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Acoustic Radiation Force Impulse (ARFI) ultrasound imaging of solid focal liver lesions

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ABSTRACT

Objective: The aim of this paper was to evaluate the application of ARFI ultrasound imaging and its potential value for characterizing focal solid liver lesions.
Materials and methods: In this multicentric prospective study, over a total non-consecutive period of four months, all patients underwent ARFI US examination. Two independent operators performed 5 measurements per each lesion and 2 measurements in the surrounding liver. According to the definitive diagnosis, a mean velocity value and standard deviations were obtained in each type of focal solid lesion, compared by using *t*-test, and the inter-operator evaluation was performed by using the Student's *t*-test. A comparison between the total mean values of each type of lesion and the mean value of the parenchyma was performed.
Results: 40 lesions were evaluated and a total of 400 measurements were obtained. The lesions were: 6/40(15%) hepatocellular carcinomas, 7/40(17.5%) hemangiomas, 5/40(12.5%) adenomas, 9/40(22.5%) metastases and 13/40(32.5%) focal nodular hyperplasias. The total mean values obtained were: 2.17 m/s in HCCs, 2.30 m/s in hemangiomas, 1.25 m/s in adenomas, 2.87 m/s in metastases and 2.75 m/s in FNHs. The inter-operator evaluation resulted non-statistically different ($p > 0.05$). A significant difference ($p < 0.05$) was always found by comparing adenomas to the other lesions. 160 measurements were obtained in the surrounding parenchyma, with a no significant difference between values measured in adenomas and in the surrounding liver.
Conclusions: ARFI technology with Virtual Touch tissue quantification could non-invasively provide significant complementary information regarding the tissue stiffness, useful for the differential diagnosis of focal solid liver lesions.

1. Introduction

Solid focal liver lesions are very common findings during abdominal examinations. The accurate characterization and the differential diagnosis between different types of focal liver lesions are important aims that all the imaging modalities available today should satisfy [1–6]. Characterization deals with the surrounding liver parenchyma. In a defined clinical setting, as cirrhosis or known primary carcinoma, the detection of a solid focal liver lesion could be considered a malignancy until proven otherwise [1,3,7]. However, in patients with known history of malignant tumor about 50% of lesions under 2 cm in size are benign [4]. On the other hand, in some cases the detection of liver metastases is the first finding in patients with unknown primitive cancer.

Conventional ultrasonography (US) is often the first imaging modality performed to screen for or study hepatic lesions because of its low cost and wide availability [7]. Color-Doppler, Tissue Harmonic Imaging and, more recently, the administration of microbubble contrast agents significantly improve the characterization of solid focal liver lesions [2,4,6,7]. Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) represent the second line examinations available to accurately characterize the lesions previously detected, but they are more expensive and less available [2,5]. These imaging modalities with the administration of contrast agents such as contrast-enhanced US, CT and MRI, assess lesion morphology and vascularization with a high diagnostic accuracy owing to their specific features, well described in literature [1–6]. Nevertheless, invasive studies are sometimes still required to make a definite diagnosis.

Acoustic Radiation Force Impulse (ARFI) imaging is a new ultrasound-based modality, integrated into a conventional US system, able to non-invasively evaluate the stiffness of deep tissues

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[8]. Since its recent introduction, only few papers in literature describe its applications in studying normal subjects [9,10] and diffuse pathologies [11,12]. Only two papers describe the application of ARFI technology in the study of solid focal liver lesions, with different results [13,14]. ARFI imaging allows quantitative and qualitative measurements in a real-time mode, giving innovative and complementary information to conventional US.

The present study was performed to evaluate the application of US ARFI imaging and its potential value for characterizing focal solid liver lesions.

2. Materials and methods

This multicenter study was approved by the Institutional Review Board of each Institute and conducted in accordance with the principles of Helsinki Declaration. A written informed consent was obtained from all patients prior to the ARFI examination.

2.1. Patients

Over a total non-consecutive period of four months, all included patients studied in the three centres involved, respectively named I, II and III, prospectively underwent ARFI examination. The non-consecutive period was due to the temporary availability of the ARFI system in the hospitals.

Inclusion criteria were: presence of a solid focal liver lesion, pathologically proved or definitely diagnosed by accordance of at least two imaging methods, such as contrast-enhanced US, CT or MR, as reported into the guidelines [7]; absence of any previous local treatments (i.e. percutaneous ethanol injection, radiofrequency ablation, trans-arterial chemo-embolization); lesion well visualized at conventional US, with a minimum diameter greater than or equal to 1.5 cm, localized at a maximum depth of 5.5 cm. Furthermore, the patients had to be compliant and able to hold their breath properly to be enrolled.

2.2. Imaging techniques

ARFI imaging was performed with an Acuson S2000 ultrasound system (Siemens, Erlanger, Germany), using convex probes (4C1), Tissue Harmonic Imaging (THI; 4 MHz) and Mechanical Index of 1.7. On a B-mode US image the lesion to be interrogated for elastic properties is identified utilizing a Region of Interest (ROI), characterized by a box with fixed dimension of 1 cm × 0.5 cm and a maximum depth of 5.5 cm. The ROI was entirely included into the lesion, in biggest ones changing the ROI location to cover the entire mass as much as possible, without including any vessels or biliary structures. The potentially presence of any degeneration (i.e. necrotic or cystic or hemorrhagic or calcified portion) or any other specific macroscopic finding, such as fibrotic scar, have not to be comprised into the ROI. Measures in the surrounding parenchyma were also performed, with the ROI within 2–3 cm from the focal lesion, taking care not to comprise any vascular or biliary structures. The target tissue is mechanically "pushed" by short-duration forces (less than 1 ms) that generate localized displacements. The shear waves produced propagate perpendicular to the acoustic pulse away from the target ROI. The calculation of the shear wave speed is expressed in meters per second.

2.3. Data analysis

Two independent operators per centre, unaware of the definitive diagnosis of the lesions and of the results derived from the other imaging modalities, performed ARFI examinations. All measurements were achieved after a short inspiration in order to improve the visualization of the lesion. Both operators performed 5 measurements per lesion and 2 measurements in the surrounding liver. As reported above, the ROI was located in different portions of the lesions, in order to evaluate the entire mass. Since Virtual Touch tissue quantification expresses the shear wave speed in solid materials as numerical values, only numerical results were taken into consideration in this study. Thus, non-valid measurements due to an erroneous ROI positioning (i.e. necrotic or cystic portion of a lesion, vessels or biliary structures within the ROI) or patient motion, expressed by the system as "N/A" (not-available) or "XXXX" or "0", were excluded.

All data supplied by the three centers were collected and analyzed by the centre "I" that coordinated the study. Wave velocity values and definitive diagnoses were compared.

2.4. Statistics

According to the definitive diagnosis, a mean wave velocity value was obtained from all measurements performed by each operator in each type of focal solid liver lesion. The inter-operator evaluation, calculated comparing all measures performed by both operators in each centre, consisted of the comparison between these mean values. The statistical analysis was performed by using the Student's *t*-test and a p value < 0.05 was considered statistically significant.

Furthermore, the total mean value and standard deviations derived from all measurements performed by both operators in each group of lesion were calculated. A statistical comparison between the total mean wave velocity values, typical for each group of lesions, was achieved by using a *t*-test. A p value < 0.05 was considered statistically significant.

Finally, a comparison between the total mean values of each type of lesion and the mean value of the surrounding parenchyma was performed.

3. Results

A total of 40 lesions underwent Virtual Touch tissue quantification, 20/40 (50%) in centre "I", 15/40 (37.5%) in centre "II" and 5/40 (12.5%) in centre "III", respectively. In patients with more than one lesion, the largest and best visualized was examined. A total of 400 valid measurements (5 per lesion per operator) were obtained.

According to the definitive diagnosis, the lesions were: 6/40 (15%) hepatocellular carcinomas (HCCs; mean size: 38 mm, range: 18–85 mm), 7/40 (17.5%) hemangiomas (mean size: 25 mm, range: 15–45 mm), 5/40 (12.5%) adenomas (mean size: 31 mm, range: 16–45 mm), 9/40 (22.5%) metastases (mean size: 35 mm, range: 15–55 mm) and 13/40 (32.5%) focal nodular hyperplasias (FNHs; mean size: 38 mm, range: 19–78 mm). The metastatic lesions derived from different primary tumors including pancreatic adenocarcinoma, pancreatic neuroendocrine tumor, gallbladder tumor, colon and breast cancers. All hemangiomas, 10/13 FNHs, 2/6 HCCs and 2/9 metastases were diagnosed based on typical findings at contrast-enhanced ultrasound (CEUS) and/or CT and/or MRI. The other lesions were pathologically confirmed after biopsy (4/6 HCCs and 7/9 metastases) or surgical resection (3/13 FNHs, owing to larger dimensions) performed immediately after ARFI examination.

The mean wave velocity values and their standard deviations derived from all measurements performed by both operators in each type of lesion are reported in Table 1. In particular, the total mean wave velocity values obtained were: 2.17 ± 0.85 m/s in HCCs (Fig. 1), 2.30 ± 0.95 m/s in hemangiomas (Fig. 2), 1.25 ± 0.37 m/s in adenomas (Fig. 3), 2.87 ± 1.13 m/s in metastases (Fig. 4) and 2.75 ± 0.95 m/s in FNHs (Fig. 5). The inter-operator evalua-