Research Elastography: Liver

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Disclosure

Esaote: expenses; speaker
Hitachi Aloka Medical, Ltd: expenses; speaker
Philips Healthcare: honorarium; speaker
Toshiba Medical Systems: expenses, speaker

Loan of ultrasound systems for research purposes:
- Twice, Esaote SpA, Genoa, Italy
- EPIQ7, Philips Medical Systems, Bothell, WA, USA
- Aplio 500, Toshiba Medical Systems, Tokyo, Japan
- Fibroscan, Echosens, Paris, France
Acoustic radiation force impulse (ARFI) Elastography

- Point Shear Wave Elastography
- 2D Shear Wave Elastography

Point Shear Wave Elastography

VTQ

ElastPQ

QElaxto

SWM
Reproducibility

**ICC: 0.84 - 0.87**

- Boursier J et al. Eur J Gastroenterol Hepatol 2010
- D’Onofrio M et al. AJR Am J Roentgenol 2010

Healthy Subjects: < 1.2 m/sec


Comparison of Transient Elastography and Acoustic Radiation Force Impulse for Non-Invasive Staging of Liver Fibrosis in Patients with Chronic Hepatitis C

139 consecutive patients with CHC were enrolled in two tertiary centers

ARFI best cutoff values:
Significant fibrosis (≥F2), ≥1.3 m/s (AUROC: 0.86)
Severe fibrosis (F3-F4), ≥ 1.7 m/s (AUROC: 0.94)
Cirrhosis (F=4), ≥2.0 m/s (AUROC: 0.89)

The average concordance rates of TE and ARFI with liver biopsy were 45.4 and 54.7%.

Rizzo L et al. Am J Gastroenterol 2011
Acoustic radiation force impulse elastography shows higher rate of reliable measurements and similar predictive value to TE for significant fibrosis and cirrhosis.

Bota S et al. Liver Int 2013
ElastPQ® (Philips Healthcare)
ElastPQ Reproducibility

**CCC:** 0.97 (95% CI, 0.96-0.98)  
Ferraioli G et al. World J Gastroenterol 2014

**ICC:** 0.80 (95% CI, 0.77-0.82)  
Ma JJ et al. J Gastroenterol Hepatol 2014

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**Healthy Subjects:** 3.5 kPa (1.08 m/s)
A Point Shear Wave Elastography Method for Assessing Liver Stiffness

Patients with mild fibrosis and healthy volunteers

Ferraioli G et al. World J Gastroenterol 2014
ROC Curves

F ≥ 2

F ≥ 3

F = 4

102 patients with chronic hepatitis C
The stage of liver fibrosis and the grade of necro-inflammatory activity were associated with higher values of ElastPQ, while liver fibrosis was the dominating factor affecting liver stiffness measured by ElastPQ.
Accuracy of the latest release of a point shear wave elastography method for staging liver fibrosis in patients with chronic hepatitis C

189 patients

For staging liver fibrosis we used the VCTE cutoffs of 7.0, 9.5 and 12.0 kiloPascal, respectively, for significant fibrosis (F≥2), advanced fibrosis (F≥3), and cirrhosis (F=4).

The diagnostic performance of ElastPQ® was assessed by calculating the area under the receiver operating characteristic (AUC) curve.
### Fibrosis stage

<table>
<thead>
<tr>
<th>Fibrosis stage</th>
<th>Cutoff (kPa)</th>
<th>Sensitivity% (95% CI)</th>
<th>Specificity% (95% CI)</th>
<th>PPV% (95% CI)</th>
<th>NPV% (95% CI)</th>
<th>LR+ (95% CI)</th>
<th>LR- (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Significant fibrosis ($F\geq2$)</td>
<td>6.76</td>
<td>91.5 (83.9-96.3)</td>
<td>96.2 (89.4-99.2)</td>
<td>96.6 (90.5-99.3)</td>
<td>90.6 (82.3-95.8)</td>
<td>24.4 (8.0-74.2)</td>
<td>0.09 (0.05-0.2)</td>
</tr>
<tr>
<td>Advanced fibrosis ($F\geq3$)</td>
<td>7.60</td>
<td>95.7 (87.8-99.1)</td>
<td>90.5 (83.2-95.3)</td>
<td>86.8 (77.1-93.5)</td>
<td>96.9 (91.3-99.4)</td>
<td>10.04 (5.6-18.1)</td>
<td>0.05 (0.02-0.1)</td>
</tr>
<tr>
<td>Liver cirrhosis ($F=4$)</td>
<td>8.93</td>
<td>91.9 (82.2-97.3)</td>
<td>91.1 (84.2-95.6)</td>
<td>85.1 (74.3-92.6)</td>
<td>95.3 (89.4-98.5)</td>
<td>10.3 (5.7-18.7)</td>
<td>0.09 (0.04-0.2)</td>
</tr>
</tbody>
</table>
Ferraioli G et al. Accuracy of the QElaXto® shear wave technique for staging liver fibrosis. Insights into Imaging 2016; 7:S394-395

2D Shear Wave Elastography

Bavu E et al. Ultrasound Med Biol 2011

Bercoff J et al. IEEE Trans Ultrason Ferroelectr Freq Control 2004
2D-SWE (SuperSonic Imagine S.A.)
Reproducibility

**CCC:**
- Inter-observer: 0.88
- Intra-observer (within day, expert): 0.95-0.93
- Intra-observer (between days, expert): 0.84-0.65

Ferraioli G et al. Eur J Radiol 2012

**ICC:**
- Inter-observer: 0.78
- Intra-observer (within day): 0.92-0.87
- Intra-observer (between days): 0.84-0.63

Hudson JM et al. Ultrasound Med Biol 2013
Accuracy of Real-Time Shear Wave Elastography for Assessing Liver Fibrosis in Chronic Hepatitis C: a Pilot Study

121 patients with chronic hepatitis C

Shear Wave Elastography

Transient Elastography

Ferraioli G et al. Hepatology 2012
**ROC Analysis and Cutoffs**

Ferraioli G et al. Hepatology 2012

<table>
<thead>
<tr>
<th>F ≥ 2</th>
<th>F ≥ 3</th>
<th>F = 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>SWE: 7.1 kPa</td>
<td>SWE: 8.7 kPa</td>
<td>SWE: 10.4 kPa</td>
</tr>
<tr>
<td>TE: 6.9 kPa</td>
<td>TE: 8.0 kPa</td>
<td>TE: 11.6 kPa</td>
</tr>
</tbody>
</table>

422 patients with chronic hepatitis C
The diagnostic performance of real-time SWE was compared to those of Fibrotest and the two Fibroscan probes.

- The performance of real-time SWE for the diagnosis of cirrhosis was similar to those of Fibrotest and TE.
- In patients with ascites, real-time SWE applicability was greater than that of TE.

Poynard T et al. J Hepatol 2013
Non-Invasive Assessment of Liver Fibrosis with Impulse Elastography: Comparison of Supersonic Shear Imaging with ARFI and FibroScan®

349 patients, mixed etiologies

<table>
<thead>
<tr>
<th></th>
<th>2D-SWE</th>
<th>TE</th>
<th>VTQ</th>
<th>AUROC</th>
</tr>
</thead>
<tbody>
<tr>
<td>mild fibrosis</td>
<td>0.89</td>
<td>0.86</td>
<td>0.84</td>
<td>0.89</td>
</tr>
<tr>
<td>significant</td>
<td>0.88</td>
<td>0.84</td>
<td>0.81</td>
<td>0.88</td>
</tr>
<tr>
<td>severe fibrosis</td>
<td>0.93</td>
<td>0.87</td>
<td>0.89</td>
<td>0.93</td>
</tr>
<tr>
<td>cirrhosis</td>
<td>0.93</td>
<td>0.90</td>
<td>0.90</td>
<td>0.93</td>
</tr>
</tbody>
</table>

Real-time 2D-SWE had a higher accuracy than TE for the diagnosis of severe fibrosis ($p = 0.002$), and a higher accuracy than VTQ for the diagnosis of significant fibrosis.
Accuracy of the latest release of a 2D shear wave elastography method for staging liver fibrosis in patients with chronic hepatitis C: preliminary results

FibroScan® as the reference standard.

Consecutive patients with chronic hepatitis C (n=73).

On the same day:

- Transient Elastography (FibroScan)
- Toshiba 2D-SWE

Ferraioli G et al. Digestive and Liver Disease 2016; Suppl 1:e62-63
**F≥2**

**2D-SWE**
- Cutoff value, 6.6 kPa
- Sensitivity, 100%
- Specificity, 94.4%
- PPV, 97.7%
- NPV, 100%
- LR+, 18.0
- LR-, 0

**VCTE**
- Cutoff value, 7.0 kPa

**AUROC**: 0.99

**F≥3**

**2D-SWE**
- Cutoff value, 9.4 kPa
- Sensitivity, 96.9%
- Specificity, 100%
- PPV, 100%
- NPV, 96.6%
- LR+, calculation not possible
- LR-, 0.03

**VCTE**
- Cutoff value, 9.5 kPa

**AUROC**: 1.00

**F=4**

**2D-WE**
- Cutoff value, 11.2 kPa
- Sensitivity, 88%
- Specificity, 97.1%
- PPV, 95.7%
- NPV, 91.9%
- LR+, 30.8
- LR-, 0.12

**VCTE**
- Cutoff value, 12.0 kPa

**AUROC**: 0.98
Sporea I et al. The performance of 2D SWE.GE compared to transient elastography for the evaluation of liver stiffness: preliminary results. Insights into Imaging 2016; 7:S395
Elastography: Confounding Factors

Stiffness increases with:

- Exacerbations of acute hepatitis associated with transaminase flares, thus the effect of necro-inflammation should be taken into account, and the results should always be evaluated in clinical settings;
- Congestive heart failure;
- Feeding;
- Extrahepatic cholestasis;
- Deep inspiration, so that transiently stopping breathing in a neutral position is optimal for measurements.
The influence of steatosis

It is still a matter of debate with conflicting results: some studies suggest that steatosis is associated to an increase in liver stiffness, whereas others do not.
The severity of steatosis influences liver stiffness measurement in patients with nonalcoholic fatty liver disease

253 patients were assessed by clinical, US, and histological features. Transient elastography was performed using the M probe.

Median LSM values were significantly higher in subjects with severe steatosis (≥66% at liver biopsy) compared to those without.

**Conclusion:** In patients with nonalcoholic fatty liver disease, the presence of severe steatosis, detected by histology or by US, should always be taken into account in order to avoid overestimation of liver fibrosis assessed by transient elastography.

Petta S et al. Hepatology 2015
Procedure*

- Fasting conditions;
- Dorsal decubitus positioning, with the right arm elevated above the head for optimal intercostal access;
- Resting respiratory position (breath-hold without deep inspiration);
- Minimal scanning pressure applied by the operator;
- ROI placement beneath Glisson’s capsule by 1.5-2.0 cm to avoid reverberation artifacts;
- ROI placement to avoid large liver vessels.

*General procedures, valid for all techniques
Limitation

Different estimates of shear wave speed in the same liver are obtained with different ultrasound systems. These differences can cause uncertainty and a lack of technology adoption in the clinical community. Given the need for serial assessment of liver fibrosis, and the impracticality of serial liver biopsy, providing a common SWS estimate among systems would speed adoption of the technology.

Several sources of bias and variance should be addressed to improve consistency of measurement results (QIBA project).

Hall TJ. RSNA/QIBA: Shear wave speed as a biomarker for liver fibrosis staging
Liver cirrhosis:
Suggested threshold in patients with hepatitis C

Advanced fibrosis and/or cirrhosis: 15 kPa (2.2 m/s)


Compensated advanced chronic liver disease:
TE values > 15 kPa

Measurement of spleen stiffness to evaluate portal hypertension and the presence of esophageal varices in patients with HCV-related cirrhosis

100 consecutive patients

Diagnostic performance of spleen stiffness (SS) measurement by transient elastography with that of liver stiffness (LS) and of other recently proposed noninvasive tests.

SS and LS were more accurate than other noninvasive parameters in identifying patients with EV and different degrees of PH.

Colecchia A et al. Gastroenterology 2012
Distribution of SS and LS values

Patients with HVPG <12 or >12 mm Hg

Patients with HVPG <10 or >10 mm Hg

Patients with or without EV

Colecchia A et al. Gastroenterology 2012
Spleen stiffness measurement can predict clinical complications in compensated HCV-related cirrhosis: A prospective study

92 patients followed-up for 2 years or until the occurrence of the first clinical decompensation (CD).
At enrolment: liver stiffness, spleen stiffness, HVPG measurements and upper endoscopy.

Univariate analysis:
Varices at enrolment, all non-invasive parameters, HVPG, and MELD resulted clinical predictors of CD.

Multivariate analysis
Only SS (p = 0.0001) and MELD (p = 0.014) resulted as predictive factors.
Ultrasound point shear wave elastography assessment of liver and spleen stiffness: Effect of training on repeatability of measurements

92 healthy volunteers (blood donors)

Point shear wave elastography (Acuson S2000, Siemens)

Measurements were performed by an expert (observer1) and a novice (observer2) at three different sites of liver and spleen.

Ferraioli G et al. Eur Radiol 2014
Both intra-observer and inter-observer agreement were higher for the liver than for the spleen.

Training improved the repeatability of spleen stiffness measurements at all sites.

A good intra-observer agreement was obtained only for measurements at lower pole of the spleen.
Real-time shear-wave elastography: applicability, reliability and accuracy for clinically significant portal hypertension

88 consecutive patients undergoing HVPG measurement (reference standard) for portal hypertension.

- LS and SS by RT-SWE were feasible respectively in 87 (99%) and 58 (66%) patients.
- Both correlated with HVPG (LS: R=0.611, and SS: R=0.514).
- Reliability of measurements was influenced by standard deviation (SD)/median ratio and depth.

Procopet B et al. J Hepatol 2015
Guidelines and Recommendations on the Clinical Use of Ultrasound Elastography

Consensus Conference on Ultrasound Elastography for Liver Fibrosis

EASL-ALEH Clinical Practice Guidelines: Non-invasive tests for evaluation of liver disease severity and prognosis

Ultrasound Med Biol, 2015

Radiology, 2015

J Hepatol, 2015