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White Paper

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Non-Invasive Staging of Liver Fibrosis with ShearWave™ Elastography Imaging

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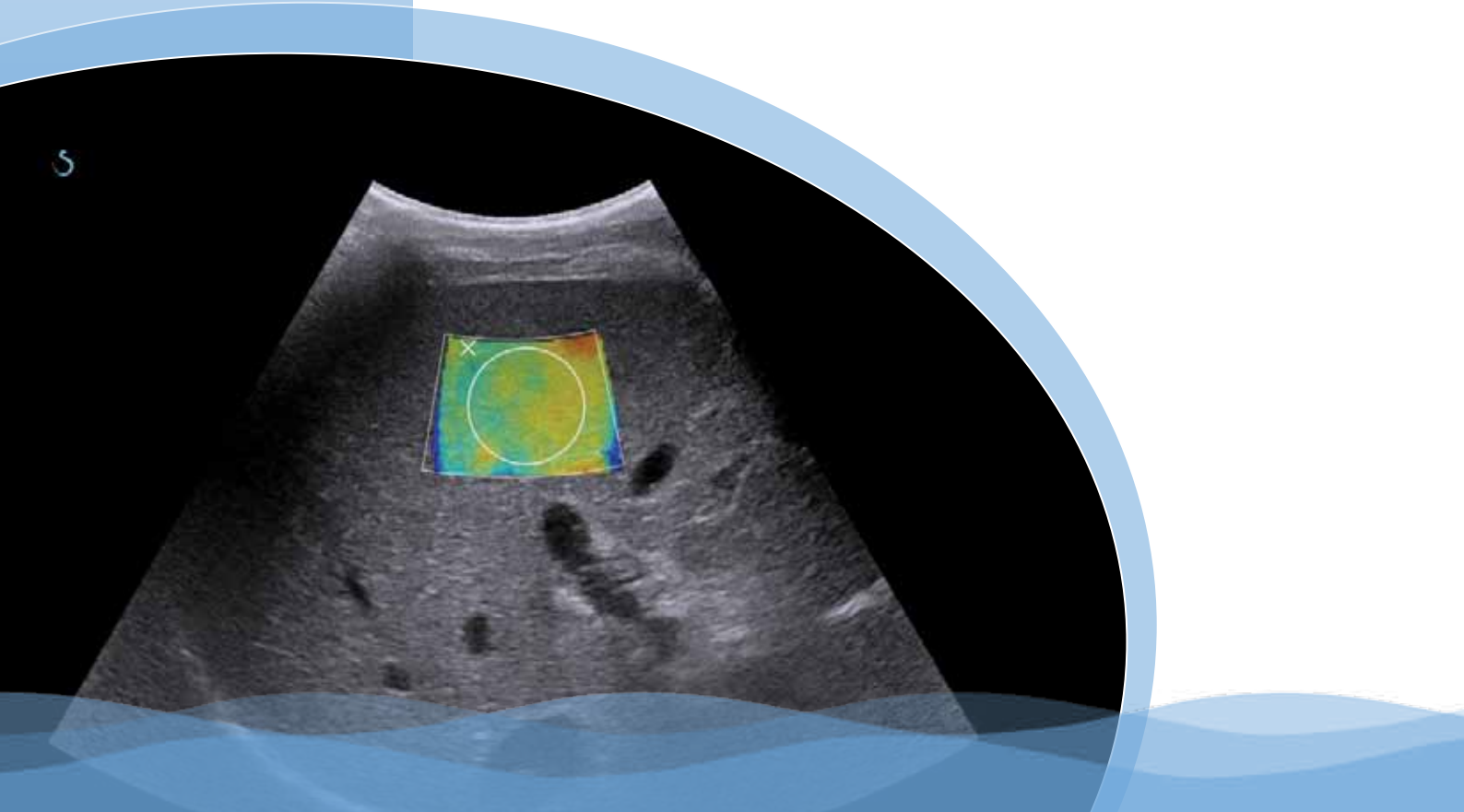

1. Introduction

Ultrasound (US) Imaging plays a major role in the diagnosis, the regular follow-up, and the therapeutic decisions of chronic liver disease. Its use covers a wide spectrum of clinical applications, such as:

- Analyzing liver parenchyma echo structure and assessing risk of chronic liver disease (such as changes in the size of individual segments or liver dysmorphia and signs of portal hypertension),
- Detecting and characterizing nodules of cirrhotic liver (and in particular identifying any suspicious lesion such as hepatocellular carcinoma (HCC)),
- Guiding while performing the percutaneous focal treatment (such as RF-ablation, cryogeny, etc…) of lesions such as HCC,
- Evaluating therapeutic response.

Quantification of hepatic fibrosis is also of critical importance in chronic hepatitis C not only for diagnosis, but also for antiviral treatment decision-making. Two end-points are clinically relevant: detection of significant fibrosis, which is an indication for antiviral treatment, and detection of cirrhosis, which is an indication for specific monitoring of complications related to portal hypertension and of an increased risk of developing HCC [1].

Today, conventional US imaging is limited by the subjective nature and the variability in assessing the hepatic parenchyma echo-texture alteration and liver dysmorphia, and therefore by its inability to accurately differentiate hepatic fibrosis stages.

ShearWave™ Elastography (SWE™) may address the current limitation of conventional US imaging to characterize liver fibrosis.

In this white paper we will focus on liver fibrosis in patients with chronic hepatitis C and present the preliminary results of the benefit of ShearWave Elastography to differentiate fibrosis stages.

2. Ultrasound Elastography Imaging

Conventional imaging techniques do not provide information on the viscoelastic properties of the organs or tumors. However, the elasticity (or, equivalently, stiffness) of body tissues varies greatly and is a parameter that can be coded to differentiate different tissues and also lesions from surrounding tissues [2]. Many disease processes result in changes in tissue elasticity. Tumors (especially malignant) are generally harder than normal tissue around them. Interstitial fibrosis, which appears in some diffuse diseases (liver cirrhosis, renal failure...), also causes a change of elasticity [3, 4]. Imaging of elasticity of the human body is a new imaging modality currently being evaluated. It proposes to replace subjective palpation by imaging the elastic properties of the human body. Static elastography is currently available on many ultrasound diagnostic imaging devices. However, it does not provide quantitative values of elastic properties of tissues. Elastography imaging is also being developed in MRI (Magnetic Resonance Elastography or elasto-MR [4-6]). Three other techniques, based on the properties of shear waves, have been developed in the last decade to quantitatively measure elastic properties of tissues. Indeed, the speed of a shear wave propagating in a medium is dependent on the longitudinal modulus of elasticity of the biological tissue; the tissue elasticity modulus can then be derived from this measurement. The first technique, called Transient Elastography (TE) is a one-dimensional method, which gives a single elasticity value from a region. Its main application has been liver fibrosis assessment. The second technique, Acoustic Radiation Force Impulse (ARFI) is also a one-dimensional technique but has been integrated onto a conventional ultrasound imaging system. The third technique is ShearWave™ Elastography (SWE™) imaging. SWE allows two-dimensional, real time, quantitative* imaging of tissue elasticity in combination with conventional ultrasound imaging. This third technique has been validated for breast lesion characterization [7-10]. In addition to the first application to help breast lesion diagnosis, SWE is currently being evaluated for other indications, such as the characterization of thyroid nodules, and prostate cancer [11-12].

Ultrasound elastography technologies have been developed based on the same approach – the measurement of deformation induced in tissue by a constraint, following three steps:

1. The generation of stress in the tissue. This stress can be internal or external and is of different origins. Some applications use a static compression; others use monochromatic vibration or impulse to shake the parenchyma.

The Aixplorer System available for sale outside the U.S. has the SWE™ quantification tool.
** The Aixplorer System legally available for sale in the U.S. does not include the quantification tool.*

2. The measurement of the displacements induced by the application of this stress, which is performed using ultrasound.

3. The estimation of the elastic modulus by physical reversal of the relationship relating the stress to the displacements.

In this white paper we will only report on the elastography techniques based on shear waves, as they are the most relevant for the quantitative evaluation of the hepatic fibrosis. As explained above, there are 3 quantitative techniques available to measure liver stiffness.

a. One-Dimensional Transient Elastography

One-dimensional TE is a non-invasive, bedside method to evaluate liver fibrosis by measuring liver stiffness. This technique is based on one-dimensional transient elastography, a technique that uses both ultrasound (around 5 MHz) and low-frequency (50 Hz) mechanically generated shear waves, whose propagation velocity is directly related to elasticity. The shear wave speed in stiff or "hard" tissue is greater than the speed in a softer region. The shear wave is generated by an external low frequency vibrator (50 Hz), which strikes the patient's skin. This external pitch is sufficient to produce a shear wave whose propagation is measured by a one-dimensional ultrasound system and provides an average elasticity. This technique is currently commercially available (FibroScan®, Echosens, Paris, France) [3]. This technique has been widely studied and validated in clinical practice to measure the elasticity of the liver parenchyma in a cylindrical volume sample [3]. The measurement is typically performed intercostally in the right liver and covers a small region of interest 30 to 40 mm long (from a given depth). However, the result is a value that corresponds to the average of elasticity in the single explored cylinder. The measurement is typically repeated 10 times and the median is considered as the representative value.

The limitations of this technique are:

- The low volume of parenchyma explored,
- The absence of ultrasound imaging to guide the measurement,
- The measurement difficulties in cases of obesity and presence of ascites,
- The lack of specificity for the distinction of significant fibrosis level,
- The learning curve in correctly performing the acquisition without imaging guidance.

b. ARFI

Recently, Acoustic Radiation Force Impulse (ARFI) Imaging has been introduced to the field of elastography [13]. Unlike TE, it relies on the mechanical excitation of tissue by providing localized, impulsive, acoustic radiation force. This results in shear-wave propagation away from the region of excitation. Using conventional beamforming architecture, beams are continuously transmitted until the passing shear wave front is detected. However, like TE, it is also a one-dimensional technique and it has other limitations such as:

- There is no elasticity map of tissue produced by this technique,
- The elasticity measurement is not real time,
- The elasticity measurement cannot be performed retrospectively,
- Only one single acquisition can be acquired at a time,
- The evaluated area of parenchyma is a small pre-determined size and cannot be modified,
- Only the average of the elasticity in the ROI is calculated, without any information on standard deviation,
- Excessive transducer heating is prevented by limiting the frequency and magnitude of push pulses, which in turn restricts the possible depth of the ROI.

c. ShearWave™ Elastography

ShearWave™ Elastography (SWE) relies on the measurement of the shear wave propagation speed in soft tissue; like ARFI, it does not require an external vibrator to generate the shear wave [14]. It is based on the generation of a radiation force in the tissue to create the shear wave. The ultrasound probe of the device produces a very localized radiation force deep in the tissue of interest. This radiation force/push induces a shear wave, which then propagates from this focal point. Several focal points are then generated almost simultaneously, in a line perpendicular to the surface of the patient's skin. This creates a conical shear wave front, which sweeps the image plane, on both sides of the focal point. The progression of the shear wave is captured by the very rapid acquisition of ultrasound images (up to 20,000 images per second), called UltraFast™ Imaging. The

acquisition takes only a few milliseconds, thus the patient or operator movement does not impact the result. A high-speed acquisition is necessary to capture the shear wave as it moves at a speed in the order of 1 to 10 m/s. A comparison of two consecutive ultrasound images allows the measurement of displacements induced by the shear wave and creates a “movie” showing the propagation of the shear wave whose local speed is intrinsically linked to elasticity. The propagation speed of the shear wave is then estimated from the movie that is created and a real-time two-dimensional color map is displayed, for which each color codes either the shear wave speed in meters per second (m/s), or the elasticity of the medium in kilopascals (kPa). This color map is accompanied by an anatomic reference gray scale (or B-mode) image. This quantitative imaging technique is a real-time imaging mode.

Moreover, using a ROI tool called the Q-Box, areas of interest can both be modified in size (1mm^2-700mm^2) and measured retrospectively. As each pixel in the color-coded map corresponds to a tissue elasticity measurement, the stiffness of the tissue is locally assessed. Additionally, the automatic standard deviation calculation provides relevant information on the stiffness value distribution within the region of interest.

3. Liver Fibrosis Staging in Chronic Liver Diseases

Chronic liver diseases usually combine hepatocyte and/or cholangiocyte necrosis/apoptosis with inflammation (the so-called necro-inflammation) and interstitial fibrosis, whose extension may result in alterations of the hepatic architecture and regeneration nodules, which define cirrhosis.

a. Liver Biopsy

Liver biopsy has traditionally been considered the reference method for assessing liver fibrosis severity in chronic hepatitis C. It can be performed percutaneously, or by a transvenous route in case of hemostasis disorder. It nevertheless has several drawbacks:

- It is an invasive technique, which is associated with significant morbidity (3%, including 0.6% severe complications),
- It is expensive since it requires a day of hospitalization [15],
- The biopsy core sample is not very large (< 25 mm in length and of 1mm diameter) and may not be representative of the liver fibrosis if its distribution is heterogeneous. With percutaneous biopsy, the diagnosis of fibrosis is underestimated in 10 to 30% of cases [16],
- The histological study is a semi-quantitative method, which has a certain inter-observer variability, despite the standardization imposed by the use of scores such as Metavir or Ishak.

In addition to these limitations, liver biopsy is not ideal for repeated assessment of disease progression. Both the progression and the regression of hepatic fibrosis over time could be of clinical significance. Recent research has demonstrated reduction in liver fibrosis with treatment even in advanced stages [17,18].

Therefore new non-invasive techniques to assess hepatic fibrosis have been an important focus of research in the hepatology field for the last 10 years. Currently available methods rely on two different approaches: a “biological” approach based on the dosage of serum biomarkers of fibrosis [19], and a “physical” approach based on the measurement of liver stiffness, using TE [3]. Although the large number of publications over the past decade confirms the growing interest regarding these new non-invasive methods, they also have limitations.

b. Serum Biomarkers

Serum markers are used to calculate a fibrosis score from the measurements of biological parameters. Fibrotest® has been extensively tested and has a diagnostic accuracy ranging from 70 to 85% [19]. It combines the dosage of 5 markers (alpha-2-macroglobulin, haptoglobin, apolipoprotein A1, total bilirubin, gamma-glutamyltranspeptidase) with an adjustment for sex and age. This test presents limitations in cases of hyperbilirubinemia, hemolysis, inflammation or concomitant illness. Another main limitation to the clinical use of serum markers of liver fibrosis is that they are not routinely available in most hospital settings. Strengths and limits are similar for the other scores like Fibrometer or Hepascore.

c. One Dimensional Transient Elastography

This technique, described in the section above, allows the diagnosis of cirrhosis and significant fibrosis. Indeed when hepatic elasticities (liver stiffness) reach values greater than 12.5 to 14.5 kPa, the diagnosis of cirrhosis can be realized with a high positive predictive value [20-23]. TE can suggest significant fibrosis for elasticity values greater than 7.1 to 8.7 kPa [20-22]. However, there is considerable variation in the performances reported for TE to predict significant fibrosis (AUROCs of 0.75 to 0.91) in the literature [24]. Moreover, the stiffness measurement with FibroScan® is difficult in obese patients, when the intercostal space is thin, or ascites is present. The majority of failed TE exams originate from variability within the acquisitions comprising a final liver stiffness measurement. The failure rate varies between 2.4% and 20% [24,25]. Non-invasive techniques, and more particularly the FibroScan®, have inferior performance for intermediate fibrosis staging [26].

d. Ideal Liver Fibrosis Method

Numerous morphological non-invasive approaches have been developed and evaluated to stage liver fibrosis in the last decade including TE, and other ultrasound and non-ultrasound based techniques. Only TE has successfully entered clinical practice, particularly in a number of European countries. Furthermore, the technique is now reimbursed in some countries. As mentioned above, there is considerable variation in the performances reported for TE to predict significant fibrosis (AUROCs of 0.75 to 0.91) [24]. The majority of failed TE exams originate from variability within the acquisitions comprising a final liver stiffness measurement.

Therefore there is a need for a better method to stage liver fibrosis. This method should have the following characteristics:

- Non-invasive,
- Rapid,
- Highly reliable/reproducible,
- Provide information on the fibrosis stage and fibro-genesis activity,
- Separate stages according to the therapeutic indications.

SWE imaging has three advantages with respect to TE:

- It is integrated into a conventional diagnostic ultrasound system and, thus, can make use of real-time B-mode imaging for the assessment of morphologic changes or detection of focal liver lesions (e.g. hepatocellular carcinoma). The use of the B-mode image to guide the SWE acquisitions (for example, to avoid large arteries corrupting the stiffness estimation) might decrease the variability of stiffness measurements,
- It should benefit from improved separation of fibrosis stages, due to the use of shear-waves with greater bandwidths,
- It provides a real-time two-dimensional quantitative map of liver tissue stiffness. The spatial heterogeneity of liver stiffness can be visualized and the region size used for a measurement can be selectively placed and/or adjusted. As a result, physiological variations of liver fibrosis can be averaged out. The measurement region placement and size can be adjusted to avoid artifacts, such as those arising from nearby pulsating vessels. The real-time acquisition of SWE enables user adjustment during acquisition for targeting a homogenous region of liver tissue. This also ensures that excessive liver motion is avoided during real-time SWE acquisitions.

These advantages might reduce the variability of measurements of hepatic stiffness performed with SWE.

To assess performances of SWE for staging liver fibrosis we performed 2 clinical studies, of which one has published results and the other is still ongoing. The first compared SWE to FibroScan® on 113 patients [27]. The second study compares the performance of SWE to both the FibroScan® and liver biopsy, with a target recruitment of 160 patients.

4. Clinical Experience

a. First Published Results

The results of this study have been published in Ultrasound in Medicine and Biology Journal [27].

MATERIALS AND METHODS

A cohort of 113 consecutive patients, with established hepatitis C virus and with no treatment, participated in the study after giving their informed consent. Each patient underwent on the same day FibroScan®, SWE imaging, and surrogate blood tests in the hepatology department of Cochin Hospital (Paris, France).

SWE™ Acquisitions

SWE measurements were performed on the right lobe of the liver, through inter-costal spaces, with the patient lying in the supine position and the right arm in maximal abduction. The same intercostal space was used for both SWE measurements. The upper edge of the SWE box was placed 1.5-2cm from Glisson's capsule in the liver and in an area of parenchyma free of large vessels. Measurements of liver stiffness were obtained from the average of a circular ROI, 2cm in diameter, when scanning conditions permitted. The mean value of four consecutive measurements was used for statistical analyses.

TE Acquisitions

TE was carried out by using FibroScan®. An operator with five years of experience performed the measurements on the right lobe of the liver through intercostal spaces, following the examination procedure previously described. A successful acquisition consisted of 10 validated measurements and the interquartile range (IQR) of less than 30% of the median liver stiffness values was included.

RESULTS

The 95% confidence intervals for SWE and TE for the 113 patients with hepatitis C are given in Table 1 according to Metavir fibrosis stage.

Table 1. AUROC and 95% confidence interval for SSI and FS according to METAVIR fibrosis stages

Method	$F \geq 2$	$F \geq 3$	$F = 4$
SSI	0.95 [0.91;0.99]	0.96 [0.92;1]	0.97 [0.90;1]
FS	0.85 [0.77;0.92]	0.86 [0.77;0.93]	0.94 [0.85;1]
FS (Castéra et al. 2005)	0.83 [0.76;0.88]	0.90 [0.85;0.94]	0.95 [0.91;0.98]
Δ	0.102 ± 0.0367	0.105 ± 0.0407	0.027 ± 0.0193
P	0.005	0.001	0.154

SSI = supersonic shear imaging; FS = FibroScan; AUROC = area under the receiver operating characteristic curve.
The results from a previous study (Castéra et al. 2005) on fibrosis staging using FS are shown for reference. Δ, the difference between AUROC for SSI and FS are also presented. The significance level *P* of the comparison between ROC curves is also given.

Table 1 : AUROC and 95% confidence interval for SWE (SSI) and TE (FS) according to Metavir fibrosis stages

Comparison of SWE and TE

Box and whisker plots of both real-time SWE and TE measurements versus Metavir stages are shown in Figure 1. The median 50% interquartile (box) and 95% interquartile (black lines) are also shown for each stage for both measurements in the plots of Figure 1. Figure 2 shows the ROCs for significant fibrosis. For significant fibrosis (F>2), a significant improvement (p=0.05) in the AUROCs was observed between SWE™ (0.95) and TE (0.85). The optimal cutoffs, obtained by ROC analysis, were 9.12 kPa and 5.8 kPa for SWE and TE respectively. The slight improvements for the AUROCs for severe cirrhosis were not significant.

DISCUSSION

The diagnosis and management of patients with hepatitis C strongly rely on an accurate assessment of the degree of liver fibrosis. Anti-viral treatment is usually initiated promptly in patients with advanced fibrosis (Metavir score F3-F4), and is carefully considered for patients with significant fibrosis (Metavir score F2). In this study, real-time SWE exhibited a significantly higher ability to identify intermediate stages of fibrosis in comparison with TE. The AUROCs in differentiating no/mild fibrosis (F0-F1) from significant fibrosis (F≥2) were 0.85 and 0.95 for TE and SWE respectively (p≤0.005). The same results were observed for severe fibrosis with AUROCs

in differentiating no/mild/significant fibrosis (F0-F1-F2) from severe fibrosis (F≥3) equal to 0.86 and 0.96 for TE and SWE respectively (p≤0.001). The performance of TE in identifying cirrhosis (F4) is already quite high. No significant difference was observed between the AUROCs of TE and SWE for cirrhosis (0.94 and 0.97 respectively). These findings suggest that SWE can be used similarly as TE is being used for the assessment of severe fibrosis and cirrhosis, with the benefit of improved assessment for significant and severe fibrosis stages.

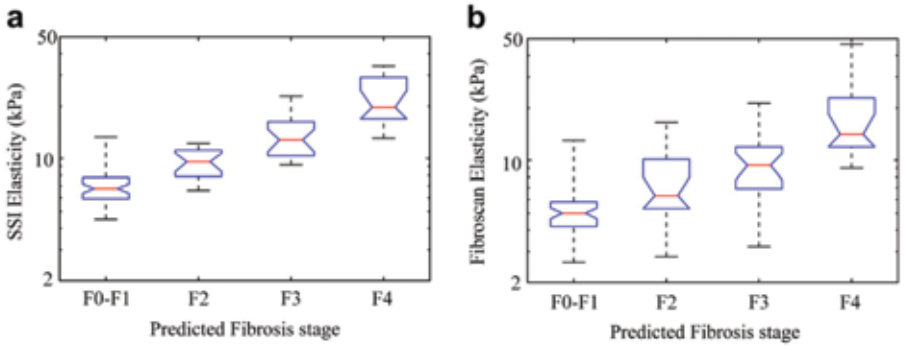

Figure 1 : Box and whisker plots of (a) SWE and (b) FibroScan® (TE) values for each fibrosis stage around the median elasticity. Each box represents the interquartile range within which 50% of the elasticity values are located.

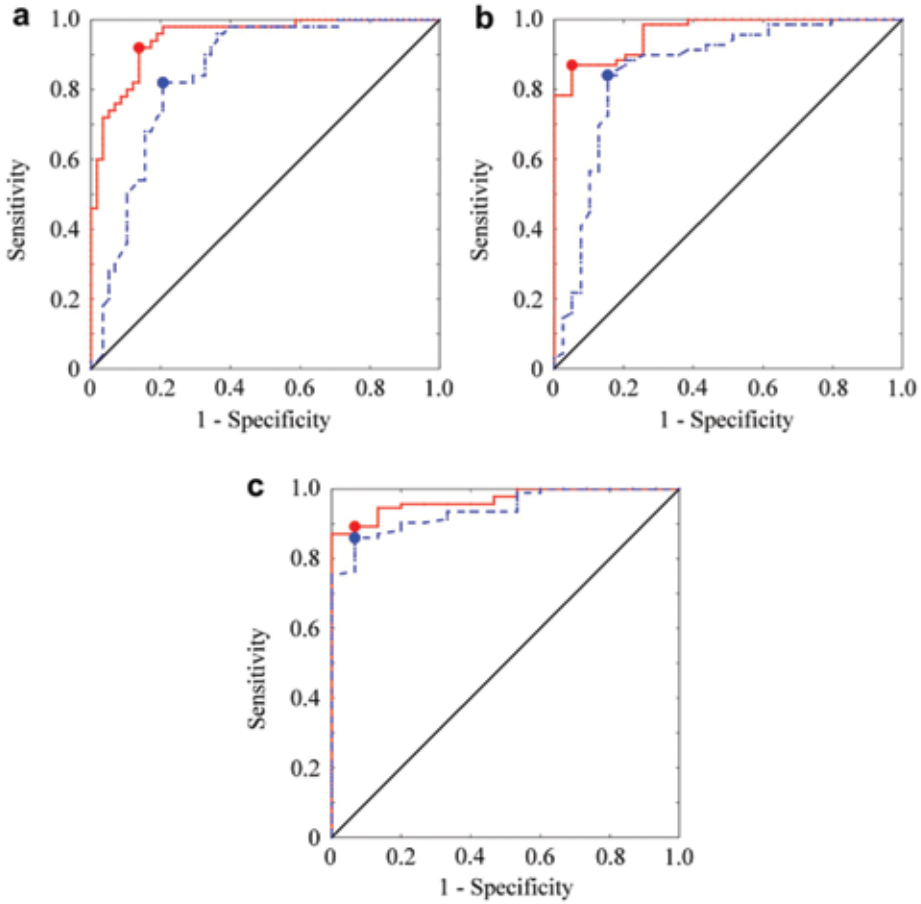

Figure 2 : ROC curves for SWE imaging (solid line) and FibroScan® (TE) (dashed line) for different fibrosis thresholds: (a) F0-F1 vs. F2-F4 (p index: 0.005), (b) F0-F2 vs. F3-F4 (p index: 0.001) and (c) F0-F3 vs. F4 (p index: 0.154). The most discriminant cutoff values in this study are shown for reference.

a. A review of five clinical cases

MATERIALS AND METHODS

Five patients were specifically chosen from the second study to be representative of the different fibrosis stages. In this study, the recruited patients have SWE imaging, TE, analysis of blood markers, and liver biopsy performed on the same day, in the hepatology department of Cochin Hospital. These patients have established hepatitis C virus and no treatment. The patients participate in the study after giving their informed consent (study approved by the French Authorities). Currently 84 patients have been included in the study.

The SWE and TE acquisitions are performed in the same manner as in the previous study with ten successive acquisitions for the SWE to be equivalent with TE acquisitions. Ultrasound-assisted percutaneous liver biopsy is performed in the same intercostal space as is used for the TE and SWE measurements. A single expert liver pathologist, blind to the results of both TE and real-time SWE results but not to the patient's clinical and biochemical data, reads the specimens on site. Fibrosis is evaluated semi-quantitatively and staged on a five-point scale from 0 to 4 according to the Metavir scoring system.

RESULTS

Four patients were specifically chosen from the current enrollment pool to represent the different fibrosis stages. Table 2 summarizes the threshold values in kPa for TE and SWE. These thresholds have been taken from the publications on TE [20-23] and SWE [27]:

Biopsy Metavir Score	Fibroscan Fibrosis Threshold in kPa	SWE Fibrosis Threshold in kPa
F1	>5.8	>6.5
F2	>7.10	>9.12
F3	>9.50	>10.08
F4	>12.50	>13.30

Table 2 : Threshold elasticity values of TE and SWE for different fibrosis stages.

Table 3 summarizes the results of the TE and SWE values for the 4 patients (referred to as a, b, c, and d). Each technique was acquired ten times, and values are presented as mean value ± IQR for TE and mean value ± standard deviation for SWE:

Patient	Biopsy Matavir Score	Fibroscan Values in kPa	Deduced Fibroscan Fibrosis Stage	SWE Mean Values in kPa	Deduced SWE Fibrosis Stage
a	F1	6.55±1.30	F1	7.65±1.07	F1
b	F2	7.50±1.25	F2	9.83±1.14	F2
c	F3	9.65±1.20	F3	11.61±1.87	F3
d	F4	15.7±1.42	F4	21.32±1.65	F4

Table 3: Comparison of TE and SWE fibrosis scores with Metavir score (obtained from liver biopsy) for patients a, b, c and, d.

The following images (figure 3) illustrate the SWE results in these patients, by presenting one single acquisition of the ten used to calculate the mean value.

Patient (a) exhibited mean elasticity values around 7.05 kPa (average of 10 acquisitions) with 1.07 standard deviation and was characterized by liver biopsy to F1A0 Metavir with no steatosis. Patient (b) with F2A2 liver fibrosis, no steatosis (confirmed by biopsy) had slightly higher SWE values around 9.83 kPa (average of 10 acquisitions) with a standard deviation of 1.14 kPa. Patient (c) had severe fibrosis (F3A2 with 10 % steatosis) with quite high SWE values around 11.61 kPa (average of 10 acquisitions) with a standard deviation of 1.87 kPa. Finally the last patient (d) had cirrhosis (F4A2 with no steatosis) with SWE values above 21.32 kPa (average of 10 acquisitions) with a standard deviation of 1.65 kPa.

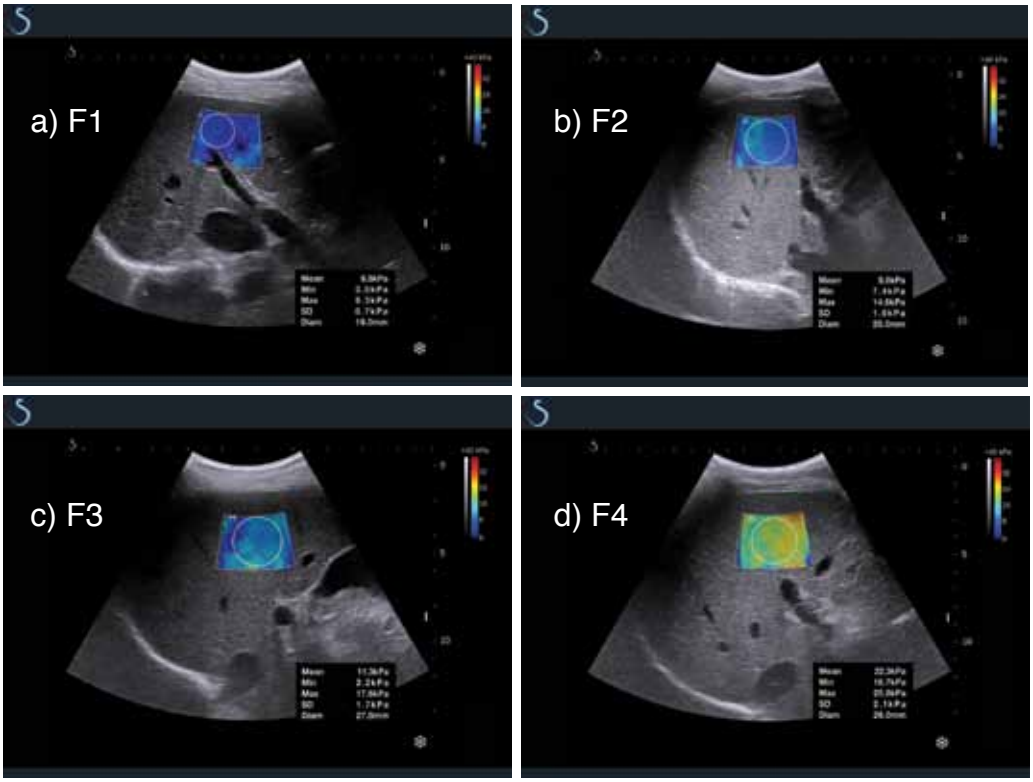

Figure 3 : Four patients (hepatitis C) with four different liver fibrosis Metavir score established by liver biopsy. One single shot elasticity map is presented in each case. a) patient with F1 liver fibrosis exhibiting SWE values around 6.8 kPa with a standard deviation of 0.7 kPa. b) patient with F2 liver fibrosis exhibiting SWE values around 9.8kPa with a standard deviation of 1.6 kPa. c) patient with F3 liver fibrosis exhibiting SWE values around 11.3 kPa with a standard deviation of 1.7 kPa. d) patient with F4 liver fibrosis exhibiting SWE values around 22.3 kPa with a standard deviation of 2.1 kPa.

The fifth clinical case illustrates the potential specificity improvement that SWE may bring to fibrosis assessment. In this case, patient (e), with F2A2 liver fibrosis, 10% steatosis (confirmed by biopsy), SWE had values around 9.76 kPa (average of 10 acquisitions) with a standard deviation of 1.37 kPa while TE underestimated the fibrosis stage with a value of 6.1±1.05 kPa which corresponds to an F1 METAVIR score.

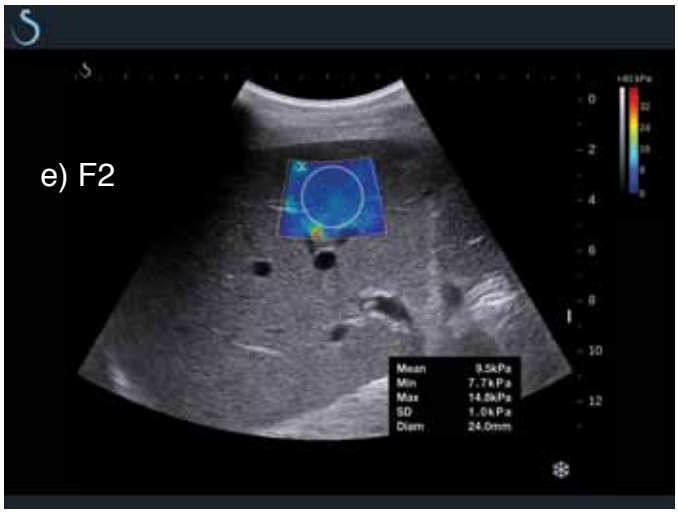

Figure 4 : Patient (e) with F2A2 liver fibrosis, 10% steatosis (confirmed by biopsy) with SWE values around 9.5 kPa (one single shot) with a standard deviation of 1.0 kPa.

DISCUSSION

These clinical cases show that SWE can correctly stage hepatic fibrosis with a small standard deviation in the measurement of the elasticity as compared to liver biopsy. It also shows that its performance is at least equivalent to TE performance in liver fibrosis staging, once the threshold values are adapted to SWE imaging, with a possibility of improvement in certain cases. As mentioned in the publication [27], the elasticity threshold and value difference between the liver elasticity values assessed by SWE and TE shows good agreement with a mean offset of less than 2 kPa. This difference between SWE and TE can be explained by the fact that the Young's modulus value (corresponding to the liver stiffness) with both SWE and TE techniques are derived from the shear group velocity. However, it is derived from the broadband (60 Hz–600 Hz) characteristic of the mechanical excitation generated using the acoustic radiation force for SWE [28,29], whereas TE elasticity values are assessed using an external vibrator acting at 50 Hz [3]. Thus, the elasticity assessed by SWE corresponds to the stiffness "felt" by higher frequency vibrations. It integrates both elasticity and viscosity properties as it averages the shear wave speed over a large bandwidth.

The larger cohort of patients of this study should confirm these results.

5. Conclusion

The diagnosis and management of patients with hepatitis C strongly rely on an accurate assessment of the degree of liver fibrosis. In these preliminary studies, SWE™ is equivalent to TE and has shown to have an increased specificity and accuracy. These improvements are related to its ease of use and its capability of real time imaging to insure that the data collected is reliable.

The assessment of liver stiffness to evaluate liver fibrosis is gaining clinical acceptance. TE has recently been added to the European Clinical Guidelines for liver fibrosis assessment in the management of hepatitis C virus infection patients [30]. Additionally, to prevent repeated biopsies in patients with hepatitis C, the French National Health Authority (HAS) and the French health care system have authorized the use of, and reimbursement for, non-invasive tests that can measure liver stiffness with a shear wave technique, such as TE or SWE for the assessment of fibrosis. In the near future, other countries may also consider authorizing and reimbursing the use of shear wave techniques, as it increasingly becomes the first intention and primary tool in combination with other non-invasive serum biomarkers for liver stiffness assessment.

The second study will demonstrate that SWE can confirm biopsy findings and has the potential to perform as well as TE. It should also confirm the SWE specificity improvements for the intermediate fibrosis stage evaluation.

Further studies in larger patient populations are needed to confirm these results.

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