Contrast enhanced voiding urosonography (ceVUS): Vesicoureteral Reflux

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Disclosures

• Lumason 12/2016 FDA approval for ceVUS

• All other contrast agents off label for ceVUS
ceVUS

What it is
What to do
What *not* to do
What it looks like
What is ceVUS?

Similar to VCUG

Use ultrasound & ultrasound contrast agents
What is ultrasound contrast?
What is ultrasound contrast?

Encapsulated gas filled MICROBUBBLES

US contrast ≠ CT contrast
US contrast ≠ MRI contrast

IV Metabolism

Gas: exhaled through lungs within 10 min
Shell: metabolized in the liver

Not nephrotoxic
Ultrasound Contrast

- **Lumason®** [Bracco, Italy]
  - **Gas:** sulphur hexafluoride
  - **Shell:** phospholipid
  - Bubble size: 1.3-2.5 um
  - Concentration: $1.5-5.6 \times 10^8$/mL
  - Dose 0.5-1% bladder filling volume

- **Optison®** [GE Healthcare, USA]
  - **Gas:** perflutren
  - **Shell:** albumin
  - Bubble size: 3-4.5 um
  - Concentration: $5-8 \times 10^8$/mL
  - Dose 0.1-0.5% bladder filling volume

*RBC 6-8 um*
Ultrasound Contrast

- **Lumason®** [Bracco, Italy]
  - *FDA approved*
  - IV CEUS Liver pediatrics 4/2016
  - ceVUS pediatric 12/2016
  - Only agent pediatric approval

- **Optison®** [GE Healthcare, USA]
  - *FDA approved*
  - Adult echo
How is it done?

- Bladder catheterization
  - Sterile technique
  - Empty bladder
- Contrast administration
  - Infusion
  - Injection
- Dedicated US settings
Contrast administration

1. Connect 180° port to bladder catheter

2. Connect syringe to 90° port

3. Connect syringe to 90° port

4. Connect 180° port to bladder catheter
Contrast administration

Infusion: 0.2% solution

Injection: 0.1 mL contrast
50 mL saline
Contrast US Modality

Low mechanical index [MI]

Other technical features:
- Color overlay
- Background subtraction
- Dual display
- Optimized for specific contrast
Kidneys

Supine, prone or both

Sitting, standing

Alternating scan right/left

Dual display useful
Pitfall: Dual Display

Decreased gray scale resolution
Pitfall: Background Subtraction

- Excessive
- Incomplete
Bladder

Monitor bladder filling

Injection small bolus of NaCl

Optimal bladder filling:

* Homogenous distribution
* No acoustic shadowing
* Visualize bladder base
* Visualize retrovesicular space
Pitfall: Inadequate bladder contrast distribution

Normal saline container: Glass
Injection angle 90° and ↑speed
Normal saline flush missing
Low or high US contrast agent dose
US scan parameters incorrect [↑MI]
US contrast vial usage duration
Preceding study with intravenous x-ray, CT or MR contrast agent
Safety: Ultrasound Contrast

Symptoms related to catheterization

<table>
<thead>
<tr>
<th>Patients</th>
<th>VCUG (n = 100)</th>
<th>RNC (n = 100)</th>
<th>DRS (n = 28)</th>
<th>Total (n = 228)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Boys and girls</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Symptoms</td>
<td>32 (32.0)</td>
<td>37 (37.0)</td>
<td>11 (39)</td>
<td>80 (35.1)</td>
</tr>
<tr>
<td>No symptoms</td>
<td>68 (68.0)</td>
<td>63 (63.0)</td>
<td>17 (61)</td>
<td>148 (64.9)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Symptom or Duration</th>
<th>VCUG (n = 100)</th>
<th>RNC (n = 100)</th>
<th>DRS (n = 28)</th>
<th>Total (n = 228)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dysuria</td>
<td>29 (29.0)</td>
<td>35 (35.0)</td>
<td>11 (39)</td>
<td>75 (32.9)</td>
</tr>
<tr>
<td>Wetting</td>
<td>1 (1.0)</td>
<td>5 (5.0)</td>
<td>1 (4)</td>
<td>7 (3.1)</td>
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<tr>
<td>Gross hematuria</td>
<td>5 (5.0)</td>
<td>3 (3.0)</td>
<td>1 (4)</td>
<td>9 (3.9)</td>
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<tr>
<td>Fever*</td>
<td>2 (2.0)</td>
<td>1 (1.0)</td>
<td>0</td>
<td>3 (1.3)</td>
</tr>
<tr>
<td>Total</td>
<td>32 (32.0)</td>
<td>37 (37.0)</td>
<td>11 (39)</td>
<td>80 (35.1)</td>
</tr>
</tbody>
</table>
# Safety: Ultrasound Contrast

<table>
<thead>
<tr>
<th>Studies</th>
<th>n</th>
<th>n</th>
<th>%</th>
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<tbody>
<tr>
<td><strong>Levovist®</strong></td>
<td>1062</td>
<td>17</td>
<td>1.6</td>
</tr>
<tr>
<td><strong>SonoVue®</strong></td>
<td>1889</td>
<td>37</td>
<td>2</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>2951</td>
<td>54</td>
<td>1.8</td>
</tr>
<tr>
<td>European survey</td>
<td>4131</td>
<td>0</td>
<td>0</td>
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<tr>
<td><strong>Grand total</strong></td>
<td>7082</td>
<td>54</td>
<td>0.8</td>
</tr>
</tbody>
</table>

### Adverse Events

- **26** Dysuria
- **15** Transient macrohematuria
- **3** Abdominal discomfort/pain
- **2** Anxiety/crying
- **2** Urinary retention
- **1** Frequency
- **1** Blood/mucous discharge
- **1** Perineal irritation
- **1** Urethral pain
- **1** Urinary tract infection
- **1** Vomiting
Safety: Ultrasound Contrast

- Prospective study
- Primary objective safety evaluation
- ONLY ceVUS with SonoVue®
- Comprehensive evaluation
- Follow-up after a week

- NO serious adverse events
- 37 (3.7%) patients minor events
- Self-limited adverse events
- Catheterization likely cause
- High safety profile!
ceVUS Reflux Grading
ceVUS vs VCUG Challenges

• VUR intermittent
• ceVUS continuous scanning, one kidney at a time
• US depicts anatomy and urinary tract dilation
• Easier to see UCA vs. x-ray contrast in dilated system
• ceVUS distal ureter
• Learning curve
Reflux Detection: first generation UCA

• Meta analysis 18 studies
• 1338 patients, 2893 kidney-ureter units
• 886 with reflux
• VUR
  • Only in ceVUS 19%
  • Only in VCUG 10%

ceVUS + 9%

Darge 2008 Pediatr Radiol 38:54-63
<table>
<thead>
<tr>
<th>V C U G</th>
<th>I</th>
<th>II</th>
<th>III</th>
<th>IV</th>
<th>V</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>17</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>II</td>
<td>28</td>
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<td>III</td>
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<tr>
<td>IV</td>
<td>0</td>
<td>1</td>
<td>3</td>
<td>44</td>
<td>1</td>
</tr>
<tr>
<td>V</td>
<td>0</td>
<td>0</td>
<td>3</td>
<td>2</td>
<td>35</td>
</tr>
</tbody>
</table>

**71.2% Grade I VCUG > Grade II ceVUS**

Darge K 2008 Pediatr Radiol 38:54-63
Reflux Detection: second generation UCA

- Papadopoulou 2009
  161 VUR/463 KUU
  ceVUS + 47%

- Kis 2010
  140 VUR/366 KUU
  ceVUS + 6.3%

- Wong 2014
  14 VUR/62 KUU
  ceVUS + 64%

Papadopoulou 2009 Pediatr Radiol 39:239-244
Kis 2010 Pediatr Nephrol 25:2289-2293
Wong 2014 Eur J Pediatric 173:1095-1101
### “Missed” Reflux

<table>
<thead>
<tr>
<th></th>
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<th>II</th>
<th>III</th>
<th>IV</th>
<th>V</th>
</tr>
</thead>
<tbody>
<tr>
<td>VCUG</td>
<td>3</td>
<td>69</td>
<td>21</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>(99)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ceVUS</td>
<td>8</td>
<td>5</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>(15)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Papadopoulou 2009 Pediatr Radiol 39:239-244
Kis 2010 Pediatr Nephrol 25:2289-2293
Wong 2014 Eur J Pediatric 173:1095-1101
ceVUS Urethral Imaging

9 yo girl
Transperineal

1 mo boy

1 mo boy
Suprapubic
4 month old girl, fever

Urine culture + E. coli

Imaging
  Renal bladder US
  Duplex left kidney
  VCUG
  Left grade 3 reflux

Antibiotic prophylaxis
18 months old follow up US

Imaging

Renal bladder US

Duplex left kidney

Urinary tract dilation

Left sag

Left trv
Bladder
Left kidney supine
Left kidney prone
VCUG at 4 months old

ceVUS at 24 months old
24 month old girl

Imaging

Renal bladder US
Duplex left kidney
VCUG/ceVUS
Left grade 3 reflux

Antibiotic prophylaxis

Follow up with ceVUS
Summary

What ceVUS is
How to do it
Pitfalls
Case example