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Acoustic Radial Force Impulse as an effective tool for a prompt and reliable diagnosis of hepatocellular carcinoma – Preliminary data

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Abstract. – ARFI (Acoustic Radiation Force Impulse) is a novel method based on the use of shear acoustic waves remotely induced by the radiation force of a focused ultrasonic beam. Recently, ARFI has been investigated as a non-invasive method for the assessment of liver fibrosis. The reproducibility of ARFI technology was proved in determining liver fibrosis: in detail, for cirrhosis Fibroscan had its best cut-off at ≥ 11 kPa (AUROC of 0.80) whereas ARFI ≥ 2.0 m/s (AUROC of 0.89). By pair-wise comparison of AUROC, ARFI was significantly more accurate than TE for a diagnosis of significant and severe fibrosis.

Due to the low amount of collagen deposition within hepatocellular carcinoma (HCC) nodules in a context of "hard" cirrhotic parenchyma, ARFI propose itself also as a novel, specific method for an early identification of primitive neoplastic nodules during the follow up of cirrhotic patients. The diagnostic accuracy can be demonstrated either versus the surrounding liver tissue or versus dysplastic or metastatic nodules. Further studies are required to confirm ARFI as a useful tool for HCC follow-up.

Key Words:
Acoustic radiation force impulse, Hepatocellular carcinoma, Cirrhotic parenchyma.

Short Report

In HCV-infected patients, the prognosis and the clinical management of chronic liver disease are dependent on the extent of fibrosis progression[1]. In fact, any kind of therapeutic approach (direct antiviral or interferon-based) raises significantly its chance of getting a successful response on the basis of how early it has been started[1,2].

Biopsy, even if invasive, painful and with potentially life-threatening complications, remains the gold standard for determining the fibrotic stage of liver disease[2]. Unfortunately, the diagnostic accuracy of a liver biopsy for assessing liver fibrosis is influenced by many factors: inconsistency in defining pathological features, variety of scoring systems, technical processing of the specimens, and variations and quality of biopsy samples[3]. As a consequence, several alternative methods, both direct and indirect, have been investigated to predict the grade of fibrosis[4,5].

Acoustic Radiation Force Impulse (ARFI) is a novel method, with original technological solutions based on the use of shear acoustic waves remotely induced by the radiation force of a focused ultrasonic beam[6]. ARFI is a registered software that runs on the hardware of a conventional ultrasound. During the course of ultrasound examination, the operator command (Push), generates mechanical energy into the examined tissue. This is achieved through a high frequency ultrasound beam that produces a mechanical deformation at the focal point of the beam (Pulse).

The micro-area of organ parenchyma affected by the compression called Region Of Excitation (ROE), undergoes a 10 to 20 microns deformation. This size of deformation is critical to trigger a shear-wave with an adequate Signal Noise Ratio (SNR).

The propagation of three-dimensional shear wave strictly depends on the medium viscoelasticity. To simplify the calculation of speed, ARFI includes as representative only the wave perpendicular (radial) to the ROE axis of symmetry. To calculate the progression of the shear wave, ARFI measures the Time-To-Peak (TTP) of the wave within a target area close to the ROE, denominated Region of-Interest (ROI). The ROI area is 0.6 × 1 cmL. The box of the ROI can be freely positioned by the operator up to a depth of 8 cm during a traditional ultrasound examination.

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Table I. Median liver ARFI velocimetric value in different clinical conditions (Rizzo L et al, unpublished data).

Clinical condition	Median ARFI value (m/sec)	Range
Normal liver	1.1	(0.8-1.4)
Chronic hepatitis F2 Metavir	1.5	(1.2-1.7)
Liver cirrhosis	2.2	(1.9-2.9)
Hepatocellular carcinoma	1.2	(1.0-1.7)

Recently, ARFI has been investigated as a non-invasive method for the assessment of liver fibrosis, with particular reference to chronic hepatitis C[6].

A number of studies confirmed ARFI as an even more reliable method than Fibroscan for analysing the progression of chronic liver disease towards cirrhosis[6].

In particular, we observed that ARFI had a significantly higher discriminatory capacity than Fibroscan for intermediate stages of fibrosis. In fact, the comparison between Fibroscan and ARFI respective AUROCs (area under the receiver operating characteristics curves of ARFI) achieved statistical significance both for significant and severe fibrosis. Even though by pairwise comparison analysis a significant difference between the two tools was not found for diagnosis of cirrhosis, the partial AUROC analysis resulted in a significantly better performance of ARFI in all three stages of fibrosis[6].

A severe complication encountered during the course of chronic hepatitis C both in immune competent and in immune defective patients (such as those coinfected with HCV and HIV-1) is the occurrence of hepatocellular carcinoma (HCC)[7]. This is the reason for a strict diagnostic follow up among individuals affected with advanced virus-related chronic liver disease, which could represent the only reasonable way to a prompt diagnosis and an early radical therapeutic approach[8-12].

Recently, ARFI elastometry proved to be useful for evaluating hepatic focal lesions. In particular ARFI showed a satisfactory specificity for discriminating malignant lesions[13,14]. In chronic hepatitis C patients with no previous oncological history, the specificity of ARFI in diagnosing or excluding malignant lesions might help to simplify the diagnostic pathway for HCC by definitively dropping or deferring other expensive and time-consuming contastographic exams during the follow up.

Since the onset and the advancement of fibrosis in the liver is known to correspond with changes in the bulk elasticity of the organ, it can be expected that in progressing CHC and in cirrhosis the background elastometric values of liver parenchyma result remarkably increased in comparison with normal livers. On the contrary, HCC has a significantly lower amount of collagen deposition, resulting much softer than the surrounding hepatic parenchyma with very low elastometric values[13]. In our, yet preliminary and unpublished caseload, median velocimetric values within the HCC nodules was 1.2 m/sec whereas in the surrounding cirrhotic livers ARFI median values were 2.2 m/sec (p = 0.05). These results were confirmed by an excellent interobserver reproducibility.

This phaenomenon allows also a prompt differential from displastic nodules which are either easily identified by morphological B-Mode methods or characterized by an elastometric velocity comparable or minimally reduced versus the surrounding parenchyma. Our yet unpublished data confirm the actual capacity of ARFI to distinguish HCC from dysplastic nodules with a specificity rate of 85%.

Moreover other Authors[14] showed also ARFI images to be superior to B-mode for evaluating both the results of Radio Frequency Ablation (RFA) of liver tumors and HCC recurrences after RFA.

Finally, ARFI proved to be useful for differentiating liver metastasis, with a specificity of 89% and a negative predictive value of 93% when 2.72 m/sec was chosen as a cutoff value[15].

In conclusion, the current availability of ARFI might simplify the echographic approach to either diffuse or focal liver diseases providing rapid and reliable results with poor expenses.

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