Clinical applications of ultrasound elastography

Background

- Ultrasonographic elastography is a noninvasive imaging technique that can be used to depict relative tissue stiffness in response to an external force.
- Stiff tissues deform less and exhibit less strain than soft tissues in response to the same applied force.
- Most pathological changes are associated with changes in tissue stiffness.

Background

The tissue deformation may be represented in an elasticity image (elastogram), or as a local stiffness measurement, in one of three ways:

- Tissue displacement by manual compression with measurements of tissue displacement - compression elastography (CE).
- Tissue displacement using external vibrator with measurements of shear wave propagation - transient elastography (TE).
- Tissue displacement using acoustic radiation force impulse (ARFI) with measurements of shear-waves propagation.
- Point shear-wave elastography without making images (pSWE)
- Color shear wave speed map, known as shear-wave elastography (SWE)

Compression elastography

Elastography (Gray-scale)

Elastography (Color-coded)
Strain Elastography

1. Tissue strain depends on the amount of applied compression and is not an intrinsic property of tissue.
2. The elastogram is an image of relative stiffness and the actual strain values cannot be compared from one elastogram to the next.
3. Because elastograms show only changes in strain from one area to another in an image, they are well suited for detection and evaluation of focal lesions and are insensitive to diffuse processes that produce the same stiffness everywhere in the image.

Transient Elastography

1. A single-element ultrasound transducer operating at 5 MHz is built on the axis of a piston-like vibrator.
2. Low-frequency (50 Hz) transient vibrations are transmitted, and the elastic shear waves that are generated propagate through underlying tissues.
3. Pulse-echo ultrasound acquisitions are used to follow the propagation of the shear wave and to measure its velocity.

Transient Elastography

- The probe induces an elastic wave through the liver.
- The velocity of the ultrasonic shear wave is a measure of elasticity (fibrosis).
- Explored volume

Transient Elastography

- The software of the device determines whether each measurement is successful.
- The entire procedure is considered to have failed when no value is obtained after 10 shots.
- Successful measurements are validated by these criteria:
  - 10 valid shots;
  - A ratio of valid shots to the total number of shots of 60% or higher;
  - Variability of measurements less than 30% of the median value of liver stiffness measurements.

Limitations

1. Transient elastography cannot technically be performed in patients with ascites.
2. High rate of failure in patients with body mass indices greater than 30 kg/m2.
3. The recent availability of the FibroScan XL probe has overcome this latter limitation.

Castéra L et al. Gastroenterology 2005
Acoustic radiation force imaging

- Acoustic radiation force creates a localized displacement of a few microns in the ultrasound axial direction.
- Sufficient force can be generated with a standard ultrasound scanner at depths of several centimeters.
- The displacement is measured at a known time after cessation of the push using RF-echo tracking.
- Results are displayed as an elastogram within a small box.

ARFI advantages

- As the ultrasound beam creates the displacements, they are less user-dependent than those in hand-induced strain imaging.
- ARFI images
  - better resolution
  - less artefacts,
  - improved SNR
  - less influenced by slip movement outside of the imaged region
ARFI limitations

- The displacement contrast depends on absorption and reflection of the pushing beam.
- The displacement contrast depends on the delay between the push and the displacement measurement.
- Substantial transducer heating from the high power needed to create the pushing beam limits the frame rate.

Shear Wave Elastography

- Real-time color-coded shear wave mapping

Shear velocity imaging

Breast elastography

Elasticity of the breast tissues

Fibroadenoma

Quantification of hepatic fibrosis is of critical importance in chronic hepatitis C.

Two end points are clinically relevant:
- Significant fibrosis (indication for antiviral treatment)
- Detection of cirrhosis (screening for esophageal varices and HCC)
Sampling error in liver biopsy

Table 3. Differences in Grading of Nonneutrophilic Activity in Diagnoses From the Right and Left Lobes (Test = 0.15) &

<table>
<thead>
<tr>
<th>Difference Between Right and Left Lobes</th>
<th>Number of Patients</th>
<th>% of Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Identical grade</td>
<td>84</td>
<td>73.5</td>
</tr>
<tr>
<td>Different grade (test)</td>
<td>30</td>
<td>24.7</td>
</tr>
<tr>
<td>Difference of one grade</td>
<td>26</td>
<td>22.6</td>
</tr>
<tr>
<td>Difference of two grades</td>
<td>5</td>
<td>4.9</td>
</tr>
<tr>
<td>3-4 in the other</td>
<td>5</td>
<td>4.9</td>
</tr>
</tbody>
</table>

In healthy volunteers, a mean normal liver stiffness is 4.9 ± 1.7 kPa (1.28 ± 0.75 m/s).

Transient Elastography

In patients with chronic hepatitis C, liver stiffness values greater than 6.8 – 7.6 kPa signify a high probability of significant fibrosis (F ≥ 2) on biopsy.

The cut-off values for predicting cirrhosis (F = 4) range between 11.0 and 13.6 kPa.

The use of TE in chronic hepatitis C has been endorsed in the recommendations for the management of viral hepatitis by the European Association for the Study of the Liver.

Liver Elastography Technique

Thresholds in Patients with Hepatitis C
Elastography techniques can be used to distinguish patients with no or minimal fibrosis (METAVIR F0, F1) and those with severe fibrosis or cirrhosis (METAVIR F3, F4).

A middle group between these cutoff values requires additional data to determine follow-up.

Additional research is needed in the areas of population differences, disease differences, spleen measurement, steatosis, and incidence of HCC related to liver fibrosis grade.

### Thyroid elastography

#### Elasticity of the thyroid tissues

<table>
<thead>
<tr>
<th>Condition</th>
<th>Elasticity Moduli (kPa)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal thyroid gland (n=24)</td>
<td>47.3 ± 17.9</td>
</tr>
<tr>
<td>Chronic thyroiditis (n=2)</td>
<td>63.3 ± 5.6</td>
</tr>
<tr>
<td>Benign thyroid tumors (n=19)</td>
<td></td>
</tr>
<tr>
<td>Papillary adenocarcinoma (n=19)</td>
<td></td>
</tr>
<tr>
<td>Follicular adenocarcinoma (n=3)</td>
<td></td>
</tr>
</tbody>
</table>

Lyshchik, A. et al. Ultrasound Imaging. 2005

#### Elasticity score

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Elasticity in the whole nodule</td>
</tr>
<tr>
<td>2</td>
<td>Elasticity in a large part of the nodule</td>
</tr>
<tr>
<td>3</td>
<td>Elasticity only at the peripheral part of the nodule</td>
</tr>
<tr>
<td>4</td>
<td>No elasticity in the nodule</td>
</tr>
<tr>
<td>5</td>
<td>No elasticity in the nodule and in the posterior shadowing</td>
</tr>
</tbody>
</table>

Rago, T. et al. JCEM 2007

#### Solid benign thyroid nodules

- adenomatous goiter
- pattern 2

Rago, T. et al. JCEM 2007

B-mode sonogram

Real-time elasticity image

http://www.hitachi-medical.co.jp/medix/pdf_sup/sup_05.pdf
Thyroid cancer

- papillary thyroid cancer
- pattern 4

Asteria et al. Thyroid, 2008

Follicular thyroid cancer

- follicular thyroid cancer
- pattern 2

http://www.hitachi-medical.co.jp/medix/pdf_sup/sup_05.pdf

B-mode sonogram

Real-time elasticity image

Thyroid ARFI


Thyroid ARFI


Interobserver variability ultrasound vs elastography

Park, SH. et al. AJR 2009
Lymph node elastography

Prostate elastography

**Prostate cancer**

- Prostate cancers are difficult to visualize on standard B-mode ultrasound.
- Elastography can be used to detect lesions in addition to classification of sonographically visible nodules.
- Prostate elastography may find use as a guidance tool for extended pattern core biopsies of the prostate where additional core samples would be taken from suspicious areas on a real-time elastography performed during the biopsy procedure.

**Elasticity of the prostate tissues**

<table>
<thead>
<tr>
<th>Elastic Moduli (kPa)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal anterior (n=32)</td>
</tr>
<tr>
<td>BPH (n=21)</td>
</tr>
<tr>
<td>Cancer (n=28)</td>
</tr>
</tbody>
</table>

Prostate cancer
Prostate Elastography

<table>
<thead>
<tr>
<th>Parameter</th>
<th>T2-Weighted Endorectal MRI</th>
<th>Real-time Sonoelastography</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity per patient, %</td>
<td>84.6 (55–98)</td>
<td>84.6 (55–98)</td>
</tr>
<tr>
<td>Sensitivity per area, %</td>
<td>50.0 (30–70)</td>
<td>57.7 (37–77)</td>
</tr>
<tr>
<td>NPV per patient, %</td>
<td>83.3 (52–96)</td>
<td>86.7 (60–98)</td>
</tr>
<tr>
<td>NPV per area, %</td>
<td>92.2 (87–96)</td>
<td>93.6 (89–97)</td>
</tr>
</tbody>
</table>

Conclusions

1. Elastography has emerged as a useful adjunct tool for ultrasound diagnosis.

2. The first and most common application of elastography is for the diagnosis of breast lesions and distinguishing cancer from benign lesions.

3. Elastography techniques can be used to distinguish patients with no or minimal fibrosis (METAVIR F0, F1) and those with severe fibrosis or cirrhosis (METAVIR F3, F4).

Other potential applications for elastography include characterization of thyroid nodules and lymph node evaluation for metastatic disease.

Prostate cancer detection is also a potential application, but obtaining high-quality elastograms may be difficult.

Other promising applications include atheromatous plaque and arterial wall evaluation, venous thrombus evaluation, renal and liver transplant rejection, and monitoring of tumor ablation therapy.