Acoustic Radiation Force Imaging (ARFI) and Transient Elastography (TE) for liver fibrosis assessment in chronic viral hepatitis

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Purpose

Liver fibrosis evaluation is an important step in clinical management of patients with chronic viral hepatitis. Prognosis assessment and treatment of these patients mostly rely on the staging of liver fibrosis. Liver biopsy (LB) is still considered the gold standard for hepatological evaluation, but in the recent years many non-invasive methods have been proposed to replace this invasive procedure in order to make liver fibrosis evaluation easier and safer for patient.

The aim of our study is to assess the effectiveness of combining two non-invasive ultrasound-based elastographic methods in staging liver fibrosis in patients with chronic viral hepatitis: acoustic radiation force impulse (ARFI) and transient elastography (TE).
Methods and Materials

Transient elastography (TE) and Acoustic Radiation Force Impulse (ARFI) elastography are non-invasive methods for the evaluation of liver fibrosis using ultrasound waves. Basically they use respectively a mechanical pulse and a ultrasonic pulse to generate shear waves into liver tissue in order to measure its elasticity. TE uses a single ultrasonic transducer that is both used as an ultrasonic emitter and receiver and as a low-frequency piston-like vibrator to generate a transient vibration. A low-frequency elastic wave is sent through the medium under investigation by the vibrator. Elasticity is derived from the velocity of the low-frequency elastic wave. The principle of ARFI elastography is that compression of the liver parenchyma induces a smaller strain in hard tissues than in softer ones. The compression is provided by an acoustic pulse, automatically generated by the ultrasound transducer, that propagates deep into the tissue generating orthogonal shearwaves. Their speed, can be quantified (in meters/second) by a proprietary implementation of ARFI technology in a precise liver segment, focusing on a region-of-interest (ROI), and is displayed on the screen. The propagation speed increases with fibrosis severity.

![Fig. 1: ARFI imaging technology. red line: high energy acoustic pulse; green box: sampling ROI for measurements; yellow arrows: shear waves generated by the](image)

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acoustic pulse and propagating orthogonally into liver parenchyma; blue lines: transducer receiving pulses.

References: - Genova/IT

PATIENTS

Our study includes 18 patients (8 males, 10 females; mean age: 61±15) with diagnosis of chronic viral hepatitis (11 HBsAg positive and 7 HCV-RNA positive). All of them underwent liver biopsy (LB) within last 6 months and TE in the last month. Fibrosis was staged on a 0-4 scale according to METAVIR score (F0: no fibrosis# F1: portal fibrosis without septa# F2: portal fibrosis and few septa extending into lobules; F3: numerous septa extending to adjacent portal tracts or terminal hepatic venules; F4: cirrhosis). Exclusion criteria were history of hepatic nodules or masses, hepatobiliary surgery, complications like ascites, pregnancy, and any other co-existing liver disease. TE was performed in all patients with a FibroScan TM device (Echosens - Paris, France) by 2 experienced physicians (more than 200 examinations each). For the 18 patients a median value of the liver stiffness (LS) was obtained, measured in kPa. Only patients with measurements obtained with a success rate of at least 60%, with an IQR<30%, were included.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
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<tbody>
<tr>
<td>Gender</td>
<td>8 Males; 10 Females</td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>61 ± 15</td>
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<tr>
<td>BMI</td>
<td>24.2 ± 5.1</td>
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</table>
| Liver Fibrosis (according to the METAVIR score classification) | F0: not included  
F1: n= 3 (16.6%)  
F2: n= 8 (44.4%)  
F3: n= 7 (38.8%)  
F4: not included |
| Mean ALT values                                      | 1.7 ± 1.9 x ULN            |
| Mean AST values                                      | 1.6 ± 2.1 x ULN            |

Table 1: Main patients characteristics.(xULN: times the upper limit of normal)
ARFI

Arfi was performed in all the patients with a Siemens Acuson S2000 TM ultrasound system provided with Virtual Touch Tissue Imaging and Quantification software. The physician selected the depth at which the liver elasticity has to be evaluated, by placing a measuring box (10 mm long and 5 mm wide) in the desired ROI. The patients were examined supine and in left decubitus in order to investigate the whole liver parenchyma and were asked to stop breathing for a moment during the shear wave velocity (SWV) measurement. ARFI measurement were performed for every liver segment and a median value expressed in meters/second (m/s) was calculated for all of them in order to have a quantitative reproducible measure of the whole liver stiffness. The most discriminating cut-off values were determined from the distribution of SWV according to METAVIR fibrosis stage and were established at 1.18(F#1), 1.28(F#2), 1.60(F#3), 2.0(F#4). The procedure was performed during normal liver examinations and took about 5 minutes per patient. No complications occurred.

Fig. 2: Example of measurement into liver segment n.2

References: Ospedale Evangelico Internazionale di Genova
Fig. 3: Example of measurement into liver segment n.3

References: Ospedale Evangelico Internazionale di Genova
Fig. 4: Example of measurement into liver segment n.4  
*References:* Ospedale Evangelico Internazionale di Genova

**STATISTICAL ANALYSIS**

The statistical analysis was performed collecting data in a Microsoft Excel file and using Med-Calc Software (MedCalc program, Belgium). For numerical variables, mean value and standard deviation were calculated. Spearman's rank correlation coefficient was used to assess the correlation between elastographic methods and with histologic findings (METAVIR scoring system, ordinal scale). Cut-off values were chosen so that sensitivity and specificity would be the highest. A p-value less than 0.05 was regarded as significant for each statistic test.
Fig. 5: Example of measurement into liver segment n.5

References: Ospedale Evangelico Internazionale di Genova
Fig. 6: Example of measurement into liver segment n.6
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Fig. 7: Example of measurement into liver segment n.7

References: Ospedale Evangelico Internazionale di Genova
Fig. 8: Example of measurement into liver segment n.8

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Results

In our preliminary study, valid ARFI measurements were performed in 100% of cases and ranged from 1.19 to 1.91 m/sec. Previous TE measurements resulted valid in 94.4% of cases and ranged from 4.3 to 9.8 kPa. On LB 3 patients had F1, 8 patients were F2, 7 patients resulted F3, no patients were F0 or F4. With our mentioned cut-offs ARFI and TE measurements presented a high correlation between the two techniques ($r=0.693$) ($p<0.0001$); a strong correlation was also found between ARFI and the grade of fibrosis ($r=0.889$) ($p<0.0001$).
Conclusion

Our preliminary study showed that ARFI in association with TE is a highly predictive method in evaluating liver fibrosis in patients with chronic viral hepatitis. ARFI showed a high correlation with the grade of fibrosis and also with TE with the established cut-offs. The combination of the two techniques could be very useful in clinical management of these patients avoiding LB.

Unlike TE, ARFI is a faster examination (about 5 minutes), can be performed also from less-experienced operators (optimal knowledge of liver segmentation is required), and in patients with ascites; it allows a more comprehensive evaluation of the whole liver tissue (right and left lobe) and grants almost zero percentage of failure. The main advantage of ARFI elastography is that this technology is integrated into an ultrasound machine that can also perform real time b-mode liver evaluation and, eventually, Doppler examination and contrast enhanced ultrasonography in the same session (Fig. 9 on page 23, Fig. 10 on page 23, Fig. 11 on page 24). The weak point of our study is the limited number of patients; anyway our preliminary results correlates with more comprehensive studies from other Authors and are encouraging for further work.
**Fig. 9:** Example of portal vein Doppler imaging conducted during a normal US liver evaluation; in the same session it's possible performing ARFI measurement.

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Fig. 10: Example of middle hepatic vein Doppler imaging conducted during a normal US liver evaluation; in the same session it’s possible performing ARFI measurement.

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Fig. 11: Example of contrast enhanced ultrasonography (CEUS) of an hepatic nodular lesion conducted during a normal US liver evaluation; in the same session it's possible performing ARFI measurement.

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References


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