Overview

• Share St. Jude experience with contrast enhanced ultrasound (CEUS) assessing solid organs in children
• Review literature regarding CEUS assessment of solid organs
Current Applications of CEUS in Solid Organs

- Liver
- Renal
- Spleen
- Pancreas
- Adrenal
Current Applications of CEUS in Solid Organs

- Liver
- Renal
- Spleen
- Pancreas
- Adrenal
European Federation of Societies for Ultrasound in Medicine and Biology
Recommendations for Spleen CEUS

- Characterize parenchymal heterogeneity or suspected lesions
- Confirm splenic infarct (non-enhancing, wedge-shaped)
- Characterize suspected accessory spleen or splenosis (enhancement identical to spleen)
- Detect malignant lesions in oncology patients
  - Malignant wash-out on delayed imaging
  - Benign persistent enhancement on delayed imaging
- Characterize splenic abscess (rim enhancement, septations)

Piscaglia F et al. Ultraschall in Med (2012);33:33-59
3 yo with Hemolytic Anemia and Splenomegaly
CEUS of Spleen Lesion

Fibrosis, granulation tissue and infarct
### Diagnostic Performance of CEUS Solid Renal Lesions

- 118 adult subjects/118 solid renal masses
- CEUS and CECT performed preoperatively
- All lesions resected

**25 benign:** angiomyolipoma (n = 20), oncocytoma (n = 3), metanephric adenoma (n = 2)

**93 malignant:** clear cell renal cell carcinoma (RCC, n = 75), papillary RCC (n = 13), chromophobe RCC (n = 2), other (n = 3)

<table>
<thead>
<tr>
<th>Modality</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
<th>AUC</th>
</tr>
</thead>
<tbody>
<tr>
<td>CEUS</td>
<td>93.5 (85.9 – 97.4)</td>
<td>68 (46.4 – 84.3)</td>
<td>91.6 (83.6 – 96.0)</td>
<td>73.9 (51.3 – 88.9)</td>
<td>0.808 (0.725 - -.875)</td>
</tr>
<tr>
<td>CECT</td>
<td>89.2 (80.7 – 94.4)</td>
<td>76 (54.5 – 90.0)</td>
<td>93.3 (85.4 – 97.2)</td>
<td>65.5 (45.7 – 81.4)</td>
<td>0.826 (0.746-0.89)</td>
</tr>
</tbody>
</table>

Diagnostic Performance of CEUS Indeterminate Renal Masses and Cysts

- 721 adults underwent CEUS of 1018 indeterminate renal lesions
- 306 lesions pathologically confirmed
- 712 followed clinically

### Diagnostic Accuracy of CEUS Lesion-by-Lesion Analysis

<table>
<thead>
<tr>
<th>Biopsied/ Followed</th>
<th>n</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biopsied</td>
<td>306</td>
<td>100% (97.4 – 100)</td>
<td>95.2% (90.8-97.9)</td>
<td>94.6%</td>
<td>100%</td>
</tr>
<tr>
<td>≥ 60 month F/U</td>
<td>191</td>
<td>100% (97.7-100)</td>
<td>96.2% (93.5-97.9)</td>
<td>92.4%</td>
<td>100%</td>
</tr>
<tr>
<td>≥ 36 mo F/U</td>
<td>290</td>
<td>100% (97.7-100)</td>
<td>96.6% (94.4-98.1)</td>
<td>91.5%</td>
<td>100%</td>
</tr>
</tbody>
</table>

Barr RG et al. Radiol (2014) 271(1);133-142
12 yo girl with Langerhan Cell Histiocytosis

T1W C-

T1W C+

STIR

Grayscale Ultrasound

Transverse

Longitudinal

CEUS
Indeterminate Renal Lesion

1 sec post injection
7 sec post injection
1 min post injection

Focal Liver Lesions (FLL)

• Commonly encountered “incidentalomas”
  – 7.2 – 33% on computed tomography
  – 10.2 – 34.5% on MRI
  – 2.3 – 6.2% on screening ultrasound
  – 20 – 50% (benign lesions) on autopsy

• Probability FLL is benign
  – Healthy person: > 95%
  – History of malignancy/chronic liver disease: 65% if lesion < 1.5 cm

Follow-up imaging 273 solid tumor patients

- 17% (46/273) developed new liver lesion
  - 30% (14/46) focal nodular hyperplasia
    - 86% (12/44) had multiple lesions
  - 15% (7/46) metastases
    - 57% (4/7) had multiple lesions
  - 54% (24/46) had other lesions

Smith et al. AJR (2012); 199:186-191
Management of FLLs in Pediatric Oncology

• Leads to further investigations
  – Detailed medical history
  – Review of prior imaging
  – Size, number, morphology of FLLs

• Often requires additional imaging
• Adds cost, time, anxiety
• Work-up should be:
  – Prompt
  – Effective
  – Non-invasive
  – Preferably avoids radiation and sedation
CEUS of Focal Liver Lesions

Figure 8. Algorithm used to diagnose a liver mass.

† DN: dysplastic nodule
‡ RN: regenerative nodule

CEUS of Focal Liver Lesions

Figure 5. Algorithm used to diagnose a liver mass.
## CEUS vs CECT for Assessment of Focal Liver Lesions

<table>
<thead>
<tr>
<th></th>
<th>Quaia\textsuperscript{1}</th>
<th>Seitz\textsuperscript{2} (DEGUM)</th>
<th>Trillaud\textsuperscript{3}</th>
</tr>
</thead>
<tbody>
<tr>
<td># cases</td>
<td>55 (indeterminate on CT)</td>
<td>267</td>
<td>123</td>
</tr>
<tr>
<td># Malignant</td>
<td>22</td>
<td>131</td>
<td>55</td>
</tr>
<tr>
<td># Benign</td>
<td>33</td>
<td>136</td>
<td>68</td>
</tr>
<tr>
<td>Sensitivity CEUS</td>
<td>89 (accuracy)</td>
<td>95.3</td>
<td>95.5</td>
</tr>
<tr>
<td>Sensitivity CECT</td>
<td>49 (accuracy)</td>
<td>90.6</td>
<td>72.2</td>
</tr>
<tr>
<td>Specificity CEUS</td>
<td>83.7</td>
<td></td>
<td>75</td>
</tr>
<tr>
<td>Specificity CECT</td>
<td>81.6</td>
<td></td>
<td>37.5</td>
</tr>
<tr>
<td>Year</td>
<td>2014</td>
<td>2009</td>
<td>2009</td>
</tr>
</tbody>
</table>


Slide courtesy Dr. Richard Barr
## CEUS vs CEMRI for Assessment of Focal Liver Lesions

<table>
<thead>
<tr>
<th></th>
<th>Seitz¹ (DEGUM)</th>
<th>Trillaud²</th>
<th>D’Onofrio³</th>
</tr>
</thead>
<tbody>
<tr>
<td># cases</td>
<td>269 (82)</td>
<td>123</td>
<td>147</td>
</tr>
<tr>
<td># Malignant</td>
<td>55</td>
<td>55</td>
<td>105</td>
</tr>
<tr>
<td># Benign</td>
<td>27</td>
<td>68</td>
<td>42</td>
</tr>
<tr>
<td>Sensitivity CEUS</td>
<td>95.8 (90.9)</td>
<td>95.5</td>
<td>90</td>
</tr>
<tr>
<td>Sensitivity CEMRI</td>
<td>(81.8)</td>
<td>81.8</td>
<td>91</td>
</tr>
<tr>
<td>Specificity CEUS</td>
<td>83.1 (66.7)</td>
<td>75</td>
<td>93</td>
</tr>
<tr>
<td>Specificity CEMRI</td>
<td>(63.0)</td>
<td>42.9</td>
<td>93</td>
</tr>
<tr>
<td>Year</td>
<td>2009</td>
<td>2009</td>
<td>2014</td>
</tr>
</tbody>
</table>


Slide courtesy Dr. Richard Barr.
13 yo boy, Treated for Stage 4 Neuroblastoma.
FLL Found on Imaging Obtained for Bowel Obstruction
Arterial Phase
Hyper-Enhancing

Centrifugal enhancement
Portal Venous Phase
Hyper-Enhancing

“Lightbulb” appearance
Portal vein

Delayed Phase
Iso-Enhancing
Delayed Phase
Iso-Enhancing

Focal Nodular Hyperplasia
12 yo girl
Newly Diagnosed Wilms Tumor
Gray-Scale
Early Arterial Phase
Iso-Enhancing
Late-Arterial Phase
Washout
Portal-Venous Phase
Washout
Portal-Venous Phase
Washout

Liver Metastasis
Primary Pediatric Liver Tumors

- Infantile hemangioma
- Hepatoblastoma
- Fibrolamellar hepatocellular carcinoma
Primary Pediatric Liver Tumors

- Infantile hemangioma
- Hepatoblastoma
- Fibrolamellar hepatocellular carcinoma

Overlapping age groups
Both may have elevated AFP
3 mo with Liver Mass Found on US for Pyloric Stenosis
Arterial Phase
Peripheral Hyper-Enhancement
Portal Venous Phase
Central Filling/Iso-Enhancing
Delayed Phase
Central Filling/Hyper-Enhancing
Delayed Phase
Central Filling/Hyper-Enhancing

Infantile Hemangioma
9 mo Boy with Beckwith-Weidemann Syndrome

- Left supra-renal masses found on surveillance ultrasound
Follow-up MRI

- 4 liver lesions in addition to suprarenal masses
- Slightly elevated AFP (813 ng/mL)
CEUS of Largest Liver Lesion

Early arterial phase: Hyperenhancing
Portal-venous Phase: Isoenhancing
Biopsy Proven
Hepatoblastoma

Early delayed phase (51 sec): Washout
Conclusions

• CEUS is:
  – Safe and well tolerated in children
  – Portable
  – Less expensive than CT/MRI
  – Provides real-time imaging and immediate results
  – Avoids sedation and radiation

• Useful for assessment of:
  – Focal liver lesions
  – Primary liver tumors
  – Renal cysts and masses
  – Other solid organs (spleen, brain)
Thank-you!