Novel Radiotracers for PET-MRI and Applications beyond FDG

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Disclosure

- I have no financial interests to disclose.
- I will be discussing radiotracers that are not FDA approved.
CHOP experience

- 18F-FDG only
  - Rhabdomyosarcoma
  - Rhabdoid tumor
  - Pelvic tumors
  - Gastric and colon cancer
  - Neurofibromatosis
  - Non-Hodgkin Lymphoma
  - CPS
  - Seizure
Novel PET radiotracers

- Review novel radiotracers
- Provide examples of protocols for pediatric applications
- Provide PET/MR examples
# Radioisotopes – *positron emitters*

<table>
<thead>
<tr>
<th>Nuclide</th>
<th>Half-Life</th>
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<tbody>
<tr>
<td>Rb-82</td>
<td>75s</td>
</tr>
<tr>
<td>O-15</td>
<td>2 min</td>
</tr>
<tr>
<td>N-13</td>
<td>10 min</td>
</tr>
<tr>
<td>C-11</td>
<td>20 min</td>
</tr>
<tr>
<td>Ga-68</td>
<td>68 min</td>
</tr>
<tr>
<td>F-18</td>
<td>110 min</td>
</tr>
<tr>
<td>Cu-64</td>
<td>12.7 h</td>
</tr>
<tr>
<td>Zr-89</td>
<td>3.26 days</td>
</tr>
<tr>
<td>I-124</td>
<td>4.2 days</td>
</tr>
</tbody>
</table>
Radiotracers

- 68Ga DOTATATE /TOC/NOC
- 18F-FDOPA
- 89Zr
- I124MIBG

* FDA Approved
68Ga-DOTATATE

somatostatin analogue

- FDA approved
- Orphan application – NET evaluation
- Increasing incidence NET
- Well-differentiated (low mitotic rate)
- Functioning and nonfunctioning
- Diagnosis, extent of disease, confirmation
- Complementary to 18FDG (high mitotic rate lesions)

- FDA approved (June 1, 2016)
68Ga-DOTATATE

- **Mechanism**
  High affinity for SSTR type II

- **Normal distribution**

- **Pitfalls**
  - Uncinate process uptake
  - Accessory splenules
  - Inflammatory LN
  - Vertebral hemangioma

Hofman MS, et al. Somatostatin Receptor Imaging with 68Ga DOTATATE PET/CT: Clinical Utility, Normal Patterns, Pearls, and Pitfalls in Interpretation
Well differentiated Neuroendocrine tumors
- Neuroblastoma
- Medulloblastoma
- Supratentorial PNET
- Meningioma
- Oncogenic osteomalacia
- Sarcoidosis
68Gallium DOTATATE vs 111In Octreoscan

- Up to 5x more sensitive than Octreoscan
- Better S/N from background clearance
- Lower radiation dose
- Single visit

68GaDOTATE 2 hrs 111In-OCTREOTIDE 2 days
NET protocol

- D/C short acting octreotide 12-24 h
- D/C long acting 4-5 weeks
- Dose – European dose card, min 14 MBq

**PET/CT**
- 60 min uptake
- Whole body CT

**PET/MR**
- 60 min uptake
- Whole body MRI
- Hepatobiliary Contrast enhanced MRI with 15 min PET acquisition, DWI, Delayed
Most common pediatric indication is Congenital Hyperinsulinism

- Variable severity, genetics and histology
- Most severe forms may have KATP channel defect associated with genetic mutations in ABCC8 and KCNJ11.
- Risk for brain damage
- Resection of focal lesion is curative.
18F-DOPA

Distribution

CBD  Normal pancreas

Mechanism

18[F]DOPA

L-amino acid transporter

AADC

18 F-L-DOPA  ➔ 18F-L Dopamine

VMAT2

vesicles

DAT
Congenital Hyperinsulinism focal lesion
Clinical evaluation

- Imaging indications
  - Diazoxide unresponsive
  - Genetics not consistent with diffuse disease
  - *Surgical candidate*


### Table 3 FDOPA PET Performance For Localization (Focal versus Diffuse Signal Uptake) in 11 Core Studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Sensitivity, n (%)</th>
<th>Specificity, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Otonkoski 2006</td>
<td>5/5 (100)</td>
<td>4/4 (100)</td>
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<tr>
<td>Ribeiro 2007</td>
<td>15/15 (100)</td>
<td>8/9 (89)</td>
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<tr>
<td>Hardy 2007</td>
<td>18/24 (75)</td>
<td>26/26 (100)</td>
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<tr>
<td>Barthlen 2008</td>
<td>9/9 (100)</td>
<td>1/2 (50)</td>
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<tr>
<td>Capito 2009</td>
<td>16/16 (100)</td>
<td>0/0</td>
</tr>
<tr>
<td>Masue 2011</td>
<td>6/9 (67)</td>
<td>3/3 (100)</td>
</tr>
<tr>
<td>Zani 2011</td>
<td>14/14 (100)</td>
<td>5/5 (100)</td>
</tr>
<tr>
<td>Ismail 2012</td>
<td>3/3 (100)</td>
<td>0/0</td>
</tr>
<tr>
<td>Laje 2013</td>
<td>45/53 (85)</td>
<td>50/52 (96)</td>
</tr>
<tr>
<td>Meintjes 2013</td>
<td>5/5 (100)</td>
<td>3/3 (100)</td>
</tr>
<tr>
<td>Kuhnen 2014</td>
<td>32/32 (100)</td>
<td>0/0</td>
</tr>
<tr>
<td>Numeric total</td>
<td>168/185 (91)</td>
<td>100/104 (96)</td>
</tr>
</tbody>
</table>

Pooled sensitivity 92.5%, specificity 94%
PET/CT Protocol

PET/CT proposed protocol

- NCCT, low dose
- PET (q 10 min x 5)
- CECT, low dose

PET/MRI

- PET (q 10 min x 5)
- MRAC, Ax Dixon, Ax dynamic CE (x 3), Ax DWI

D/C diazoxide. Octreotide and glucagon can be continued if necessary.
Do not use carbidopa
Continue IV glucose infusion
Sedation/GA recommended
Alternative applications

- Pheochromocytoma
- Paraganglioma
- Neuroendocrine tumors
- Neuroblastic tumors
- Brain tumors
High diagnostic accuracy in patients with pheochromocytoma/paraganglioma
18F-DOPA

Neuroendocrine tumors

- high sensitivity in midgut neuroendocrine tumors
- lower sensitivity in foregut neuroendocrine tumors (including bronchial, gastric, duodenal and pancreatic neuroendocrine tumors).
18F-DOPA
Neuroblastic tumors

- High sensitivity/specificity
- Complementary to 123I-MIBG scintigraphy
- Uptake in neuroblastic tumors significantly correlated with AADC expression and urinary VMA excretion

18F-DOPA, NBL in BWS
I$^{124}$ MIBG – NBL
PET alternative to I$^{123}$ MIBG

- Pre-therapy/dosimetry
- Recurrence
- Problem solving with equivocal lesion
- Better evaluation of skull
- Higher radiation dose
  - $^{124}$I-MIBG (0.25 mSv/MBg)
  - $^{123}$I-MIBG (0.019 mSv/MBg)

- not FDA approved
NBL with pulmonary metastasis
$I^{123}$ vs $I^{131}$ vs $I^{124}$ MIBG

124I-MIBG

- Dosimetry option prior to therapy
- T1/2 4.2 days
Multiparametric, Multitracer Targeted therapeutics

- 18F-MFBG
- 124I MIBG
- 18F-MIBG
- 18F-FDOPA
- 18F-FDG
- 68Ga-DOTATATE
- 177 Lu-DOTATATE Therapy

- Somatostatin receptors
- Norepinephrine transporter
- Glut transporter
- L-amino acid transporter

MRI- DWI
Heterogeneity analysis
Dynamic contrast enhancement

Dynamic contrast enhancement

Genomics
Molecular Drug Imaging

89Zr Bevacizumab treatment of Diffuse Intrinsic Pontine Glioma

Targeted radiotracers in combination with MRI techniques such as DWI, hepatobiliary contrast agent, ferumoxytol, arterial spin labeling, and functional imaging will drive changes in diagnosis, surveillance and treatment and pave the way to personalized medicine.