PET/MRI can be useful for lateralization and general localization in the pediatric population

- *PET/MRI may provide crucial data that guide surgical resections of the epileptogenic zone even in the absent of anatomical abnormalities*
PET/MRI in Pediatric Neuroimaging
2-year old with refractory epilepsy for presurgical

EEG: left lateral interictal discharges
Prior MRI: no definite focal abnormality
Quantitative analysis and cortical surface projections

Unilateral Sylvian Fissure Syndrome

PET/MRI in Pediatric Neuroimaging

2-year old with refractory epilepsy for presurgical

EEG: left lateral interictal discharges
Prior MRI: no definite focal abnormality
Unilateral Sylvian Fissure Syndrome

**EEG:** left lateral interictal discharges
**Prior MRI:** no definite focal abnormality

**Teaching Points:**
- **Cortical malformations** may *not be visible or missed* on MR imaging in children less than 2 years old, because of immature myelination and poor gray matter–white matter differentiation.

- **PET/MRI plays an important role allowing identification of cortical malformation which is the major cause of seizures in children detecting subtle changes on MR images that may initially be reported as normal.**
PET/MRI in Pediatric Neuroimaging
6 year-old with refractory seizures

**EEG:** generalized seizures and infantile spasms

Past medical history is withheld
Findings ? Differential Diagnosis?
Autosomal dominant
- Prevalence is 1 in 6-12,000
- Clinical neurological manifestations: epilepsy and cognitive impairment

Brain imaging features:
- Cortical/subcortical tubers
- Subependymal nodules
- SGCAs

In Nuclear Medicine:
- F18FDG-PET, Ictal-interictal
- Tc99m-ECD/HMPAO SPECT
- [α11C-methyl-L-tryptophan PET] (currently not available at most institutions)*

Other features:
- Cardiac rhabdomyoma
- LAM
- Renal cysts and AMLs
- Ash leaf spots
- Shagreen patches, angiofibromas

Teaching Point:
- Tuberous Sclerosis/epileptic spasms
  - FDG: cortical tubers are seen as multifocal areas of hypometabolism
  - FDG: hypometabolism in cortical dysplasia (MRI:-)
  - FDG: can not distinguish between epileptogenic and nonepileptogenic tubers

SISCOM (subtraction ictal SPECT coregistered to MR imaging)
6 year-old boy with epilepsy with newly drug resistant epilepsy

**EEG:** The seizure had electrographic onset in the left frontocentral region

**MRI:** No structural abnormalities to explain this patient's seizures
Why?
Radiolabeled amino acids in neuro-oncology: \([^{18}F]FDOPA\)

- Targets system L amino acid transport
- Crosses the intact blood-brain barrier (BBB) therefore visualizes both enhancing and non-enhancing tumors
- Can visualize the entire tumor volume

**Amino acid Agents**

- \([^{18}F]FDOPA\)
- \([^{18}F]FDG\)
F-FDOPA-PET/MRI for monitoring early clinical response to bevacizumab in children with recurrent brain tumors: initial experience

Karen Gauvain et al. Neuro-Oncology Practice, in press 2017
8-year-old with a right thalamic grade IV small cell astrocytoma

This patient has had the smallest decrease with the MTV.
This patient progressed very rapidly following the start of therapy, receiving only eight weeks of treatment.
18F-FDOPA-PET/MRI was well-tolerated by all patients. All tumors were well visualized with 18F-FDOPA on the initial study with peak tumor uptake occurred approximately 10 min after injection. The maximum and mean SUVs were not predictors of response at 3 months. Changes in MTVs after therapy ranged from 23% to 98% (n=5). There is a trend towards the percent MTV change seen on the 4-week scan correlating with progression-free survival.

Conclusion:
18F-FDOPA PET/MRI was well-tolerated in pediatric patients and merits further investigation as an early predictor of response to therapy.
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- **Summary**
15-year-old boy presents with hypertensive urgency

19 year old with osteosarcoma of the left distal femur status post resection
FDG-PET/MRI has similar performance as FDG-PET/CT in pediatric oncology

PET/MRI provides significant radiation dose reduction in pediatric imaging

PET/MRI is very well suited to pediatric neuroimaging

Non-FDG PET tracers have potential to expand the use of PET and PET/MRI in pediatric populations

Several unanswered questions