Elastography of liver and thyroid

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Why tissue stiffness?

- Palpation – practice of feeling the stiffness of tissues
Principle of palpation

- Focal mass
- Soft mass is deformed by pressure from finger
- Hard mass is not deformed by pressure from finger and is palpable.

- Stress is
  - higher on fingers overlying a superficial "hard" lesion
  - lower on receptors of fingers overlying softer surrounding tissues

Hall TJ. Beyond the basics: elasticity imaging with US. Radiographics. 2003;23:1657Y1671
Tissue Stiffness

- Limitation of palpation:
  - Subjective
  - Deeper lesions
  - Small lesions
  - Qualitative not quantitative
Ultrasound Elastography

- US elastography
  - Strain Elastography
  - Shear wave Elastography

- Usually quantitative
- Operator dependent
- Insufficient for diffuse diseases

- Quantitative
- Higher repeatability
Strain Elastography

Technique:
Strain elastography detects local deformation (strain) under slight pressure.
Pressure performed by hand held US transducer or physiologic movements (carotid pulsation)
Elastogram – color coded image superimposed on Bmode image displayed.
Strain Elastography

- 2 kinds of elasticity assessments:
  - Visual scoring of colors - Color based elastograms – 4-5 scale scoring systems
Strain Elastography in Thyroid

- 2 kinds of elasticity assessments:
  - Quantitative assessment
    - Strain ratio calculation – 2 ROIs – one over target region and 2nd over adjacent reference region.
  - Increasing strain ratio – suggests increasing likelihood of malignancy
Shear wave Elastography

- New technique
- Shear wave displaces tissues
- Ultrafast scanner (frame rate - 20kHz) – receives information
- Map of shear-wave time-of-arrival can be created
- Final image of shear-wave speed
Step 1: **Volumetric force creation using ultrasound beam focus**

Step 2: **Ultra fast imaging of the displacement generated by ultrasounds**

Step 3: **Image acquisition and processing**

- Ultrasonic beam
- US images
- 1D Cross-correlation
- $U_z(x,t)$
## Shear wave Elastography

<table>
<thead>
<tr>
<th>pSWE</th>
<th>2D SWE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Short duration acoustic radiation force (less than 1ms)</td>
<td>Color Coded display over a B-mode</td>
</tr>
<tr>
<td>Conventional Bmode imaging</td>
<td>Larger FOV, one or more ROI</td>
</tr>
<tr>
<td>Generates localized displacements in ROI box 1 x 0.5cm</td>
<td>Qualitative or quantitative</td>
</tr>
<tr>
<td>Quantitative</td>
<td></td>
</tr>
<tr>
<td>Wave velocity values m/a</td>
<td>m/s or kPa</td>
</tr>
</tbody>
</table>
PQ – 1.35 m/s
EQI – 1.34 m/s
Diffuse liver disease

- Cirrhosis – 2 distinct clinical stages
  - Not easily diagnosed clinically

- Chronic liver disease
  - Median survival >12 years

- Compensated cirrhosis
  - Variceal hemorrhage
  - Ascites
  - Encephalopathy
  - Jaundice
  - Median survival - 2 years

- Decompensated cirrhosis
  - Death

D’Amico et al J Hepatol 2006
D’Amico, Garcia-Tsao. J Hepatol 2006
Why is staging important in management?

- Prognostication
  - Assessment of urgency for Rx
- Surveillance (e.g. HCC, varices) in cirrhotic patients
- Baseline for monitoring of Rx efficacy
- Tailoring of treatment algorithm (e.g. prolonged Rx duration in HCV cirrhosis)
- Drug reimbursement
No or minimal fibrosis

- No immediate treatment needed. F/U based on clinical factors.

Mild to moderate fibrosis

- Treatment and F/U based on other clinical factors.

Severe fibrosis or cirrhosis

- Screening for HCC
  - Compensated
    - NL HVPG
  - Decompensated
    - ABNL HVPG
Increasing liver stiffness is associated with increasing fibrosis stages.

<table>
<thead>
<tr>
<th>F0</th>
<th>F1</th>
<th>F2</th>
<th>F3</th>
<th>F4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>Portal Fibrosis</td>
<td>Peri-portal fibrosis</td>
<td>Septal fibrosis portal-portal “bridging”</td>
<td>Cirrhosis</td>
</tr>
</tbody>
</table>

Normal portal pressure → Increased portal pressure
Liver Fibrosis Staging systems

- Periportal fibrosis
- Bridging fibrosis
- Nodularity

Diffuse liver disease

- Liver fibrosis – need accurate measurement
  - Plan therapy
  - Assess response to therapy
  - Assess risk of malignancy
Liver Elastography

- Liver biopsy – “gold standard”
  - Invasive
  - Potential complications – severe
  - Sampling error – specimen represents 1/50000\textsuperscript{th} of liver volume
  - Inter and Intraobserver variability at microscopic evaluation

- Elastography
  - Noninvasive
  - No complications
  - Larger volume of liver sampled
Technique of elastography - Liver

- Supine position with right arm in maximal extension
- Transducer in intercostal space
- Right lobe of the liver – without large vessels or artifacts
- ROI placed minimum of 1-2 cm and maximum 6 cm from liver capsule.
- Transient breath-hold in a neutral breathing position
- Fasting
- 10-20 minutes of rest
Place the Circle Caliper in areas of the ROI that display the majority of one COLOR.
Place the Circle Caliper in areas of the ROI that display the majority of one COLOR.
Liver Elastography

- Take measurements in same location or various locations
- Liver fibrosis – heterogeneous process
- Best accuracy – measurements from multiple locations
How many measurements?

- Literature suggests 10
  - Delete obvious bad numbers
  - Delete highest and lowest number
- SRU guidelines recommend 10 as well
- Make sure that the IQR/median ratio is <30% or 0.3
  - Monitor sonographer quality
  - Improvement with experience
SRU consensus suggested thresholds in HCV

<table>
<thead>
<tr>
<th>Device</th>
<th>No Clinically Significant Fibrosis: METAVIR Stage ≤ F2, Unlikely to Need Follow-up</th>
<th>Advanced Fibrosis and/or Cirrhosis: METAVIR Stage of F4 and Some Stages of F3—Clinically Significant Fibrosis</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>TE FibroScan (Echosens)</td>
<td>&lt;7 kPa (1.5 m/sec)</td>
<td>&gt;15 kPa (2.2 m/sec)</td>
<td>42,91,92,95,64,115–117</td>
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<tr>
<td>Siemens pSWE</td>
<td>1.2 m/sec (Siemens suggests &lt;1.34 m/sec, &lt;5.6 kPa)</td>
<td>&gt;2.2 m/sec (&gt;15 kPa)</td>
<td>38,91,45</td>
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<tr>
<td>Philips pSWE</td>
<td>&lt;5.7 kPa (1.37 m/sec)</td>
<td>&gt;2.2 m/sec (&gt;15 kPa)</td>
<td>109</td>
</tr>
<tr>
<td>2D SWE (SuperSonic Imagine)</td>
<td>&lt;7 kPa (1.5 m/sec)</td>
<td>&gt;2.2 m/sec (&gt;15 kPa)</td>
<td>36</td>
</tr>
<tr>
<td>MR elastography (GE, Siemens, Philips)</td>
<td>&lt;3.0 kPa* (27–30)</td>
<td>&gt;5.0 kPa*</td>
<td>29–32</td>
</tr>
</tbody>
</table>

Note.—The location for Echosens is Paris, France.

* MR elastography is reported as shear modulus, while US elastography techniques are reported in Young modulus. The Young modulus is three times the shear modulus.
Suggested thresholds in HCV

<table>
<thead>
<tr>
<th>Liver Fibrosis Staging</th>
<th>Ultrasound based methods</th>
<th>MR based method</th>
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<tr>
<td></td>
<td>Philips(100)</td>
<td>MRE (GE, Siemens, Philips)(29)</td>
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<tr>
<td>F=&gt;2</td>
<td>1.22 m/s (5.2 kPa)</td>
<td>3.5 kPa*</td>
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<td></td>
<td>1.34 m/s (5.7 kPa)</td>
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<td>1.5 m/s (7.1 kPa)</td>
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<tr>
<td></td>
<td>7.2 kPa</td>
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<tr>
<td></td>
<td>1.66 m/s (8.29 kPa)</td>
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<tr>
<td></td>
<td>3.5 kPa*</td>
<td></td>
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<tr>
<td>F=&gt;3</td>
<td>1.49 m/s (7.0 kPa)</td>
<td>4.0 kPa*</td>
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<td>1.55 m/s (7.3 kPa)</td>
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<td>1.7 m/s (8.7 kPa)</td>
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<td>Not available</td>
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<tr>
<td></td>
<td>9.6 kPa</td>
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<tr>
<td></td>
<td>1.77 m/s (9.40 kPa)</td>
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<tr>
<td>F=4</td>
<td>2.21 m/s (12.3 kPa)</td>
<td>5.0 kPa*</td>
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<td></td>
<td>1.80 m/s (10 kPa)</td>
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<td></td>
<td>1.9 m/s (10.4 kPa)</td>
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<td></td>
<td>2.23 m/s (15 kPa)</td>
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<td></td>
<td>14.5kPa</td>
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</tr>
<tr>
<td></td>
<td>1.99m/s (11.9 kPa)</td>
<td></td>
</tr>
</tbody>
</table>

*Shear modulus

**Publication by the manufacturer, and not in peer reviewed literature
How to report the results

- SRU consensus Best Practices
- Report median stiffness value
- Report IQR/median as quality of measurements
- Template:

  - *In the context of a diagnosis of XXXX, the above results suggest a degree of fibrosis/cirrhosis of XXX.*
  - *Normal*=F0 (0.81-1.22m/s), *Non-fibrotic/Mild*=F0-F1 (1.23-1.37m/s), *Moderate*=F2F3 (1.38-2.00m/s), *Severe*=F3-F4 (2.01-2.64)
How to interpret the results

- Elastography detects liver stiffness
- Liver stiffness ≠ Liver fibrosis
  - Increased with inflammation – elevated transaminase levels
  - Cholestasis, severe alcoholic hepatitis, drug-induced liver failure, acute viral hepatitis, reactivation of hepatitis B.
  - Congestion from right heart failure, Budd Chiari syndrome and even recent meal
Pitfalls

- Obesity – thick subcutaneous layer
- Air filled intestines
- Liver movement caused by breathing
- Large amount of ascites
- Narrow intercostal spaces
- Technique
Artifact – Lack of Color Fill

Problem
• Poor ROI placement

Impact
• Suboptimal SW propagation = loss of color fill vertically

Solution
• Position your ROI in the center of the image
• Ensure your transducer is perpendicular with good contact
Problem
• Reverberation or persistence of sound caused by multiple reflections from the liver capsule

Impact
• The reverberations are displayed in the ROI as an area of increased stiffness

Solution
• Move ROI deeper or resize the ROI box so the top edge is away from the liver capsule
Problem
  • Motion due to vessel pulsation

Impact
  • Increased stiffness values at motion site

Solution
  • Avoid vessels when possible
  • If there is adequate tissue stability in other areas of the ROI, place measurements on the stable tissue
  • Do not place measurements on the artifact
**Problem**
- Motion due to patient breathing

**Impact**
- Suboptimal SW propagation = loss of color fill

**Solution**
- Ask patient to PAUSE their breathing
- For patients that are unable to comply, it may be necessary to obtain an image during shallow breathing
Problem
• Shadowing due to bone, air or poor transducer contact

Impact
• Suboptimal shear wave propagation = loss of color fill

Solution
• Ensure the patient is positioned to increase intercostal space and transducer contact is good
• Reposition the ROI to avoid shadowing
Narrow intercostal spaces  

Ascites
Elastography training at UW

- Sonographers – perform elasto on at least 10 people to learn the technique
- Standard protocol
- Super user (either the chief technologist or radiologist) – reviews, instructs and correct as necessary
- Perform Elasto on routine liver screen cases as well for larger numbers
- Elasto images need to be perfect:
  - >1cm away from rib shadow, vessels
  - >2cm from liver surface
  - Perpendicular to liver edge
  - Not too far from the center
  - IQR/median <0.3
Why Thyroid

Superficial organ

Carotid artery - pulsation
Trachea – hard area
The problem

- **FNA** – standard procedure
  - Invasive procedure
  - Inadequate samples – 10-20%
Normal thyroid
Papillary carcinoma
Follicular lesion

Multinodular goiter
Strain Elastography in Thyroid

- Quantitative assessment

- Strain ratio calculation
  - 2 ROIs – one over target region and 2nd over adjacent reference region.
    - PNSR – parenchyma to nodule strain ratio
    - MNSR – Muscle to nodule strain ratio
Thyroid Elastography

- Nodular goiter
- Papillary carcinoma

TSI = 16.86
TSI = 41.15
TSI = 16.86
TSI = 41.15

B-mode

Strain
### Strain Elastography in Thyroid

<table>
<thead>
<tr>
<th>Study</th>
<th>Number of nodules</th>
<th>Sensitivity %</th>
<th>Specificity %</th>
<th>Reference standard</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rago et al., 2007 [29]</td>
<td>92</td>
<td>97</td>
<td>100</td>
<td>Surgery</td>
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<tr>
<td>Asteria et al., 2008 [28]</td>
<td>86</td>
<td>94</td>
<td>81</td>
<td>FNAB or surgery</td>
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<tr>
<td>Tranquart et al., 2008 [60]</td>
<td>108</td>
<td>100</td>
<td>93</td>
<td>FNAB</td>
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<tr>
<td>Hong et al., 2009 [23]</td>
<td>145</td>
<td>88</td>
<td>90</td>
<td>Surgery</td>
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<tr>
<td>Rubaltelli et al., 2009 [32]</td>
<td>51</td>
<td>82</td>
<td>86</td>
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<td>Lippolis et al., 2011 [49]</td>
<td>102</td>
<td>89</td>
<td>6</td>
<td>Presurgery of indeterminate cytology (follicular)</td>
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<td>Moon et al., 2012 [44]</td>
<td>703</td>
<td>65</td>
<td>58</td>
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<td>Azizi et al., 2013 [31]</td>
<td>912</td>
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<td>Ko et al., 2014 [61]</td>
<td>367</td>
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<td>Mehrotra et al., 2013 [62]</td>
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<td>79</td>
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</table>
### Shear-wave imaging of thyroid

<table>
<thead>
<tr>
<th>Study ID</th>
<th>No. of Patients</th>
<th>No. of Nodules Available for Analysis</th>
<th>Mean Diameter of Nodules (mm)</th>
<th>Percentage of Malignant Nodules %</th>
<th>Percentage of nodules referred to histopathological examination %</th>
<th>Diagnosis Parameter</th>
<th>Diagnosis Criteria</th>
<th>TP</th>
<th>FP</th>
<th>FN</th>
<th>TN</th>
<th>Sensitivity %</th>
<th>Specificity %</th>
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<tbody>
<tr>
<td>Bhatia et al. 2012</td>
<td>74</td>
<td>59</td>
<td>13.94*</td>
<td>23.73</td>
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<td>E</td>
<td>&gt;28.9kPa</td>
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<td>6</td>
<td>7</td>
<td>39</td>
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<td>Bojunga et al. 2012</td>
<td>138</td>
<td>158</td>
<td>20.00</td>
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<td>40.51</td>
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<td>Ni et al. 2013</td>
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<td>81.7</td>
</tr>
</tbody>
</table>
Diffuse thyroid disease

• Strain
  – Thyroiditis – stiff gland
  – Lower cut-off values to be used
  – MNSR gave better results than PNSR

• SWE
  – Less problematic in DTD
  – ARFI performed better than SWE
Pitfalls

Both Papillary Carcinoma.

21 kPa

76.7 kPa
kPa = 126.9

FNA – Follicular lesion with Hurthle cell changes – cannot exclude neoplasia.

Histopath – Nodular hyperplasia (multinodular goiter) background of lymphocytic thyroiditis.
Artifacts in Elastography

Elastography artifacts:
1. Lack of penetration
2. Color scale set incorrectly
3. Near field artifact
4. Compression artifact

Nodule characteristics:
1. Cystic nodule
2. Rim Calcified nodule
3. Large nodule
Near Field artifact
Avoided by stand off pad

Compression artifact:
Finger like projections

Extends through the image
Effect of compression

Mean - 7.4kPa ➔ 12.2kPa
Ratio – 0.5 ➔ 0.7

Case courtesy –
Dr Antonio Masciotra, Campobasso, Italy
Color gain set incorrectly

Overgain

Lack of adequate contact

Undergain

Cystic areas in a nodule.
Lack of penetration – deep nodules.

Calcified nodules.
Ultrasound, elastography (List separately in addition to code for primary procedure)

(Use 0346T in conjunction with 76536, 76604, 76641, 76642, 76700, 76705, 76770, 76775, 76830, 76856, 76857, 76870, 76872, 76881, 76882)

(For liver elastography mechanically induced shear wave technique without imaging, use code 91200)

A separate limited ultrasound study or complete abdominal ultrasound study may be billed if a separate complete or limited exam is ordered, medical necessity is documented, and all elements required for a limited or complete abdominal ultrasound study are described in the medical report. Code 91200 can be used for all forms of shear wave liver elastography, including both those using mechanical (transient elastography - Fibroscan®) or acoustic (ARFI) techniques to generate the shear waves. The shear wave speed can be reported in meters/second (m/s) or converted to KiloPascals (kPa) making appropriate assumptions.
Conclusion

- Detection of significant fibrosis and cirrhosis is important for diagnosing, determination of treatment, prognosis and follow up of chronic liver disease.
- Adherence to strict protocol is required
- Both patient factors and scanning factors effect results
- Thyroid elastog – further studies needed to assess utility in routine practice
Acknowledgement:
Excellent sonographers and sonologists at UW dedicated to improving patient care.