Cutoff Values for Alcoholic Liver Fibrosis Using Magnetic Resonance Elastography Technique

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ABSTRACT

Background: Due to the lack of cut-off values validated for specific liver diseases, the purpose of this study was to set up specific Magnetic Resonance Elastography (MRE) cut-off values for asymptomatic liver fibrosis in alcoholic patients.

Methods: Ninety patients underwent three clinical exams. The liver stiffness was measured locally with the Fibroscan, and globally through cartographies of shear modulus generated with MRE. The Fibroscan method was chosen as the gold standard in order to classify the fibrosis. The liver score was also obtained with the Fibrometer A, and the diagnostic performance of the methods was analyzed with ROC curves and cut-off values were calculated.

Results: Spearman correlation and AUROC revealed that MRE is a better diagnostic method than the Fibrometer A, to identify various levels of fibrosis. The results showed that the Fibrometer A was adapted for severe fibrosis. The MRE cut-off values are: F1 : 2.20 kPa, F2 : 2.57 kPa, F3 : 3.31 kPa and F4 : 4 kPa and was not influenced by the GOT level. By using the ultrasound cut-off values attributed for alcoholism, 66% of patients had a similar liver fibrosis diagnosis as the MRE cut-offs. However, both imaging techniques did not provide the same distribution for minor fibrosis.

Conclusions: None of the imaging techniques (Fibroscan, MRE) could replace the gold standard of the biopsy. However, due to the risk and the unnecessary procedure for the present recruited alcoholic patients, the Fibroscan method was chosen as the reference. Since MRE is currently being used as a clinical exam, the present MRE cut-offs could aid clinicians with their diagnosis of liver fibrosis for alcoholism disease.

Key Words: alcoholic liver stiffness, magnetic resonance elastography, Fibroscan, cut-offs.

INTRODUCTION

Alcoholism disease concerns more and more people and becomes a major public healthcare problem with a relevant social and economical impact. Alcohol is the main cause of chronic liver disease, which may end up to cirrhosis, and new treatments such as baclofene are clinically test to fight this addiction (Paille, 2011).

To determine the stage of the liver fibrosis, biopsies have remained the gold standard. However, due to the invasive process and the risk incurred by the patients for the small harvested liver sample, other biochemical tests (Fibrotest, Fibrometer A) and imaging techniques (ultrasound and magnetic resonance elastography) have been developed in order to estimate the liver stiffness. Alcoholic liver disease (ALD) present various clinical settings (Mathurin et al., 2012; Mueller and Sandrin, 2010) such as inflammation (Arena et al., 2008; Mueller et al., 2010; Sagir et al., 2008), cholestasis and venous pressure (Millonig et al., 2008), which could influence the liver stiffness.

Serum markers such as Fibrotest and Fibrometer A are accurately able to identify high level stages of liver fibrosis or cirrhosis, but are not accurate with regard to identifying intermediate levels of liver fibrosis (Morra et al., 2008; Rockey and Bissell, 2006). Moreover, Naveau et al. (2009) showed that the Fibrometer A, which is specific for alcoholic liver disease, provided similar results as the Fibrotest.

In a way to better depict the intermediate liver stages and to avoid invasive procedures, elastography techniques have been used to assess the liver stiffness. Thus, the transient elastography (TE) method was used for alcoholic patients (Nahon et al., 2008; Trabut et al. 2012), and Gelsi et al. (2011) found changes in liver stiffness according to the consumption or the cessation of alcohol, suggesting the usefulness of the transient elastography to follow the consequence of this pathology (Gelsi et al., 2011). Transient elastography was therefore extensively applied for the measurement of liver fibrosis stiffness, and Janssens et al. (2010)

have analyzed the influence of the cut-off values, previously validated for chronic hepatitis C, on liver stiffness classification for other etiologies such as alcoholism (Janssens et al., 2010). It was concluded that these cut-offs were able to predict severe fibrosis (≥ F3) for alcoholic patients. In the literature, only Nguyen-Khac et al. had set up all of the intermediate cut-off values for asymptomatic liver fibrosis in alcoholic patients using the Fibroscan technique (Nguyen Khac et al., 2008). It should be noted that these cut-offs are now used in clinical practice for alcoholic patients, but ultrasound elastography techniques are difficult to use accurately on obese patients and on persons exhibiting a narrow rib interspace (Nguyen and Talwalkar, 2011).

Magnetic Resonance Elastography (MRE) which is not limited by these factors (obesity, ascite, rib space) allows for a more global characterization of liver stiffness compared to the local measurements performed using ultrasound elastography techniques (Bensamoun et al., 2008). However, MRE results can also be altered by other criteria such as severe hepatic iron and portal hypertension and it therefore remains a more restrictive method which can be performed at the same time as an MRI test (Siegel, 2011). The MRE technique has been applied to patients with chronic liver disease and Huwart et al. (2007) showed that it more accurately depicts liver fibrosis staging compared to biochemical tests and ultrasound elastography (Huwart et al., 2008). Recently, Shire et al. (2011) performed a study focused only on the repeatability of the MRE technique to estimate the liver stiffness and has demonstrated the reproducible behavior of MRE to assess liver stiffness in HCV patients, and its capability to differentiate moderate fibrosis (≥ F2) from that of healthy liver (Shire et al., 2011). The cut-off values, for the MRE technique, was determined for different liver etiologies such as chronic hepatitis C and B, alcohol abuse, autoimmune disease, α1-antitrypsin deficiency among others (Huwart et al., 2007). To our knowledge, no MRE studies have proposed cut-off values for specific liver diseases. Due to the lack of cut-off values, the

purpose of this study was to set up specific MRE cut-off values for asymptomatic liver fibrosis in alcoholic patients using Nguyen-Khac et al. cut-off data base (Nguyen Khac et al., 2008), defined specifically for alcoholic patients using the fibroscan, as the reference. Obviously, none of the imaging techniques could replace the gold standard of the biopsy, even though biopsy may also provide an error and may not be representative of the entire liver volume. However, due to the risk of this invasive exam for the patients, and the unnecessary procedure for the present recruited alcoholic patients, the Fibroscan method was chosen as the gold standard (Kircheis et al., 2012). Subsequently, the diagnostic performance of the MRE technique was compared to the fibroscan and fibrometer A.

I. MATERIALS AND METHODS

Patients

Ninety patients (68 men and 22 women, mean age: 44.7 years, mean Body Mass Index: BMI = 23.8 ± 3.9 kg/m^2) currently enrolled in alcohol dependence programs were recruited from 2009 to 2012 at the alcoholism department. Patients were hospitalized for 3 weeks for purposes of detoxification and to ensure that they followed a specific program for rehabilitation. During the first week, all patients underwent a blood test and the level of transaminase was analyzed (Glutamic Oxaloacetic Transaminase (GOT) = 83.2 ± 88.8 U/L, Glutamic Pyruvic Transaminase (GPT): 70.9 ± 72.5 U/L, Gamma-glutamyltransferase (GGT): 448.9 ± 780.5 U/L, Alkaline Phosphatase (ALP): 97.3 ± 82.4 U/L). During the second week a Fibroscan exam was performed and patients satisfying the following exclusion criteria: claustrophobia, mental instability, existence of hepatitis, suspicion of hemochromatosis (coefficient of saturation > 45%) and invalidated Fibroscan test were selected for a MRE and Fibrometer A tests performed only few days after the Fibroscan. The study was approved by the Institutional Review Board and written informed consent was obtained.

Classification of the liver fibrosis staging using Fibroscan

The experimental setup was designed similar to Bensamoun's study (Bensamoun et al., 2008), who compared liver stiffness as measured by two different imaging techniques (Fibroscan and MRE) and is briefly summarized here. During the Fibroscan experiment, the subjects laid down with the right arm in maximal abduction. An ultrasound probe (3.5 MHz) was placed between intercostal spaces and perpendicularly to the skin. A vibrator located on the probe sent low-frequency (50 Hz) shear waves into the right liver lobe. This specific probe

is an emitter-receptor that measures the velocity of the waves propagated within the liver tissue.

The signal recorded during the ultrasound test is represented through an elastogram reflecting the depth of propagation as a function of the acquisition time. The liver stiffness (Young's modulus) is represented by the slope of the straight line. Young's modulus was calculated as an average of 20 validated measurements, corresponding to a success ratio ≥ 60% with an interquartile ranges (IQR) < 30%. Moreover, the acquisitions were defined as valid when the shape of the signal recorded during the ultrasound test revealed a crimp behavior reflecting the hepatic tissue. The waves were propagated at a depth of 60 mm and Young's modulus was calculated with the following equation: $E=3\mu$.

Biopsy being a risky and an unnecessary procedure for alcoholic patients, the fibroscan exam was used as the reference technique to identify the level of fibrosis (F_S), and the distribution of the patients was composed as follow: $F0_S$ (N=18), $F1_S$ (N=20), $F2_S$ (N=27), $F3_S$ (N=12), $F4_S$ (N=13).

Magnetic Resonance Elastography (MRE)

The subjects lay supine on a 1.5 T Signa HDx MRI machine (General Electric, Milwaukee, WI, USA) and the center of a cylindrical acoustic driver (diameter: 16 cm) was placed at the same level as the diaphragm and positioned in contact with the rib cage. The body coil was used and the acoustic driver had a long hose connected to a large active loudspeaker. This system created time-varying pressure waves propagating shear waves within the abdomen at 60 Hz. MRE images were collected with a motion-sensitized gradient-echo sequence, collected at two time offsets (phase offsets) between the start of the motion and the motion encoding gradients, using a single number of gradients. Two offsets were recorded in a row, and during this acquisition the subjects held their breathing to avoid the

motion of the liver caused by the displacement of the diaphragm. The total scan time recorded was 32s corresponding to 2 breath-holding periods of 16s.

The acquisition matrix was 256x64 (which was interpolated to 256x256), the flip angle was 30°, the field of view was between 34 and 48 cm in function of the morphology of the subject, the receiver bandwidth was 15.63 kHz and the frequency direction was R/L. According to the MRE parameters, the TR was 100 ms and the TE corresponded to the minimum echo time (26.8 ms) that allowed for motion encoding.

MRE axial images were recorded for each patient in the same liver region where the Fibroscan was performed. Phase images (Fig. 1A,C,E) showed the shear wave displacement within the liver tissue and the cartography of the shear modulus (μ) (Fig. 1B,D,F) revealed the distribution of the liver stiffness. The mapping of stiffness was automatically generated from the masked wave displacement image (pre-filtered with a 4^{th} order bandpass filter) using the local frequency estimation algorithm (Manduca et al., 2001). Assuming that the liver tissue is locally homogeneous, the regions of interest (ROI), which were composed of two front waves, were placed around fibrotic areas in order to measure the average stiffness and to analyze the localization of the fibrosis within the liver. Minor fibrosis (F1 and F2) exhibited smaller wavelength (Fig. 1A) than severe fibrosis (Fig. 1E), therefore the ROI was placed in the superior right lobe (i.e. in the anterior liver area: Fig. 1D) while larger ROI, representing the entire liver, were drawn for severe (F3 and F4) fibrosis. Repeatability of MRE acquisitions was conducted on each subject, on the same day but at different times.

Laboratory tests

In addition to the stiffness measurement, a laboratory test was analyzed to assess the fibrosis level. Thus, the fibrometer A (BioLiveScale, Angers, France) calculated the intermediate stages (F0, F0/1, F1/2, F2/3 and F4) of the liver fibrosis for each patient, as a

function of the following parameters: prothrombin time (PT), Alpha2 macroglobulin (A2M), hyaluronic acid (HA) and the age of the patient (Calès et al., 2005). It should be noted that the fibrometer A is a test which provides a combination of the intermediate grades.

Statistical analysis

A Spearman correlation test was used to evaluate the correlation between the level of fibrosis and the imaging (Fibroscan, MRE) techniques as well as the laboratory test (Fibrometer A).

Paired t-tests were performed in order to compare the stiffness measurements between the successive intermediate (from F0 to F4) liver stages measured for each technique. In addition, paired t-tests were also used to compare the liver stiffness data, at each intermediate level, obtained between the Fibroscan and MRE techniques.

The diagnostic performance of the MRE technique as well as the Fibrometer A were performed by using the cut-offs of the Fibroscan, validated for alcoholic patients, and with the receiver-operating characteristic (ROC) curves leading to the analysis of the following parameters: sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV). Moreover, the area under the ROC curve (AUROC) was analyzed in order to define the performance of the applied methods. Then, from the ROC curve, the Youden index, equal to the sensitivity + specificity -1, was maximized in order to quantify the cut-off values for the MRE and the Fibrometer A.

All the statistical tests were significant for a $P<0.05$ as calculated using the software Statgraphics 5.0 (Sigma Plus, Maryland, USA).

II. RESULTS

Comparison of the liver stiffness obtained with imaging (Fibroscan, MRE) techniques and the laboratory (Fibrometer A) test using the fibroscan alcoholic cut-offs.

The Spearman correlation revealed that the MRE technique is a better method ($r = 0.817$), to identify the different levels of fibrosis for alcoholism disease compared to the Fibrometer A ($r = 0.496$) tests.

Figure 1 shows an increase of the wavelength with the level of fibrosis, leading to stiffer areas located within the cartography of the shear modulus. It can be noticed that alcoholic patients F2s revealed a stiffer region (about 1kPa) in the anterior area of the liver (Fig. 1D), indicating the possible starting point of the fibrosis. Figure 2 also showed the evolution of the liver fibrosis characterized with the three different tests, which revealed an increase in the stiffness measurement and an increase in the liver score with the level of fibrosis. As expected, the Fibroscan technique revealed a significant liver stiffness difference (Fig. 2A) between all the intermediate stages, while the MRE technique did not succeed to differentiate the stages F1s from F2s (Fig. 2B) by using the cut-off values previously established for the fibroscan. The results obtained with the Fibrometer A (Fig. 2C) showed only significant ($P<0.05$) score differences between the severe (F3 and F4) fibrosis levels.

Figure 3 compared the mean shear stiffness measured with the imaging (MRE and Fibroscan) techniques. The results were in the same range even though it was determined that there was a slight but significant difference ($P<0.05$) in stiffness between both techniques, for all fibrosis levels. The present comparison is in agreement with the literature (Bensamoun et al., 2008; Huwart et al., 2008). A strong increase in the shear stiffness was revealed for both imaging techniques in alcoholic patients F4s due to the composition of this group made up of more severe fibrosis, and other factors such as hepatic inflammation, portal pressure, and so

on. In addition, the comparison of the standard deviation between MRE and Fibroscan techniques revealed a higher variation for the fibroscan.

Comparison of the diagnostic performance between MRE and Fibrometer A tests

Figure 4 shows the results of the areas calculated under the ROC curve and it was found that the MRE technique is a method with a high diagnostic performance for the identification of all the intermediate alcoholic liver stages while the Fibrometer A is adapted to identify only severe alcoholic fibrosis (F4).

Table 1 summarizes the different MRE parameters (cut-off, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV)) obtained from the ROC analysis dedicated to alcoholism disease. The result of the MRE cut-off for all patients are $F1_{MRE}$: 2.20 kPa, $F2_{MRE}$: 2.57 kPa, $F3_{MRE}$: 3.31 kPa and $F4_{MRE}$: 4 kPa. It must be noticed that the GOT level did not influence the MRE cut-off values. The calculated Fibrometer A cut-off values were: $F1_{Fibrometer}$: 0.63 kPa, $F2_{Fibrometer}$: 0.71 kPa, $F3_{Fibrometer}$: 0.27 kPa and $F4_{Fibrometer}$: 0.64 kPa. It can be noticed that the cut-offs did not vary from the level $F1_{Fibrometer}$ to $F4_{Fibrometer}$, indicating that the fibrometer A is not adapted to depict intermediate liver fibrosis.

Then, a new distribution of the fibrosis levels for alcoholic patients was made using the MRE cut-offs (table 2). The results showed that 66% of patients had a similar liver fibrosis as those defined with the Fibroscan cut-offs attributed to alcoholism. Table 2 indicates that Fibroscan and MRE provide a similar distribution for inexistent fibrosis (F0) and for severe fibrosis (F3). However, these imaging techniques did not provide the same distribution for minor fibrosis (F1 and F2). Indeed, 20 and 27 patients were classified as $F1_S$ and $F2_S$, with the Fibroscan technique, respectively, while the new MRE classification indicated 17 and 22 patients for the groups $F1_{MRE}$ and $F2_{MRE}$, respectively.

DISCUSSION

The originality of this study is to take into consideration the etiology of the liver pathology in order to set up cut-off values to properly differentiate the intermediate levels of fibrosis for alcoholic patients which can ultimately be used for accurate non-invasive clinical diagnosis.

The comparison of the three different tests (Fibroscan, MRE, and Fibrometer A) revealed that the Fibrometer A test can be used to depict severe alcoholic fibrosis while both imaging techniques were able to differentiate the intermediate fibrosis levels. Fibroscan and MRE are complementary imaging techniques characterizing locally and globally the liver tissue, respectively. In a previous study (Bensamoun et al., 2008), similar stiffnesses were found between Fibroscan and MRE methods for healthy subjects demonstrating the capability of the MRE technique to measure healthy liver. The same conclusion was found in the present study for alcoholism liver disease. Standard deviations for F4 patients showed a greater variation for the Fibroscan technique, revealing its sensitivity to local stiffness measurements. Indeed, F4 patients presenting liver tissue changes such as thicker subcutaneous fat tissue above the ribs, a more important blood flow circulation as well as a high heterogeneous local tissue, the placement of the ultrasound probe, as well as the twenty recorded acquisitions, could be difficult leading to a higher range of liver stiffness obtained with the Fibroscan compared to the MRE technique, which is less influenced by the intrinsic liver modifications. MRE method provides cartography of stiffness allowing for the visualization of fibrotic regions within the entire liver and this information is of importance for the follow up of liver disease. Moreover, the cartographies of stiffness, corresponding to F2s patients, and revealing fibrotic areas in the anterior zone could be used as an indicator for the clinician to investigate possible areas of fibrosis (for patient F2s) by placing the ultrasound probe in this region.

In the literature, studies have characterized the area under the ROC curve (AUROC) and it was demonstrated that the Fibroscan technique was found to be more adapted than the Fibrometer A for alcoholism liver pathology (Nguyen Khac et al., 2008), and less adapted than magnetic resonance elastography (MRE) technique from a study performed on different liver etiologies (Huwart et al., 2008). AUROC were mainly built using the biopsy as the gold standard while in the present study the Fibroscan was used as the reference. However, due to the risk of this exam for the patients, and the unnecessary procedure for the present recruited alcoholic patients, the Fibroscan method was chosen as the gold standard. We are conscious that none of the imaging techniques could replace the gold standard of the biopsy, even though biopsy may also provide an error of 25% (Friedman, 2008), and the extracted sample may not be representative of the entire liver volume. The AUROC corresponding to the Fibrometer A and calculated for the intermediate fibrosis levels of the present study were in the same range as the one of Nguyen-Khac's study until stage F3, while a higher performance was found for the most severe stage F4 (0.950 vs 0.85 for Nguyen-Khac's study). This may be due to the lower number of F4 patients recruited in the present study. Moreover, the comparison of the AUROCs obtained with MRE technique revealed similar data as Huwart et al. (2008) for patients suffering of different liver pathologies, suggesting that the AUROC is not sensitive to the liver etiology.

According to this present study, the MRE cut-off values, calculated for all patients, cannot be correlated to those found by Nguyen-Khac's study, for the same type of liver disease, using the standard equation $E_{\_cut\text{-}offs\_TE} = 3\ \mu_{\_cut\text{-}offs\_MRE}$ (Table 3). The comparison of MRE and transient elastography cut-offs revealed that patients will be more easily diagnosed F1 using the Fibroscan ($F1_{Nguyen\text{-}Khac}$: 1.96kPa) while using MRE cut-offs ($F1_{MRE}$: 2.2 kPa) the patients will be diagnose healthy, i.e F0 (table 3). Conversely, F4 patients will be more easily diagnosed at this level with MRE cut-offs ($F4_{MRE}$: 4 kPa) than using the Fibroscan ($F4_{Nguyen\text{-}}$

$_{Khac}$: 6.5 kPa) technique. The comparison of the present MRE cut-offs for alcoholic patients, with those already established by Huwart's study (2008) using MRE tests performed on liver disease from different etiologies, revealed a higher stiffness difference between the cut-offs of levels F1 and F2 ($\Delta_{F1/2\_Alcoholism}$ = 0.37 kPa vs $\Delta_{F1/2\_Huwart}$ =0.07 kPa), indicating a better accurate evaluation of moderate fibrosis using the new set up of MRE cut-offs (table 3). Indeed, by using Huwart's MRE cut-offs it is almost impossible to differentiate the fibrosis level F1 from F2 (Huwart et al., 2008). Concerning the stiffness interval between the cut-offs for the levels F2 and F3, the present stiffness difference ($\Delta_{F2/3\_Alcoholism}$ = 0.74 kPa) is in agreement with Huwart's study (Huwart et al., 2008). However, the stiffness difference between the cut-offs of levels F3 and F4 remaining stable ($\Delta_{F3/4\_Alcoholism}$ = 0.69 kPa) for the present alcoholism study, compared to Huwart's study who exhibited a larger interval ($\Delta_{F3/4\_Huwart}$ = 1 kPa). Thus, with the new set up of MRE cut-offs, it is more difficult to classify patients F≥ 3 compared to the MRE cut-offs of Huwart. In order to characterize the impact of the cut-offs on the liver staging, a new distribution of the present alcoholic patients were made using the MRE cut-off values of Huwart's studies. The result showed that only one patient was diagnosed as F1 using Huwart's cut-offs, while a total of 17 patients were diagnose F1 with the present MRE cut-offs (table 2). Even if these changes of distribution concerns moderate fibrosis, the present study demonstrates an effect of the cut-off values on the liver fibrosis classification. In addition, it must be noticed that the variation of the cut-offs values obtained between the MRE techniques may be due to the different protocols which vary in frequency, inversion algorithm (LFE, PG, MSDI), ROI placement in the right or left liver lobes and so on. For instance, a recent study has demonstrated a correlation between the applied range of frequency and the materiel properties of the clinical liver driver (Leclerc et al., 2012). All these factors may induce a mis-classification of the patients.

The present MRE protocol has been standardized (frequency, liver driver, inversion algorithm, …) to be currently used in Europe and the United State as a clinical exam (Nguyen and Talwalkar, 2011). Thus, the present MRE cut-offs could assist clinicians with regard to the diagnosis of liver fibrosis resulting from alcoholism disease. Furthermore, it is necessary to establish cut-off values for the various stages of liver disease in order to accurately diagnose these patients.

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Figure legends

Fig. 1. Phase images (A, C, E), showing the propagation of the shear waves (λ: wavelength) inside the liver of alcoholic patients, and the corresponding cartography of shear modulus (μ) (B, D, F) representing the liver stiffness measured inside selected regions of interest (ROI).

Fig. 2. Evolution of the alcoholic liver fibrosis using imaging techniques (A: Fibroscan and B: MRE) and laboratory test (C: Fibrometer A) (* $P < 0.05$).

Fig. 3. Comparison of the mean shear stiffness measured with the Fibroscan and MRE techniques. (* $P < 0.05$) for all the intermediate liver fibrosis.

Fig. 4. Comparison of the ROC curves obtained from MRE experiments and Fibrometer A test for moderate and severe liver fibrosis. Areas under the ROC curves (AUC) for both tests were measured with 95% confident interval, for the different intermediate liver alcoholic fibrosis, using the Fibroscan technique as the reference.

TABLES

		$F1_{MRE}$	$F2_{MRE}$	$F3_{MRE}$	$F4_{MRE}$
MRE Cut-off (kPa)	All patients	2.20	2.57	3.31	4.00
	GOT < 100 U/L	2.20	2.59	3.31	4.00
	GOT < 50 U/L	2.20	2.59	3.31	4.00
Sensitivity	All patients	0.889	0.788	0.960	1.000
	GOT < 100 U/L	0.894	0.786	1.000	1.000
	GOT < 50 U/L	0.969	0.800	1.000	1.000
Specificity	All patients	0.889	0.789	0.954	0.922
	GOT < 100 U/L	0.889	0.811	0.981	0.949
	GOT < 50 U/L	0.875	0.857	1.000	0.933
PPV	All patients	0.970	0.837	0.889	0.684
	GOT < 100 U/L	0.955	0.759	0.923	0.667
	GOT < 50 U/L	0.939	0.800	1.000	0.500
NPV	All patients	0.667	0.732	0.984	1.000
	GOT < 100 U/L	0.762	0.833	1.000	1.000
	GOT < 50 U/L	0.933	0.857	1.000	1.000

Table 1. MRE cut-offs values, as well as the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) obtained for all alcoholic patients (N = 90) and subsequently for patients with a GOT < 100U/L (N = 65), and patients with GOT < 50 (N = 48).

Initial distribution with Nguyen-khac's cut-offs (Nguyen Khac et al., 2008) (F_S)	Fibrosis stage with Magnetic Resonance Elastography				
	$F0_{MRE}$ [0 – 2.20]	$F1_{MRE}$ [2.20 – 2.57]	$F2_{MRE}$ [2.57 – 3.31]	$F3_{MRE}$ [3.31 – 4.00]	$F4_{MRE}$ [4.00 - ∞]
$F0_S$ (N = 18)	**16**	1	1		
$F1_S$ (N = 20)	3	**10**	6	1	
$F2_S$ (N = 27)	5	6	**14**	1	1
$F3_S$ (N = 12)			1	**6**	5
$F4_S$ (N = 13)					**13**
Distribution with MRE cut-offs (F_{MRE})	24	17	22	8	19
Distribution with Huwart's cutoff (Huwart et al., 2008) (F_{Huwart})	36	1	22	16	15

Table 2. New distribution of the intermediate fibrosis levels for the alcoholic patients using the present MRE cut-offs. Number in bold correspond to the same liver fibrosis classification measured with the Fibroscan and MRE techniques.

		Cut-offs referenced in the literature							
		F1		F2		F3		F4
MRE Technique	Huwart et al. 2008 (F_{Huwart})	2.42	0.07 ←→	2.49	0.64 ←→	3.13	1.00 ←→	4.13
MRE Technique	Present cut-offs for alcoholism disease ($F_{Alcoholism}$)	2.20	0.37 ←→	2.57	0.74 ←→	3.31	0.69 ←→	4.00
Fibroscan	Nguyen-khac et al. 2008 ($F_{Nguyen-khac}$)	1.96	0.64 ←→	2.60	1.10 ←→	3.66	2.80 ←→	6.50

Table 3. Comparison of the published cut-off values from magnetic resonance and ultrasound elastography techniques.

Figures

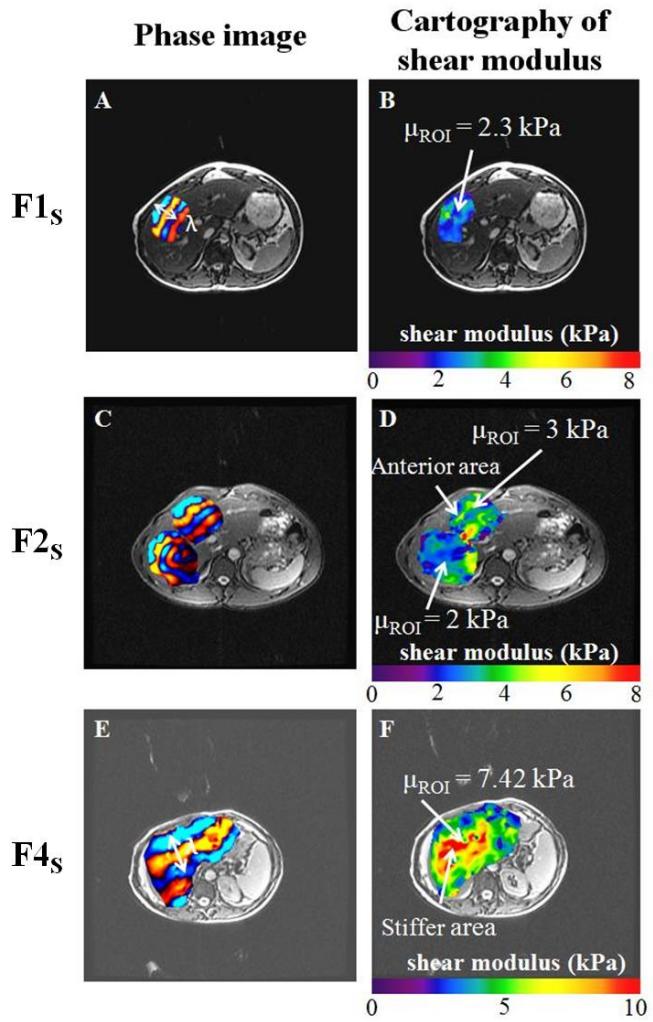

Fig. 1. Phase images (A, C, E) showing the propagation of the shear waves (k: wavelength) inside the liver of alcoholic patients, and the corresponding cartography of shear modulus (l) (B, D, F) representing the liver stiffness measured inside selected regions of interest (ROIs).

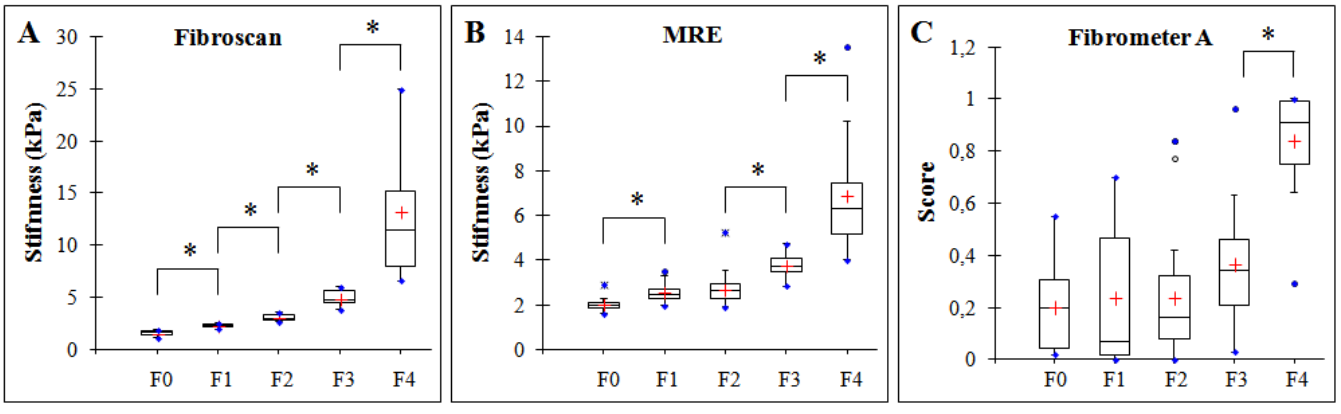

Fig. 2. Evolution of the alcoholic liver fibrosis using imaging techniques (A: Fibroscan and B: MRE) and laboratory test (C: Fibrometer A) (*p < 0.05).

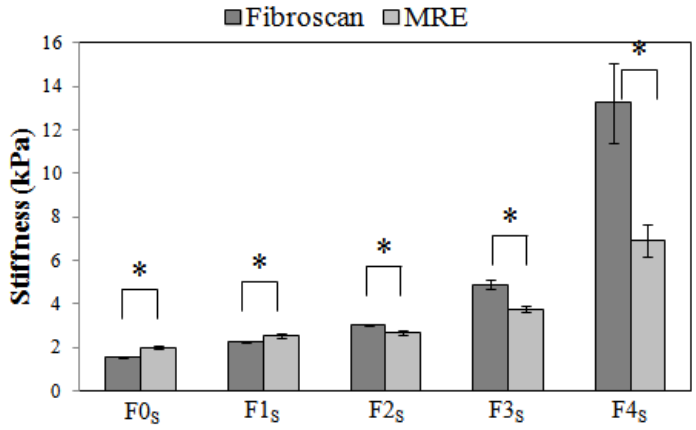

Fig. 3. Comparison of the mean shear stiffness measured with the Fibroscan and MRE techniques (*p < 0.05) for all the intermediate liver fibrosis.

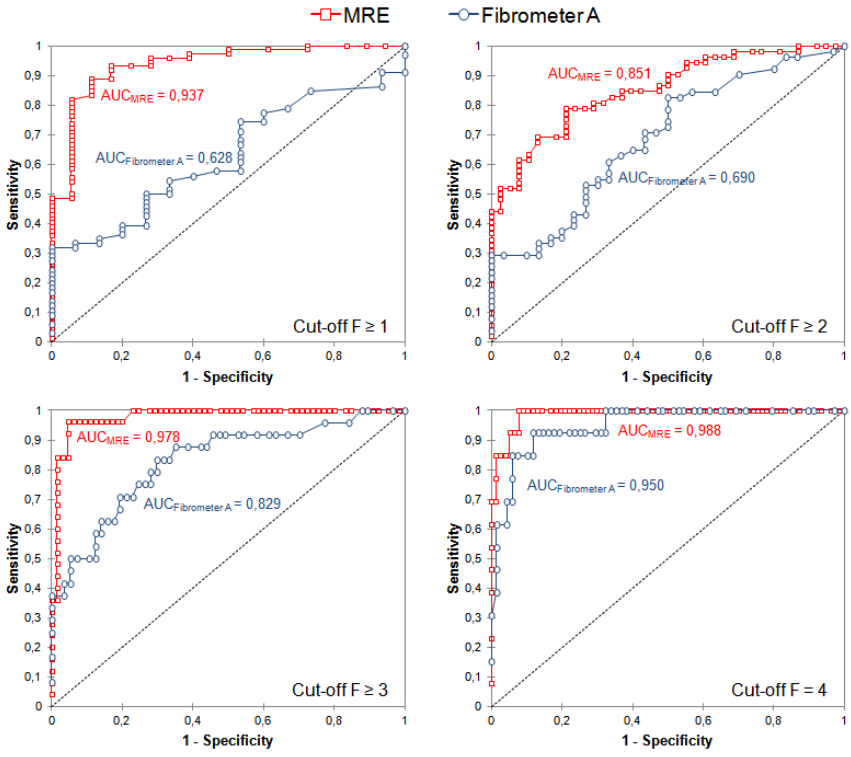

Fig. 4. Comparison of the ROC curves obtained from MRE experiments and Fibrometer A test for moderate and severe liver fibrosis for all patients. Areas under the ROC curves (AUCs) for both tests were measured with 95% confident interval, for the different intermediate liver alcoholic fibrosis, using the Fibroscan technique as the reference.