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Disclosures

• Investigator-initiated research support from:
  – Siemens US
  – Canon (Toshiba) US
Learning Objectives

1. Understand basic physics behind ultrasound (US) shear wave elastography (SWE)
2. Appreciate difference between “point” & “2D” US SWE & know vendor-specific approaches
3. Understand how to obtain reliable, high-quality US SWE data from liver
4. Learn how to report results based on SRU consensus statement
5. Understand clinical applications/limitations
Liver Fibrosis & Biopsy

- “Gold” standard for fibrosis detection/measurement
  - Invasive, high cost, sampling error
- Staged semi-quantitatively (e.g., Metavir, Ishak, NASH CRN)
  - Imperfect inter-pathologist agreement

Unmet Need

• Noninvasive, rapid, well-tolerated method for 1) detecting, 2) measuring, and 3) following liver fibrosis
Elasticity Imaging

• Analogous to palpation
• Unique form of image contrast at US & MRI
• Indirectly detects/measures liver fibrosis
• 2 basic approaches:
  – Strain-based
  – Shear wave-based
US Strain Elastography

• Assesses tissue hardness based on deformation with stress

• Soft objects deform; hard objects translate

• Semi-quantitative
  – Normalize to adjacent tissue

Courtesy of Jonathan Rubin, MD, PhD
University of Michigan, Department of Radiology
Present – Imaging of Liver Fibrosis

Shear Wave Elastography (SWE)

• Based on measurement of shear wave speed (SWS) propagation through tissue

• SWS is related to Young’s modulus, $E$ (kPa)
  – Defines relationship between stress (force) and strain (deformation) for material

• Wide dynamic range!

$$SWS \ (m/s) \approx \sqrt{\frac{E}{3\rho}}$$
Acoustic Radiation Force Impulse (AKA: “ARFI”, push pulse, acoustic burst)
“Point” SWE (<1 ml ROI)

1. Focused push pulse
2. Shear waves generated
3. Tracking beams
detect shear wave peak
4. Linear regression performed
5. Confidence interval check
6. Shear velocity computed
“2D” SWE (>20 ml ROI)

Source: Canon (Toshiba) Website
Shear Wave Imaging – US vs. MRI

- **US advantages:**
  - Cost (infrastructure & exam)
  - Length of exam
  - No sedation/GA
  - Portable
  - Better spatial resolution

- **MRI advantages:**
  - Imaging depth/more global look at tissue
  - Fat quantification
  - Reliability?
DIFFERENT VENDOR APPROACHES
(ALPHABETICAL ORDER 😊)
What Images Look Like:
GE (Shear Wave Elastography)

Elastogram (color map of liver shear wave speed)
What Images Look Like:
Philips (ElastPQ, ElastQ)

Elastogram (color map of liver shear wave speed)

5.09 ± 0.82 kPa
What Images Look Like: Siemens (VTQ, VTIQ)

Virtual Touch Quantification (VTQ)

Virtual Touch IQ (VTIQ)

Elastogram (color map of liver shear wave speed)
What Images Look Like:
Supersonic Imagine (ShearWave Elastography)

Elastogram
(color map of liver shear wave speed)
What Images Look Like:
Toshiba

Elastogram (color map of liver shear wave speed)

Shear wave propagation map (used to judge quality/ID artifacts)
KEYS TO TECHNICAL SUCCESS/ ACQUISITION OF HIGH-QUALITY DATA
1. Image supine or slight left lateral decubitus, arm up
2. Orient transducer parallel to liver capsule
3. Image ≥1-2 cm deep to liver capsule
4. Observe near-complete elastogram “fill-in”
   - No? – throw-out and repeat
   - Respiratory motion, “bad window”, imaging over vessel or rib shadow?
Bad ROI Placement (Reject)

- ROI/measurement too close to liver capsule
  - Orange area spuriously increases SWS measurement
  - Artifact from shear wave reverberation/“boundary effect”
Bad Tracking/Ineffective Push Pulse (Reject)
SRU CONSENSUS STATEMENT/ REPORTING

Elastography Assessment of Liver Fibrosis: Society of Radiologists in Ultrasound Consensus Conference Statement¹
SRU Consensus

• Acquire 10 SWS measurements from **SAME LOCATION** in right lobe, intercostal approach
  – **NPO** (4-6 hours)
  – Suspend respiration (shallow breathing)

• Present **MEDIAN** in m/s

• Present data interquartile range (IQR) / median
  – <0.3 = reliable/“good quality” data

• Report US system, transducer, and positioning

Barr et al. *Radiology* 2015; 276:845-861
[# of attempts] shear wave speed measurements were acquired using a right intercostal approach, with a median of [Median] m/s (range, [Minimum] – [Maximum] m/s). The IQR/median value is [IQR/median]. Measurements were obtained using a [Transducer] transducer.

IMPRESSION:

1. Impressions
2. Median liver shear wave speed = [Median speed] m/s.

Based on a recently published consensus document (Barr et al. Radiology 2015), liver shear wave speeds (in adult patients with Hepatitis C) <1.5 m/sec suggest no clinically significant fibrosis (<=F2). Measurements >2.2 m/s suggests significant fibrosis (F3/F4).

Note, ultrasound shear wave speed measurements may also be affected by the presence of hepatic congestion, steatosis, and inflammation. Shear wave speed measurements should be interpreted in conjunction with other available clinical data, and they should not be considered interchangeable with MRI-derived stiffness measurements at this time.
CLINICAL APPLICATIONS & LIMITATIONS
Existing Peds Literature

• Discrimination of no/minimal from advanced fibrosis (F0/F1 vs. F3/F4)

• Discrimination of biliary atresia from other causes of neonatal cholestasis
  – May predict need for liver transplantation post-Kasai

• Assessment of progression of chronic liver disease over time?
  – Post-Kasai, post OLT, PSC, autoimmune hepatitis, Fontan-associated liver disease, TPN liver disease, others?
  – *Perhaps most important role (need more research)*
Liver Fibrosis

- N=126 children
  - 50 controls / 76 chronic liver disease

- Supersonic SWE

- AUC F0 vs. ≥F2 = 0.96
  - Cut-off value = 1.85 m/s
    - No healthy control had SWS >1.85 m/s

- **Conclusions:**
  - SWE identifies liver fibrosis, although exact staging is difficult

Tutar et al. *JPGN* 2014; 750-755
Liver Fibrosis

Tutar et al. JPN 2014; 750-755
Systematic Review

• Performed to assess US SWE ability to distinguish healthy vs. fibrotic liver in children
  – MEDLINE, EMBASE, Cochrane Library and Web of Science

• 27 articles included
  – 12 with liver biopsy

• CONCLUSIONS:
  – Able to diagnose cirrhosis and distinguish healthy from fibrotic liver
  – Low accuracy when attempting to distinguish between grades
  – No fibrosis-specific cut-offs identified

Andersen et al. JPGN 2016; 63:389-399
Discriminating Fibrosis Grade

Figure 7: Graph of shear wave stiffness measurements for METAVIR stages based on the meta-analysis (38) in which median and IQR data were used.

Barr et al. Radiology 2015; 276:845-861
MRE – Meta-Analysis

# US SWE Variability

## Table 1

### Sources of Variability in Elastography

<table>
<thead>
<tr>
<th>Category</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Origin of the underlying disease</td>
<td>Hepatitis B, hepatitis C</td>
</tr>
<tr>
<td>Patient comorbidities</td>
<td>Acute chronic liver disease (44), congestive heart failure (45), extrahepatic cholestasis (46)</td>
</tr>
<tr>
<td>Modality being used</td>
<td>MR imaging, transient elastography (TE), shear wave elastography (SWE), point quantification SWE (pSWE)</td>
</tr>
<tr>
<td>System-specific factors</td>
<td>Depends on the manufacturer</td>
</tr>
<tr>
<td>Machine-specific factors</td>
<td>Machines and probe variability from individual manufacturers</td>
</tr>
<tr>
<td>Measurement variability</td>
<td>Location in the liver, intra- and interobserver variability</td>
</tr>
<tr>
<td>Patient physical factors</td>
<td>Obesity, ascites</td>
</tr>
<tr>
<td>Indication for study</td>
<td>Thresholds will be different, depending on the need for the study (fibrosis detection, staging, or follow-up) to optimize characterization of certain populations</td>
</tr>
<tr>
<td>Disease prevalence</td>
<td>Will affect measures of accuracy, positive predictive value, and negative predictive value</td>
</tr>
<tr>
<td>Patient sex</td>
<td>Male vs female (47)</td>
</tr>
<tr>
<td>Postprandial state</td>
<td>Fasting vs nonfasting (48,49)</td>
</tr>
<tr>
<td>Breath-hold technique</td>
<td>Valsalva maneuver can increase stiffness values (50)</td>
</tr>
</tbody>
</table>

Barr et al. *Radiology* 2015; 276:845-861
Inter-/Intra-System Agreement

Hall et al. *IEEE IUS* 2013; 397-400

Pediatric Cut-Off Values

- Established for certain vendors (Siemens, SSI), but not for others
- Exact values likely to vary by vendor, point vs. 2D methodology, and disease
- “Rules of thumb”:
  - <1.5 m/s, likely normal or very mild liver disease
  - >2.0-2.2 m/s, considerable liver stiffening (fibrosis vs. other)
- Change over time likely to be equally important
Neonatal Cholestasis

Biliary Atresia

Alagille Syndrome
A Study…

• 20 with neonatal cholestasis
  – 10 with BA

• BA vs. no BA:
  – $2.2 \pm 0.4 \text{ m/s vs. } 1.7 \pm 0.6 \text{ m/s}$
    $(p=0.049)$

• Using cut-off 2 m/s, 3 FP and 3 FN for BA
  – Sensitivity = 70%
  – Specificity = 70%

Hanquinet et al. *Pediatr Radiol* 2015; 45:1489-1495
Another Study…

- 38 BA, 17 hepatitis, and 31 healthy babies

Take Away: Need More Research

- Sensitivity = 97.4%, specificity = 100%

DO NON-FIBROTIC PROCESSES CAUSE LIVER STIFFENING?
The Fontan Operation

Stage 2

Acute Hepatic Congestion

Stage 3
Pre/Post Stage 3 Fontan

DiPaola et al. *Eur Radiol* 2017; 27; 2434-2442
Pre/Post Stage 3 Fontan

Take-Away: Other Processes Can Cause Liver Stiffening
Adult Fontan Patient... a Dilemma
Final Word of Caution...

Avoid Regenerative Tissue
Conclusion

• US SWE is feasible in children of all ages
• Stiffness changes in response to variety of histologic changes
  – Fibrosis, inflammation, congestion
• Need continued research
  1. Normative data
  2. Correlation with meaningful outcomes
  3. New applications