Non-invasive liver fibrosis assessment using a new ultrasonographic method: Acoustic radiation force elastography

Poster No.: C-0001
Congress: ECR 2010
Type: Scientific Exhibit
Topic: Abdominal Viscera (Solid Organs) - Biliary Tract
Authors: M. Lupso-Platon, R. Badea, H. Stefanescu, A. Maniu, H. Branda, Z. Sparchez, A. Serban; Cluj-Napoca/RO
Keywords: Acoustic Radiation Force Impulse (ARFI) Imaging, Ultrasonography, Virtual Touch Tissue quantification, liver fibrosis
Keywords: Abdomen, Biliary Tract / Gallbladder
DOI: 10.1594/ecr2010/C-0001

Any information contained in this pdf file is automatically generated from digital material submitted to EPOS by third parties in the form of scientific presentations. References to any names, marks, products, or services of third parties or hypertext links to third-party sites or information are provided solely as a convenience to you and do not in any way constitute or imply ECR's endorsement, sponsorship or recommendation of the third party, information, product or service. ECR is not responsible for the content of these pages and does not make any representations regarding the content or accuracy of material in this file.

As per copyright regulations, any unauthorised use of the material or parts thereof as well as commercial reproduction or multiple distribution by any traditional or electronically based reproduction/publication method is strictly prohibited.

You agree to defend, indemnify, and hold ECR harmless from and against any and all claims, damages, costs, and expenses, including attorneys’ fees, arising from or related to your use of these pages.

Please note: Links to movies, ppt slideshows and any other multimedia files are not available in the pdf version of presentations.
Purpose

Nowadays, there is an increasing interest in finding new non-invasive methods for the evaluation of chronic hepatitis C (CHC) patients, as an alternative to needle biopsy, with focus on the elastographic methods.

ARFI technology ("Acoustic Radiation Force Impulse Imaging") is increasingly studied for its uses in different clinical applications, including tumoral conditions of the breast, liver, kidney, colon and rectum, the characterizing of atherosclerotic plaques, as well as for the monitoring of radiofrequency ablation (1-10). As for the assessment of diffuse liver diseases, studies are now in progress (11-12).

ARFI technology involves the mechanical excitation of tissue using short-duration acoustic pulses (push pulses) in a region of interest chosen by the examiner, producing shear waves that spread away from the region of interest, perpendicularly to the acoustic push pulse, generating localized, micron-scale displacements in the tissue. Simultaneously, detection waves of lower intensity than that of the push pulse are generated. The moment of interaction between the shear waves and detection waves marks the period of time elapsed between the generating of shear waves and their entire crossing of the region of interest. By recording the shear wavefront at several locations and correlating these measurements with the elapsed time, the shear wave velocity - SWV (m/s) can be quantified; generally, the stiffer a region in the tissue, the greater the SWV as it travels through this region. Thus, the measured SWV is an intrinsic and reproducible property of the tissue.

A single transducer on a diagnostic scanner is used both to generate radiation force and to track the resulting displacement. Since this technique is implemented via additional software imaging control and detection algorithms, the method can provide co registered B-mode, color Doppler and ARFI images.

This study aims to evaluate the performance of a new elastographic method (ARFI technology) in the assessment of fibrosis in a group of CHC patients who have undergone liver biopsy.
Methods and Materials

Patients

112 CHC patients examined in the 3rd Medical Clinic, University of Medicine and Pharmacy Cluj-Napoca, Romania were prospectively included in this study. All of them had positive HCV-RNA and underwent percutaneous liver biopsy (LB) for grading and staging the diseases. All patients were referred SWV measurement 1 day prior to LB.

The exclusion criteria were:

• co-infection with HBV and/or human immunodeficiency virus
• active infectious diseases other than HCV
• pregnancy

ARFI technology

SWV measurement was performed in the right intercostal space, 4 cm in depth, using an Acuson S2000 unit (Siemens) equipped with a 4 MHz frequency transducer, with the ARFI technology implemented via additional software imaging control and detection algorithms.

For fibrosis quantification, the "Virtual Touch (VT) tissue quantification" application was used, allowing for the measurement of SWV (m/s) within the interest area chosen by the examiner, according to the principles described in the Introduction section. The higher the tissue stiffness, the higher the shear wave velocity.

When VT tissue quantification was enabled on the S2000 system, the feature was in a setup mode. Whenever the operator pressed the update key, one VT tissue quantification measurement was acquired.

The equipment listed the shear wave velocity (m/s) in the region of interest as well as the depth at which the measurement was performed (figure 1).

When no valid measurement could be acquired, the monitor would display the "X-X-X-X" symbol.

The median value of 10 valid measurements of the shear wave velocity was considered.
Histological study

A liver biopsy examination was performed by using the TruCut technique with a 1.8 mm (14G) diameter automatic needle device - Biopty Gun (Bard GMBH, Karlsruhe, Germany).

Liver biopsy specimens were fixed in formalin and embedded in paraffin. Only biopsy specimens with more than 6 intact portal tracts were eligible for evaluation.

Liver fibrosis and necroinflammatory activity were evaluated semiquantitatively according to the METAVIR scoring system (13, 14).

Fibrosis was staged on a 0-4 scale as follows:
- F0 - no fibrosis
- F1 - portal fibrosis without septa
- F2 - portal fibrosis and few septa
- F3 - numerous septa without cirrhosis
- F4 - cirrhosis.

Necroinflammatory activity was graded as follows:
- A0 - none
- A1 - mild
- A2 - moderate
- A3 - severe.

Steatosis was categorized by visual assessment as:
- 0 - none
- 1 - steatosis in <33% of hepatocytes
- 2 - steatosis in 33% to 66% of hepatocytes
- 3 - steatosis in > 66% of hepatocytes

Statistical analysis

The statistical analysis was performed using the SPSS software version 15.0 (SPSS Inc., Chicago, IL, USA). The difference of means was tested with the Anova analysis of
variance and the Kruskal-Wallis test, while the relationship between different parameters - through Spearman correlation coefficients.

The diagnostic performance of SWV was assessed using sensitivity (Se), specificity (Sp), positive predictive value (PPV), negative predictive value (NPV), accuracy, likelihood ratios (LR) and receiver operating characteristic (ROC) curves. Optimal cut-off values for SWV were chosen to maximize the sum of sensitivity and specificity, and positive and negative predictive values were computed for these cut-off values.
Results

Of the 112 examined patients, 10 (8.92%) did not yield any valid measurement through the ARFI technique.

SWV ranged from 0.75 to 4.15 m/s (median 1.70 m/s)

**Correlation between liver stiffness and different histological parameters.** SWV measured through the ARFI technique is correlated only with fibrosis ($r=0.717$, $p<0.0001$) and necroinflammatory activity ($r=0.328$, $p=0.014$), not with steatosis ($r=0.122$, $p=0.321$)

Fibrosis is the principal factor correlating with SWV. On the whole, there is a significant increase of SWV in parallel with the increase in fibrosis stage ($p<0.0001$). However, there is a certain degree of overlap between consecutive stages: 1.09±0.15 (for F0-F1), 1.50±0.89 (F2), 1.52±0.57 (F3), respectively 2.55±0.78 (F4).

Therefore SWV does not change significantly between F0-F1 ($p=0.493$), F1-F2 ($p=0.072$), F2-F3 ($p=0.965$).

Figure 2 shows box-plots of SWV values according to different stages of fibrosis.

**The most discriminate cut-off values** were determined from the distribution of SWV according to fibrosis stage. Table 1 shows the optimal cut-off values as well as corresponding sensibility, specificity, positive and negative predictive values. (Se sensitivity, Sp specificity, PPV positive predictive value, NPV negative predictive value, +LR Positive likelihood ratio, -LR Negative likelihood ratio, AUROC area under ROC curve)

<table>
<thead>
<tr>
<th></th>
<th>F0 vs F1234</th>
<th>F01 vs F234</th>
<th>F012 vs F34</th>
<th>F0123 vs F4</th>
</tr>
</thead>
<tbody>
<tr>
<td>SWV cutoff value (m/s)</td>
<td>&gt; 1.19</td>
<td>&gt; 1.34</td>
<td>&gt; 1.61</td>
<td>&gt; 2.00</td>
</tr>
<tr>
<td>Se (%)</td>
<td>62.07</td>
<td>67.80</td>
<td>79.07</td>
<td>80.00</td>
</tr>
<tr>
<td>Sp (%)</td>
<td>85.71</td>
<td>92.86</td>
<td>94.83</td>
<td>95.45</td>
</tr>
<tr>
<td>+LR</td>
<td>4.34</td>
<td>9.49</td>
<td>15.29</td>
<td>17.60</td>
</tr>
<tr>
<td>-LR</td>
<td>0.44</td>
<td>0.35</td>
<td>0.22</td>
<td>0.21</td>
</tr>
<tr>
<td>PPV</td>
<td>96.4</td>
<td>93.0</td>
<td>91.9</td>
<td>90.3</td>
</tr>
<tr>
<td>NPV</td>
<td>26.7</td>
<td>67.2</td>
<td>89.9</td>
<td>90.0</td>
</tr>
<tr>
<td>------</td>
<td>------</td>
<td>------</td>
<td>------</td>
<td>------</td>
</tr>
<tr>
<td>AUROC</td>
<td>0.725</td>
<td>0.869</td>
<td>0.900</td>
<td>0.936</td>
</tr>
</tbody>
</table>

The optimal SWV cut-off values for each fibrosis stage in CHC patients

Figure 3 shows the ROC curves of SWV according to four different fibrosis stage thresholds.
Fig. 0: The ultrasound image used to quantify the shear wave velocity 4 cm below the skin level.

© Ultrasonography, University of Medicine and Pharmacy - Cluj-Napoca/RO
Fig. 0: Variation of the SWV depending on the stage of fibrosis, measured through the ARFI technique 4 cm below the skin level. The top of the bottom of the boxes are the first and third quartiles, respectively. The length of the box represents therefore the interquartile range including 50% of the values. The line through the middle of each box represents the median. The error shows the minimum and maximum values (range).

© Ultrasonography, University of Medicine and Pharmacy - Cluj-Napoca/RO
**Fig. 0:** ROC curves according to four different fibrosis stage thresholds: F0 versus F1-F4 patients, F0-F1 versus F2-F4 patients, F0-F2 versus F3-F4 patients and F0-F3 versus F4 patients.

© Ultrasonography, University of Medicine and Pharmacy - Cluj-Napoca/RO
**Conclusion**

ARFI technology allows the quantification of the shear wave velocity, in strong correlation with the fibrosis stage. Steatosis does not influence the shear wave velocity.

ARFI could be used as a new noninvasive method especially for the prediction of severe fibrosis and cirrhosis.
Personal Information

Dr. Monica Lupșor

Ultrasonography Dept., 3rd Medical Clinic, 19 - 21 Croitorilor street, Cluj-Napoca, Romania

monica.lupsor@umfcluj.ro