68Ga-DOTATOC PET in Pediatric Oncology

Presenter

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Medical Imaging

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Conflict of Interest

- No conflicts to declare
Learning Objectives

- Review theory of receptor targeted imaging
- Examine radiation doses in children
- Learn which pediatric tumors express somatostatin receptors
- Discuss use of $^{68}$Ga-DOTATOC PET in diagnosis, staging, and restaging
Molecularily targeted PET using $^{68}\text{Ga}$-DOTATOC

- High receptor expression
- Native peptide sequence known
- High affinity/specificity/avidity for target
- Synthetically feasible (<50 residues)

Concept & design by M Schultz
OctreoScan SPECT and DOTATOC PET tracers

\[ ^{111}\text{In} \quad \text{DTPA-CO-NH-D-Phe-Cys} \quad \text{Phe} \quad \text{D-Trp} \quad \text{Lys} \quad \text{In-111 DTPA-Octreotide} \]

\[ ^{68}\text{Ga} \quad \text{DOTA-CO-NH-D-Phe-Cys} \quad \text{Tyr} \quad \text{D-Trp} \quad \text{Lys} \quad \text{Ga-68 DOTA-Tyr3-Octreotide} \]
68Ga-DOTA-TOC PET vs OctreoScan + CT

- 84 patients studied prospectively
  68Ga-DOTATOC, OctreoScan, high resolution CT

- Three indications for scan
  Detection of unknown primaries (n=13)
  Initial tumor staging (n=36)
  Post therapy follow up (n=35)

- TP, TN, FP, and FN
  Based on all path, imaging, and follow-up

Results for $^{68}$Ga-DOTATOC PET

- 97% sensitivity and 92% specificity
- 96% accuracy overall

Conclusion

“$^{68}$Ga-DOTATOC-PET showed a significantly higher detection rate compared with conventional somatostatin receptor scintigraphy (OctreoScan) and diagnostic CT with clinical impact in a considerable number of patients.”

## Comparison between Octreoscan SPECT & Ga-68 DOTATOC PET

<table>
<thead>
<tr>
<th></th>
<th>In-111 DTPA Octreotide SPECT</th>
<th>Ga-68 DOTATOC PET</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resolution</td>
<td>10-15 mm</td>
<td>4-6 mm</td>
</tr>
<tr>
<td>Binding Affinity * (IC50)</td>
<td>22  3.6</td>
<td>2.5  0.5 (TOC) 0.2  0.04 (TATE)</td>
</tr>
<tr>
<td>Radiation Dose to Pt</td>
<td>2.6 rem</td>
<td>0.4 rem</td>
</tr>
<tr>
<td>Radioisotope Production</td>
<td>Cyclotron</td>
<td>Generator</td>
</tr>
<tr>
<td>Convenience</td>
<td>2 day procedure; 3 visits</td>
<td>90min procedure, single visit</td>
</tr>
</tbody>
</table>

Which pediatric tumors express somatostatin receptors?

- Neuroblastoma
- Neuroendocrine tumors
- Brain tumors
  - Medulloblastoma
  - Supratentorial PNET
Somatostatin Receptors in Neuroblastoma

- mRNA expression and sst2 binding in 80-90% of neuroblastoma
- sst2 positivity is a good prognostic factor
- Octreoscan > bone scan
- No $^{68}$Ga-DOTATOC PET available for imaging neuroblastoma in US
**68**Ga-DOTATATE PET in Neuroblastoma

## Molecular classification of medulloblastoma

<table>
<thead>
<tr>
<th>Age@Dx</th>
<th>Sst2 positivity</th>
<th>Risk Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>SHH 0-3 YR; 15+ YR</td>
<td>50%</td>
<td>Standard</td>
</tr>
<tr>
<td>WNT 0-2 YR</td>
<td>60%</td>
<td>Excellent</td>
</tr>
<tr>
<td>Group 3 (n-myc?) 3-12 YR</td>
<td>75%</td>
<td>High risk</td>
</tr>
<tr>
<td>Group 4 (c-myc?) ANY AGE</td>
<td>80%</td>
<td>High risk</td>
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</tbody>
</table>
Pre-surgical diagnosis of medulloblastoma with MRI & OctreoScan

Khanna et al., Ped Blood Cancer 2008
FDG PET diagnosis of medulloblastoma

MRI-T1, gadolinium

MRI-T1, gadolinium

True + FDG PET

True – FDG PET

Gururangan et al. Neurosurg 55:1280, 2004
Pre-biopsy prediction of recurrent medulloblastoma

Khanna et al., Ped Blood Cancer 2008
Somatostatin Receptors (sst2) in Medulloblastoma

- sst2 binding in a portion of each of 4 genetic subgroups

- sst2 positivity is a good prognostic factor

- Molecularly targeted PET better than FDG PET in brain tumors
Neuroendocrine Tumors in Kids?

• More common than Ewing’s
• More common than Medulloblastoma
• Nearly as common as Neuroblastoma

Navalkele, O’Dorisio, Zamba, Lynch
Ped Blood Cancer, 2011
Small Bowel NET (primary) identified by OctreoScan in 16 yo

Anterior

Posterior
Initial Treatment based on Octreoscan and Diagnostic CT

- Surgical removal of small bowel primary

- Removal of 8 regional nodes (5+)

- Wedge resection of 2 right lobe liver lesions identified by CT/Octreoscan

- Sandostatin-LAR initiated
Restaging 16 yo with small bowel NET using $^{68}$Ga-DOTATOC PET and MRI

- C7 vertebral lesion on low resolution CT
- Lesion positive on $^{68}$Ga-DOTATOC PET
- Lesion confirmed as C7 on MRI
Restaging 16 yo with small bowel NET using $^{68}$Ga-DOTATOC PET and MRI
Restaging MRI of liver confirms 68Ga-DOTATOC PET
Restaging MRI identifies 3rd liver lesion, confirmed by Ga-DOTATOC
Restaging MRI identifies 3$^{rd}$ liver lesion, confirmed by Ga-DOTATOC
Safety and Efficacy of $^{68}\text{Ga}$-DOTATOC PET

Iowa Experience Results to Date

- Between August 1, 2012 – January 24, 2013, 81 scans performed
- No adverse events nor change in chemistries have been observed
- 19 Unknown Primary NETs identified
- Pediatric Brain Tumor Study in progress
Advantages of $^{68}$Ga-DOTATOC PET

• 3-5 fold more sensitive than Octreoscan

• Lower radiation dose than Octreoscan

• Single visit PET vs multi-visit SPECT

• Superior to FDG PET in brain

• Precisely predicts response to PRRT
Iowa Molecularly Targeted Tumor Imaging Team

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