Contrast Enhanced Ultrasound in Pediatric Oncology

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Disclosures

• I receive product support from GE Healthcare
Learning Objectives

• Biomarkers of tumor blood flow
• Benefits of contrast enhanced ultrasound (CUES) in pediatric oncology
• Limitations of CEUS in assessing tumor blood flow
Angiogenesis is critical for:

- Tumor growth
- Survival
- Metastasis
Targeted anti-angiogenic therapy

- Interfere with steps in angiogenic signaling pathways
- Inhibit binding of factors required for structural integrity of immature vessels
- Cytostatic not cytotoxic
- Conventional methods of assessing tumor response not suitable
Assessing tumor response to anti-angiogenic agents

• Crucial need for functional modalities, quantitative methods
  – Dynamic contrast enhanced CT
  – $^{15}$O-labeled water PET-CT
  – Dynamic contrast enhanced MRI
  – Dynamic contrast enhanced US (CEUS)
Benefits of Dynamic CEUS in Pediatric Oncology

- Small body habitus → better image
- Avoids exposure to ionizing radiation
- Does not require sedation
- Intravascular contrast agent
- Less expensive
- Portable
Dynamic CEUS

- Outer shell
  - Lipid
  - Protein
  - Polymer
- Inner Gas
  - Perfluorocarbon
- Remain in vascular space
- Highly reflective, very small doses (<1 mL)
- Contrast specific software allows quantitation

### Doses and reported adverse events of intravenously administered ultrasound contrast agents in a pediatric population

<table>
<thead>
<tr>
<th>Author</th>
<th>Number of children</th>
<th>Age (y)</th>
<th>Contrast agent</th>
<th>Contrast agent dose (mL)</th>
<th>Adverse events</th>
</tr>
</thead>
<tbody>
<tr>
<td>McMahon et al. 2005</td>
<td>20</td>
<td>Median: 15 y (9–18)</td>
<td>Optison</td>
<td>&lt;20 kg: 0.3 mL &gt;20 kg: 0.5 mL</td>
<td>4 mild</td>
</tr>
<tr>
<td>Bonini et al. 2007</td>
<td>40</td>
<td>Mean: 2.0 y (2 mo–10 y)</td>
<td>SonoVue</td>
<td>0.5 mL (up to three injections)</td>
<td>None</td>
</tr>
<tr>
<td>Valentino et al. 2008</td>
<td>27</td>
<td>Mean: 8.9 y (4–13 y)</td>
<td>SonoVue</td>
<td>2 × 2.4 mL</td>
<td>None</td>
</tr>
<tr>
<td>Jacob et al. 2013</td>
<td>44</td>
<td>Median: 11.5 (4–18)</td>
<td>SonoVue</td>
<td>1.2–2.4 mL</td>
<td>None</td>
</tr>
<tr>
<td>Coleman et al. 2014</td>
<td>34</td>
<td>Median: 8.7 (8 mo–20.7 y)</td>
<td>Optison</td>
<td>0.07–0.73 mL or &lt;20 kg: 0.3 mL &gt;20 kg: 0.5 mL</td>
<td>3 mild</td>
</tr>
<tr>
<td>Piskunowicz et al. 2015</td>
<td>137</td>
<td>Mean: 10.2 (0–18)</td>
<td>SonoVue</td>
<td>0.1–1.8 mL</td>
<td>1 severe</td>
</tr>
</tbody>
</table>
5 yo girl with recurrent Wilms tumor
Dynamic CEUS Tumor Imaging

- First, confirm lesion is visible on grey-scale
- Identify landmarks for follow-up CEUS
Quantitating the data

Time-intensity curve

Limitations of CEUS in Tumor Assessment

• Limits number of target lesions that can be followed
• Not all lesions will be visible with US
• Motion artifact
Conclusions

• Dynamic CEUS is a promising biomarker of tumor blood flow

• Particularly well-suited for pediatric use:
  – Avoids exposure to ionizing radiation
  – No sedation
  – Smaller body habitus