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Chapter

Liver Fibrosis Assessment by Point Shear-Wave Elastography Techniques

Roxana Șirli, Alina Popescu and Ioan Sporea

Abstract

Point shear-wave elastographic (pSWE) techniques use acoustic radiation force impulse (ARFI) to stimulate the liver tissue and to generate shear waves that propagate into the liver. The shear-wave velocity (SWV) increases with the severity of fibrosis. The first type of pSWE was Virtual Touch Quantification (VTQ) developed by Siemens, followed by ElastPQ by Philips, and nowadays pSWE is available on other systems (Hitachi, Esaote, Samsung). To evaluate liver fibrosis by pSWE, ten valid measurements are performed in the right liver lobe; a median value is calculated, with the results expressed in meters/second or in kilopascals (kPa) (if the operator chooses). VTQ is a reproducible method, the intraclass correlation coefficient (ICC) for inter- and intraobserver measurements ranging from 0.81 to 0.87. Confounding factors for VTQ are non-fasting conditions, elevated aminotransferases, congestive heart failure, and extrahepatic cholestasis. In patients with chronic hepatopathies, the AUROCs for predicting significant fibrosis range between 0.75 and 0.85 and for predicting cirrhosis between 0.85 and 0.95. There were promising results regarding the value of VTQ to predict liver cirrhosis complications, especially portal hypertension. ElastPQ is a newly developed point shear-wave elastographic method (from Philips). Only few data were published but with promising results.

Keywords: liver fibrosis, liver elastography, point shear-wave elastography, Virtual Touch Quantification, ElastPQ

1. Introduction

Evaluation of liver fibrosis severity is essential in chronic hepatopathies, especially for prognosis, but also for decision regarding treatment in some cases or for follow-up [1]. For a long time, liver biopsy was considered to be the reference method for fibrosis assessment. Not only mainly due to its invasiveness [2] but also due to issues regarding inter-observer variability and sampling errors [3], noninvasive methods have been developed to assess the severity of liver fibrosis. These methods can be either biological or elastographic [1].

Elastographic techniques are based on an intrinsic property of tissue elasticity. When an extrinsic force is applied to a tissue, it deforms more or less according to its elasticity. Less elastic, stiffer tissue deforms less when subjected to an external force. Elastographic techniques measure tissue displacement when subjected to

an external force. In chronic hepatopathies, as fibrosis progresses, the liver tissue becomes stiffer, less elastic; thus, liver stiffness (LS) is considered to be an indicator of liver fibrosis severity [1, 4, 5]. Elastographic techniques can be ultrasound-based or based on magnetic resonance imaging.

According to the latest guidelines [4–9], ultrasound-based elastographic techniques are divided into strain elastography (which measures longitudinal displacement) and shear-wave elastography (SWE—which measures the speed of the shear waves generated into the tissue when an external force is applied). Based on the type of impulse that generates the shear waves, SWE is subdivided into transient elastography (TE—where a mechanical stimulus is applied to the tissue) and acoustic radiation force impulse (ARFI) techniques (where the stimulus deforming the tissue is an acoustic "push pulse" generated by the transducer). Subsequently, ARFI elastography is subdivided into point SWE (in which LS is measured in a region of interest (ROI)) and multidimensional SWE (2D-SWE and 3D-SWE—in which a color-coded elastogram is obtained and shear-wave speed is also measured in a region of interest).

In the following pages, we will present point shear-wave elastography techniques.

2. Point shear-wave elastography: basic principles

pSWE is a type of SWE in which tissue stimulation is performed at a certain depth by an acoustic radiation force impulse generated by the transducer (ARFI technology), which generates shear waves that propagate into the tissue, perpendicularly on the axis of the initial pulse. Shear-wave velocity (SWV), expressed in meters/second (m/s), is measured in a predefined ROI chosen by the operator while performing B-mode ultrasonography. The average propagation speed of the shear waves, from a point placed on the lateral margin of the ROI to an opposite point on the ROI, can be measured by detecting its time of arrival at that point, relative to the acoustic "push" pulse [5]. The stiffer the tissue, the higher the shear-wave velocity [4–9].

Most systems performing pSWE allow the choice to express measurement results either in m/s or in kilopascals (kPa). Kilopascal is the unit of the elastic modulus, obtained by converting the SWV to an elastic modulus, using an equation that assumes that the tissue density is always the same and also that the elastic modulus is not influenced by the magnitude, frequency, and direction of the applied force [5]. Thus, even if kPa is the unit to which users are the most familiar (since it was used for Transient Elastography), the most correct one is m/s [5–7].

Two types of pSWE have been more thoroughly evaluated, the ones developed by Siemens (Virtual Touch Quantification) and by Philips (ElastPQ). Currently other manufacturers also offer pSWE on their systems: Esaote, Hitachi, and Samsung [5].

3. Point shear-wave elastography (pSWE): examination technique

First of all, before performing SWE the *operator should be trained* [5, 6, 8, 9]. If for TE training means performing more than 100 examinations under supervision [10], what training means is less precise for pSWE. A study published by Boursier concluded that there is no training effect on the accuracy of LS measurements by VTQ (ARFI) [11]. Concerning ElastPQ, a published study concluded that after a 1-year learning curve, or 130 examinations, the accuracy of ElastPQ matches that

of TE [12]. Considering that adequate B-mode image is a must for reliable pSWE measurements [5, 9], it is sensible to consider that training not only in elastographic measurements but also in ultrasonography is needed.

According to the guidelines, the *recommended technique* of pSWE measurements is with the patient in supine position with the right arm in maximal extension, through an intercostal approach, during breath hold, avoiding deep inspiration or expiration [5, 6, 8]. The transducer should be perpendicular on the liver capsule, and the ROI should be placed in the right liver lobe, as to avoid large blood vessels and masses, at a depth of minimum 1 cm below the liver capsule, best at 4–5 cm from the transducer [5, 6, 8, 9] (**Figures 1** and **2**).

A study published by our group demonstrated that the best correlation of VTQ measurements with histology was obtained for SWV measurements made 1–2 and 2–3 cm beneath the liver capsule but with a lower feasibility for deeper measurements [13]. Several studies observed higher SWV by VTQ in the left liver lobe vs. the right liver lobe [14–16]. Regarding ElastPQ, measurements made in liver segment V had the lowest coefficient of variation, and SWVs at the end-expiration were significantly higher than that at the end-inspiration [17].

For an appropriate estimation of fibrosis, the guidelines recommend to perform ten pSWE measurements and to calculate the median (M) value [5, 6, 8, 9]. When VTQ was launched, the manufacturer did not recommend *quality criteria*, but several studies demonstrated that there is a better correlation between histologic fibrosis and pSWE measurements if quality criteria such as interquartile range (IQR) and success rate (SR) are met. Regarding VTQ, an IQR/M ≥ 30% was associated with a discordance of at least two stages of fibrosis between SWV and histologic fibrosis [18]. In another study from our group, a very strong correlation of VTQ measurements with histologic fibrosis was observed when quality parameters (IQR < 30% and SR ≥ 60%) were met (r = 0.722, p < 0.0001); if not, there was no significant correlation (r = 0.268, p = 0.07) [19]. Also, standard deviation (SD) of the mean of ten valid SWV measurements by VTQ was evaluated as a quality criterion. Exclusion of patients in whom the SD was higher than 30% lead to an improved accuracy of VTQ [20]. Regarding ElastPQ®, IQR/M ≤ 30% is also the most important quality criterion [21, 22]. European guidelines recommend as quality criterion for pSWE an IQR/M ≤ 30% [5, 8], while the WFUMB guidelines
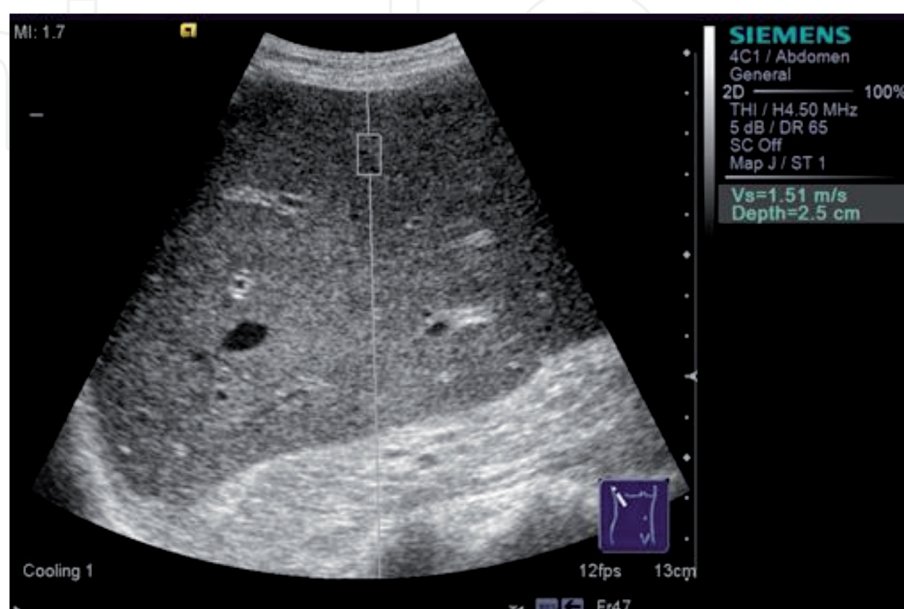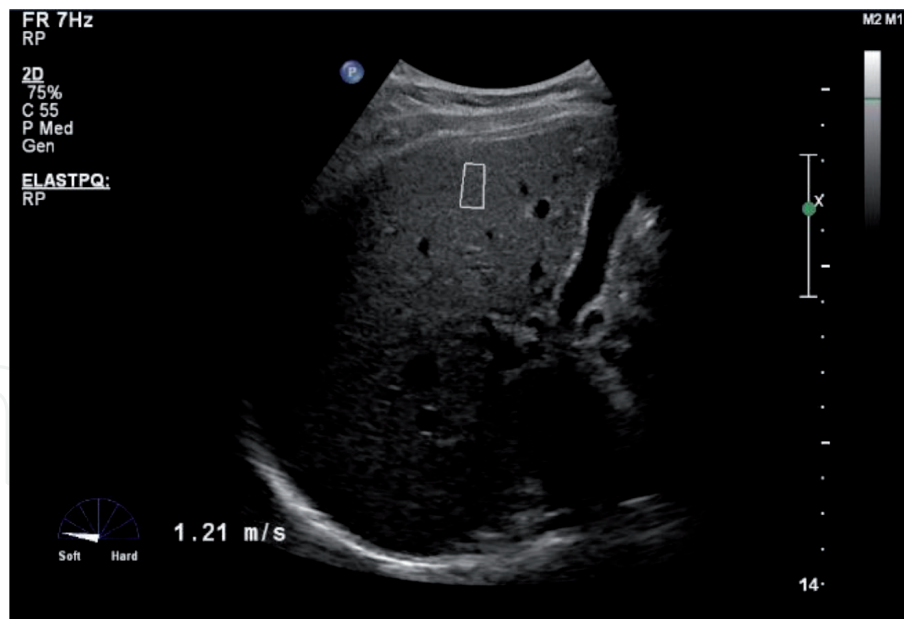

Figure 1.
VTQ measurement.

Figure 2.
ElastPQ measurement.

recommend an even smaller IQR/M, of less than 15%, if results are expressed in m/s [9]. A new multicenter study with ElastPQ® showed that the median value of five measurements with an IQR/M ≤ 30% is accurate enough for daily practice [22].

4. Point shear-wave elastography (pSWE): feasibility and reproducibility

As opposed to TE, pSWE is *feasible* in patients with ascites [5, 6, 8, 9]. Furthermore, in published studies, the feasibility is better as compared to TE, being higher than 92%, both in VTQ [11, 23–25] and in ElastPQ [26, 27]. In a multicenter study on VTQ, older age, higher BMI, and male gender were associated with failed and unreliable measurements [25].

Regarding *reproducibility* of VTQ, several studies demonstrated very good inter- and intraobserver reproducibility, with intraclass correlation coefficients (ICC) higher than 0.81 [10, 28, 29]. A study that evaluated factors that influenced reproducibility found out that intraoperator reproducibility was better than the inter-operator one (ICC of 0.90 vs. 0.81) [28]. Both intra- and inter-operator reproducibilities were better in men than in women, in patients with lower BMI, and in patients with no ascites and in cirrhotic than in non-cirrhotic patients [28].

ElastPQ was also proved to be a reproducible method, reported ICC ranging from 0.798 [30] to 0.96 [31]. In a study published by Fraquelli, the reproducibility was influenced by training, but not by age, gender, BMI, liver enzymes, and liver etiology [12].

5. Point shear-wave elastography (pSWE): confounding factors

One of the first confounding factors that should be taken into consideration is examination in *non-fasting* conditions. In a study published by our group, it was demonstrated that food intake can lead to a significant increase in SWVs measured by VTQ in healthy volunteers 1 hour post meal, the values decreasing to baseline 3 hours after the meal [32]. Even if no data was published regarding ElastPQ, the

observation in VTQ was similar to what happens with TE measurements in non-fasting patients, and thus the guidelines recommendation that pSWE measurements should be performed in fasting patients [5, 6, 8, 9].

Another factor that can lead to a falsely increased SWV measured by VTQ is *physical exercise* [33]. Thus, the EFSUMB guidelines recommend that SWE should be performed after a minimum 10 minutes of rest [5].

An important confounding factor for SWE is liver necroinflammation, objectified by *elevated aminotransferase levels*. Several studies demonstrated that elevated aminotransferase levels are associated with higher SWVs by VTQ for the same severity of liver fibrosis, as compared to those observed in patients with normal or only slightly elevated aminotransferases [34, 35]. Also, a significant decrease in SWVs was observed in a case report of acute liver failure, in parallel to the normalization of liver function tests [36].

The influence of necroinflammation on SWVs measured by ElastPQ is controversial. In a study by Ma et al., the grade of necroinflammatory activity was independently associated with higher ElastPQ values [30], while in the study of Ferraioli et al., it had no influence [31].

Similar to TE, other confounding factors, which falsely increase SWVs by pSWE are *right heart failure* [37] and the *presence of extrahepatic cholestasis* [38].

Considering all the studies mentioned above, EFSUMB and WFUMB guidelines caution about the confounding factors for pSWE and state that liver inflammation (indicated by AST and/or ALT elevation >5 times the normal limits), obstructive cholestasis, liver congestion, acute hepatitis, and infiltrative liver diseases should be excluded before pSWE to avoid overestimation of fibrosis and/or should be considered when interpreting the results [5, 9].

6. Point shear-wave elastography (pSWE): normal values in a healthy liver

The SWV by pSWE in healthy livers were evaluated by several authors. Regarding VTQ, normal SWV values ranged between 1.07 and 1.19 m/s [15, 39–42], and they were not influenced by gender and age, but higher values were observed in the left liver lobe than in the right liver lobe [15].

Regarding ElastPQ, normal values are in the same range as for VTQ [17, 31, 43], but a study found higher values in men than in women [17].

Current guidelines state that SWE measurements in the liver in normal range can rule out significant fibrosis if they are in accordance with clinical and biologic data [5, 9].

7. Point shear-wave elastography (pSWE) in patients with chronic hepatopathies

7.1 Mixed cohorts

Multiple studies have been published regarding the value of VTQ elastography in patients with chronic liver diseases, considering biopsy as the reference. We summarized some of them in **Table 1**.

Four meta-analyses were published regarding the value of VTQ for liver fibrosis assessment. The first one, by Friedrich-Rust et al., included 518 patients with hepatopathies of various etiologies. The summary AUROCs of VTQ for predicting significant fibrosis (F ≥ 2), severe fibrosis (F ≥ 3), and cirrhosis were 0.87, 0.91,

Study	Etiology	F2		F4	
		AUROC TE	Cutoff AUROC VTQ	AUROC TE	Cutoff AUROC VTQ
Friedrich-Rust et al. [44]	86 patients HBV + HCV	0.86	1.37 m/s 0.86	0.91	1.75 m/s 0.91
Sporea et al. [45]	223 patients Healthy + HBV + HCV	0.953	1.27 m/s 0.890	0.985	1.7 m/s 0.931
Takahashi et al. [46]	80 patients Healthy + HBV + HCV	—	1.34 m/s 0.94	—	1.8 m/s 0.96
Goertz et al. [47]	57 patients HBV + HCV	—	0.85	—	0.87
Ebinuma et al. [48]	131 patients Mixed	0.871	1.3 m/s 0.891	0.817	1.88 m/s 0.888
Colombo et al. [49]	68 Healthy + mixed	0.897	0.922	0.815	0.934
Cassinotto et al. [50]	349 Mixed	0.84	0.81	0.90	0.90

Table 1.
Performance of VTQ in the assessment of liver fibrosis in cohorts of patients with mixed etiologies of chronic hepatopathies, considering LB as the reference method.

and 0.93, respectively. TE performed significantly better than VTQ for F2 and cirrhosis, while for F3 the performances evaluated by AUROC were similar [51].

The second one included 1163 patients with chronic hepatopathies evaluated by LB, TE, and VTQ [52]. The first conclusion was that VTQ had a better feasibility than TE (unreliable measurements in 2.1 vs. 6.6% cases, respectively, $p < 0.001$). The diagnostic odds ratios were similar for VTQ and TE for detection of significant fibrosis and cirrhosis. The mean optimal cutoff value of VTQ for the detection of F2 was 1.30 ± 0.07 m/s, and for cirrhosis, it was 1.80 ± 0.16 m/s.

The third meta-analysis included 3951 patients with liver biopsy as reference method. The AUROCs of VTQ for predicting the presence of F2, F3, and cirrhosis were 0.84, 0.89, and 0.91, respectively [53].

Finally, the fourth meta-analysis including 2691 patients calculated global sensitivity and specificity of VTQ to predict any stage of fibrosis to be 79 and 86%, respectively. The performance of VTQ was higher for more advanced fibrosis: for $F \geq 3$ 84% Se and 90% Sp (AUROC—0.94), while for F4 86% Se and 84% Sp (AUROC—0.91) [54].

Regarding *ElastPQ*, few data are available. In a study that compared ElastPQ to TE considered as reference, ElastPQ had a better feasibility than TE: 98.7% vs. 90.7%. The AUROCs calculated for significant fibrosis, severe fibrosis, and cirrhosis were 0.94, 0.97, and 0.97, respectively [27].

7.2 Chronic hepatitis C

There is a lot of published data regarding the performance of VTQ elastography for the assessment of liver fibrosis in patients with chronic hepatitis C, as shown in **Table 2**.

To summarize, according to EFSUMB guidelines, VTQ® cutoffs of 1.21–1.34 m/s predict significant fibrosis ($F \geq 2$) (AUROC 0.85–0.89), while VTQ® cutoffs between 1.55 and 2 m/s (AUROC 0.89–0.93) predict cirrhosis [5]. Furthermore,

Study	Reference method	F ≥ 2		F ≥ 3		F = 4	
		Cutoff (m/s)	AUROC	Cutoff (m/s)	AUROC	Cutoff (m/s)	AUROC
Friedrich-Rust et al. [44]	LB—64 p	1.35	0.86	1.55	0.93	1.75	0.95
Lupșor et al. [23]	LB—112 p	1.34	0.851	1.61	0.869	2	0.945
Sporea et al. [55]	LB—274 p	1.21	0.893	1.58	0.908	1.82	0.937
Sporea et al. [56]	LB—914 p	1.33	0.792	1.43	0.829	1.55	0.842
Rizzo et al. [57]	LB—139 p	1.3	0.86	1.7	0.94	2	0.89
Chen et al. [58]	LB—127 p	1.55	0.847	1.81	0.902	1.98	0.831
Li et al. [59]	LB—128 p	1.53	0.775	1.79	0.901	1.79	0.792

Table 2.
Performance of VTQ in the assessment of liver fibrosis in patients with chronic hepatitis C.

according to recommendation 17 of the same guidelines, "pSWE as demonstrated with VTQ® can be used as the first-line assessment for the severity of liver fibrosis in patients with chronic viral hepatitis C. It performs best with regard to the ruling out of cirrhosis."

Data regarding the value of ElastPQ for the assessment of liver fibrosis severity in chronic hepatitis C is scarce. In a pilot study, the AUROCs of VTQ for predicting F2, F3, and F4 were 0.80, 0.88, and 0.95, respectively [31]. Similar results have been obtained in a more recent study [60].

Following successful antiviral HCV treatment, a significant decrease of VTQ values was observed in a study performed by Goertz et al. [61].

7.3 Chronic hepatitis B

Several studies have been published regarding the value of VTQ for liver fibrosis assessment in chronic hepatitis B, as shown in **Table 3**.

Sub-analysis of data regarding patients with HBV chronic hepatitis from the Nierhoff meta-analysis on VTQ calculated AUROCs of 0.88 for F2 and 0.93 for F4, with cutoffs of 1.35 and 1.87 m/s, respectively [53].

Data regarding ElastPQ and chronic HBV hepatitis is scarce, and validation is needed. In a study that compared ElastPQ to liver biopsy in chronic hepatitis B, the authors calculated an AUROC of 0.94 with a cutoff of 6.99 kPa for F2 and an AUROC of 0.89 with a cutoff of 9.00 kPa for cirrhosis [30].

Regarding HBV chronic hepatitis and pSWE, EFSUMB guidelines state that "pSWE as demonstrated with VTQ is useful in patients with CHB to identify those with cirrhosis" [5].

7.4 Nonalcoholic fatty liver disease (NAFLD)

Several studies have been published regarding VTQ in the evaluation of liver fibrosis in NAFLD patients. Data is presented in **Table 4**.

Study	Reference method	F ≥ 2		F ≥ 3		F = 4	
		Cutoff (m/s)	AUROC	Cutoff (m/s)	AUROC	Cutoff (m/s)	AUROC
Friedrich Rust et al. [62]	LB—133 p	—	0.69	—	0.83	—	0.96
Zhang et al. [63]	LB—180 p	1.63	0.764	1.74	0.852	2	0.825
Dong et al. [64]	LB—81 p	1.29	0.762	1.54	0.882	1.83	0.732

Table 3.
Performance of VTQ in the assessment of liver fibrosis in patients with chronic hepatitis B.

Study	Reference method	F ≥ 3		F = 4	
		Cutoff (m/s)	AUROC	Cutoff (m/s)	AUROC
Yoneda et al. [65]	LB—54 p	1.77	0.973	1.9	0.976
Friedrich-Rust et al. [66]	LB—61 p	—	0.71	—	0.74
Fierbinteanu et al. [67]	LB—64 p	—	0.944	—	0.984

Table 4.
Performance of VTQ in the assessment of liver fibrosis in patients with nonalcoholic fatty liver disease.

A recently published meta-analysis including 723 patients who evaluated VTQ as a predictor of liver fibrosis in NAFLD patients calculated a summary sensitivity and specificity of VTQ in detecting significant fibrosis of 80.2 and 85.2%, respectively, with a pooled diagnostic odds ratio of 30.13 and with an AUROC of 0.898 [68].

Considering all these data, EFSUMB guidelines conclude that VTQ can be used to exclude cirrhosis in NAFLD patients [5].

8. Point shear-wave elastography (pSWE) for the prediction of liver cirrhosis complications

Cirrhosis is the final stage of chronic hepatopathies and can have severe complications such as portal hypertension, hepatocellular carcinoma, decompensation, etc. The measurement of hepatic vein pressure gradient (HVPG) is the most accurate method for portal hypertension assessment, but it is an invasive method. HVPG >10 mm Hg means clinically significant portal hypertension (CSPH), while HVPG >12 mm Hg is predictive for variceal bleeding [69].

8.1 Portal hypertension

An initial study found a good correlation (r = 0.709) of VTQ measurements to HVPG measurements in 48 patients, with the AUROC for predicting CSPH being 0.874 [70]. In a Romanian study in 145 patients, the mean value of VTQ measurements in patients with grades 2 and 3 esophageal varices (EV) was significantly higher than the one in patients with no or small EV (3.06 ± 0.67 vs. 2.81 ± 0.80, p = 0.03) [71].

Several studies have evaluated SWVs in the spleen for the prediction of portal hypertension, with conflicting results. In the study by Rifai et al., spleen SWVs performed better than liver SWVs for predicting CSPH [72]. In the study by Vermehren et al., spleen SWV and liver SWV had similar AUROCs for predicting the presence of at least grade 2 EV, but multiple regression analysis showed that spleen measurements performed better [73]. In the study of Takuma et al., spleen VTQ measurements also performed better than in the liver to predict the presence of varices in a cohort of 340 cirrhotic patients [74].

No data is available regarding ElastPQ.

However, according to the EFSUMB guidelines "reliable cut-offs are not available yet and no strong recommendation regarding the cut-offs to be used can be made due to the limited evidence" [5].

8.2 Hepatocellular carcinoma (HCC)

Published data showed only poor value of VTQ to predict the occurrence of HCC, with an AUROC of 0.54 [73].

There is no data regarding ElastPQ.

9. Point shear-wave elastography (pSWE): perspectives

Even if pSWE is currently implemented in other systems than from Siemens and Philips, published studies are small or missing altogether.

pSWE technique implemented on the Hitachi Ascendus system was evaluated by a study published in 2017 [75]. Reliable SWV measurements (SWM) were obtained in 87.2% of the 445 patients included. Considering TE as the reference method, cutoff values for pSWE from Hitachi had been calculated to rule in and rule out patients with significant fibrosis (F ≥ 2) and cirrhosis, respectively. SWV were converted to elastic modulus and expressed in kPa. To rule in F ≥ 2, the SWM cutoff was 6.78 kPa, while to rule it out, it was 5.55 kPa (AUROC—0.92). To rule in cirrhosis, the SWM cutoff was 9.15 kPa, and to rule it out, it was 8.41 kPa (AUROC—0.94).

A very interesting idea is to combine several techniques in order to assess not only fibrosis severity but also steatosis and inflammation using the same ultrasound machine. pSWE was combined with strain elastography on a Hitachi system. A study evaluated 388 patients with this combined technique, considering liver biopsy as reference method [76]. The AUROCs to predict fibrosis stage were 0.87, 0.80, 0.83, and 0.80 for F1, F2, F3, and F4, respectively, while the AUROCs for activity grade were 0.94, 0.74, and 0.76 for A1, A2, and A3, respectively.

10. Conclusion

pSWE is an easy to perform elastographic technique, integrated into a standard ultrasound machine, with similar performance to TE to predict fibrosis severity in patients with hepatopathies of various etiologies, the performance increasing with the fibrosis severity.

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References

[1] European Association for Study of Liver, Asociacion Latinoamericana para el Estudio del Higado. EASL-ALEH clinical practice guidelines: Non-invasive tests for evaluation of liver disease severity and prognosis. Journal of Hepatology. 2015;**63**(1):237-264

[2] Piccinino F, Sagnelli E, Pasquale G, Giusti G. Complications following percutaneous liver biopsy. A multicentre retrospective study on 68,276 biopsies. Journal of Hepatology. 1986;**2**(2):165-173

[3] Regev A, Berho M, Jeffers LJ, Milikowski C, Molina EG, Pyrsopoulos NT, et al. Sampling error and intraobserver variation in liver biopsy in patients with chronic HCV infection. The American Journal of Gastroenterology. 2002;**97**(10):2614-2618

[4] Bamber J, Cosgrove D, Dietrich CF, Fromageau J, Bojunga J, Calliada F, et al. EFSUMB guidelines and recommendations on the clinical use of ultrasound elastography. Part 1: Basic principles and technology. Ultraschall in der Medizin. 2013;**34**(2):169-184

[5] Dietrich CF, Bamber J, Berzigotti A, Bota S, Cantisani V, Castera L, et al. EFSUMB guidelines and recommendations on the clinical use of liver ultrasound Elastography, update 2017 (long version). Ultraschall in der Medizin. 2017;**38**(4):e48

[6] Ferraioli G, Filice C, Castera L, Choi BI, Sporea I, Wilson SR, et al. WFUMB guidelines and recommendations for clinical use of ultrasound elastography: Part 3: Liver. Ultrasound in Medicine & Biology. 2015;**41**(5):1161-1179

[7] Shiina T, Nightingale KR, Palmeri ML, Hall TJ, Bamber JC, Barr RG, et al. WFUMB guidelines and recommendations for clinical use of ultrasound elastography: Part 1: Basic principles and terminology. Ultrasound in Medicine & Biology. 2015;**41**(5):1126-1147

[8] Sporea I, Bota S, Saftoiu A, Sirli R, Gradinaru-Tascau O, Popescu A, et al. Romanian national guidelines and practical recommendations on liver elastography. Medical Ultrasonography. 2014;**16**(2):123-138

[9] Ferraioli G, Wong VW, Castera L, Berzigotti A, Sporea I, Dietrich CF, et al. Liver ultrasound Elastography: An update to the world Federation for Ultrasound in medicine and biology guidelines and recommendations. Ultrasound in Medicine & Biology. 2018;**44**(12):2419-2440

[10] Boursier J, Konate A, Gorea G, Reaud S, Quemener E, Oberti F, et al. Reproducibility of liver stiffness measurement by ultrasonographic elastometry. Clinical Gastroenterology and Hepatology. 2008;**6**(11):1263-1269

[11] Boursier J, Isselin G, Fouchard-Hubert I, Oberti F, Dib N, Lebigot J, et al. Acoustic radiation force impulse: A new ultrasonographic technology for the widespread noninvasive diagnosis of liver fibrosis. European Journal of Gastroenterology & Hepatology. 2010;**22**(9):1074-1084

[12] Fraquelli M, Baccarin A, Casazza G, Conti CB, Giunta M, Massironi S, et al. Liver stiffness measurement reliability and main determinants of point shear-wave elastography in patients with chronic liver disease. Alimentary Pharmacology & Therapeutics. 2016;**44**(4):356-365

[13] Sporea I, Sirli RL, Deleanu A, Popescu A, Focsa M, Danila M, et al. Acoustic radiation force impulse elastography as compared to transient elastography and liver biopsy in patients

with chronic hepatopathies. Ultraschall in der Medizin. 2011;**32**(Suppl 1):S46-S52

[14] Piscaglia F, Salvatore V, Di Donato R, D'Onofrio M, Gualandi S, Gallotti A, et al. Accuracy of VirtualTouch acoustic radiation force impulse (ARFI) imaging for the diagnosis of cirrhosis during liver ultrasonography. Ultraschall in der Medizin. 2011;**32**(2):167-175

[15] Karlas T, Pfrepper C, Wiegand J, Wittekind C, Neuschulz M, Mossner J, et al. Acoustic radiation force impulse imaging (ARFI) for non-invasive detection of liver fibrosis: Examination standards and evaluation of interlobe differences in healthy subjects and chronic liver disease. Scandinavian Journal of Gastroenterology. 2011;**46**(12):1458-1467

[16] Toshima T, Shirabe K, Takeishi K, Motomura T, Mano Y, Uchiyama H, et al. New method for assessing liver fibrosis based on acoustic radiation force impulse: A special reference to the difference between right and left liver. Journal of Gastroenterology. 2011;**46**(5):705-711

[17] Ling W, Lu Q, Quan J, Ma L, Luo Y. Assessment of impact factors on shear wave based liver stiffness measurement. European Journal of Radiology. 2013;**82**(2):335-341

[18] Bota S, Sporea I, Sirli R, Popescu A, Jurchis A. Factors which influence the accuracy of acoustic radiation force impulse (ARFI) elastography for the diagnosis of liver fibrosis in patients with chronic hepatitis C. Ultrasound in Medicine & Biology. 2013;**39**(3):407-412

[19] Bota S, Sporea I, Sirli R, Popescu A, Danila M, Sendroiu M. Factors that influence the correlation of acoustic radiation force impulse (ARFI), elastography with liver fibrosis. Medical Ultrasonography. 2011;**13**(2):135-140

[20] Goertz RS, Sturm J, Pfeifer L, Wildner D, Wachter DL, Neurath

MF, et al. ARFI cut-off values and significance of standard deviation for liver fibrosis staging in patients with chronic liver disease. Annals of Hepatology. 2013;**12**(6):935-941

[21] Ferraioli G, Maiocchi L, Lissandrin R, Tinelli C, De Silvestri A, Filice C, et al. Accuracy of the ElastPQ technique for the assessment of liver fibrosis in patients with chronic hepatitis C: A "real life" single center study. Journal of Gastrointestinal and Liver Diseases. 2016;**25**(3):331-335

[22] Ferraioli G, De Silvestri A, Reiberger T, Taylor-Robinson SD, de Knegt RJ, Maiocchi L, et al. Adherence to quality criteria improves concordance between transient elastography and ElastPQ for liver stiffness assessment—A multicenter retrospective study. Digestive and Liver Disease. 2018;**50**(10):1056-1061

[23] Lupsor M, Badea R, Stefanescu H, Sparchez Z, Branda H, Serban A, et al. Performance of a new elastographic method (ARFI technology) compared to unidimensional transient elastography in the noninvasive assessment of chronic hepatitis C. preliminary results. Journal of Gastrointestinal and Liver Diseases. 2009;**18**(3):303-310

[24] Fierbinteanu-Braticevici C, Andronescu D, Usvat R, Cretoiu D, Baicus C, Marinoschi G. Acoustic radiation force imaging sonoelastography for noninvasive staging of liver fibrosis. World Journal of Gastroenterology. 2009;**15**(44):5525-5532

[25] Bota S, Sporea I, Sirli R, Popescu A, Danila M, Jurchis A, et al. Factors associated with the impossibility to obtain reliable liver stiffness measurements by means of acoustic radiation force impulse (ARFI) elastography—analysis of a cohort of 1,031 subjects. European Journal of Radiology. 2014;**83**(2):268-272

[26] Sporea I, Mare R, Lupusoru R, Popescu A, Danila M, Bende F, et al. Comparative study between four ultrasound shear waves Elastographic methods for liver fibrosis assessment. Medical Ultrasonography. 2018;**20**(3):265-271

[27] Mare R, Sporea I, Lupusoru R, Sirli R, Popescu A, Danila M, et al. The value of ElastPQ for the evaluation of liver stiffness in patients with B and C chronic hepatopathies. Ultrasonics. 2017;**77**:144-151

[28] Bota S, Sporea I, Sirli R, Popescu A, Danila M, Costachescu D. Intra- and interoperator reproducibility of acoustic radiation force impulse (ARFI) elastography—Preliminary results. Ultrasound in Medicine & Biology. 2012;**38**(7):1103-1108

[29] Guzman-Aroca F, Reus M, Berna-Serna JD, Serrano L, Serrano C, Gilabert A, et al. Reproducibility of shear wave velocity measurements by acoustic radiation force impulse imaging of the liver: A study in healthy volunteers. Journal of Ultrasound in Medicine. 2011;**30**(7):975-979

[30] Ma JJ, Ding H, Mao F, Sun HC, Xu C, Wang WP. Assessment of liver fibrosis with elastography point quantification technique in chronic hepatitis B virus patients: A comparison with liver pathological results. Journal of Gastroenterology and Hepatology. 2014;**29**(4):814-819

[31] Ferraioli G, Tinelli C, Lissandrin R, Zicchetti M, Dal Bello B, Filice G, et al. Point shear wave elastography method for assessing liver stiffness. World Journal of Gastroenterology. 2014;**20**(16):4787-4796

[32] Popescu A, Bota S, Sporea I, Sirli R, Danila M, Racean S, et al. The influence of food intake on liver stiffness values assessed by acoustic radiation force impulse elastography-preliminary

results. Ultrasound in Medicine & Biology. 2013;**39**(4):579-584

[33] Gersak MM, Sorantin E, Windhaber J, Dudea SM, Riccabona M. The influence of acute physical effort on liver stiffness estimation using virtual touch quantification (VTQ). Preliminary results. Medical Ultrasonography. 2016;**18**(2):151-156

[34] Bota S, Sporea I, Peck-Radosavljevic M, Sirli R, Tanaka H, Iijima H, et al. The influence of aminotransferase levels on liver stiffness assessed by acoustic radiation force impulse Elastography: A retrospective multicentre study. Digestive and Liver Disease. 2013;**45**(9):762-768

[35] Yoon KT, Lim SM, Park JY, Kim DY, Ahn SH, Han KH, et al. Liver stiffness measurement using acoustic radiation force impulse (ARFI) elastography and effect of necroinflammation. Digestive Diseases and Sciences. 2012;**57**(6):1682-1691

[36] Kuroda H, Takikawa Y, Onodera M, Kakisaka K, Yoshida Y, Kataoka K, et al. Serial changes of liver stiffness measured by acoustic radiation force impulse imaging in acute liver failure: A case report. Journal of Clinical Ultrasound. 2012;**40**(2):99-104

[37] Goertz RS, Egger C, Neurath MF, Strobel D. Impact of food intake, ultrasound transducer, breathing maneuvers and body position on acoustic radiation force impulse (ARFI) elastometry of the liver. Ultraschall in der Medizin. 2012;**33**(4):380-385

[38] Attia D, Pischke S, Negm AA, Rifai K, Manns MP, Gebel MJ, et al. Changes in liver stiffness using acoustic radiation force impulse imaging in patients with obstructive cholestasis and cholangitis. Digestive and Liver Disease. 2014;**46**(7):625-631

[39] Popescu A, Sporea I, Sirli R, Bota S, Focsa M, Danila M, et al. The mean values of liver stiffness assessed by acoustic radiation force impulse elastography in normal subjects. Medical Ultrasonography. 2011;**13**(1):33-37

[40] Son CY, Kim SU, Han WK, Choi GH, Park H, Yang SC, et al. Normal liver elasticity values using acoustic radiation force impulse imaging: A prospective study in healthy living liver and kidney donors. Journal of Gastroenterology and Hepatology. 2012;**27**(1):130-136

[41] Goertz RS, Amann K, Heide R, Bernatik T, Neurath MF, Strobel D. An abdominal and thyroid status with acoustic radiation force impulse Elastometry—A feasibility study: Acoustic Radiation Force Impulse Elastometry of human organs. European Journal of Radiology. 2011;**80**(3):e226-e230

[42] Madhok R, Tapasvi C, Prasad U, Gupta AK, Aggarwal A. Acoustic radiation force impulse imaging of the liver: Measurement of the normal mean values of the shearing wave velocity in a healthy liver. Journal of Clinical and Diagnostic Research. 2013;**7**(1):39-42

[43] Sporea I, Bota S, Gradinaru-Tascau O, Sirli R, Popescu A. Comparative study between two point shear wave Elastographic techniques: Acoustic radiation force impulse (ARFI) elastography and ElastPQ. Medical Ultrasonography. 2014;**16**(4):309-314

[44] Friedrich-Rust M, Wunder K, Kriener S, Sotoudeh F, Richter S, Bojunga J, et al. Liver fibrosis in viral hepatitis: Noninvasive assessment with acoustic radiation force impulse imaging versus transient elastography. Radiology. 2009;**252**(2):595-604

[45] Sporea I, Badea R, Sirli R, Lupsor M, Popescu A, Danila M, et al. How efficient is acoustic radiation force impulse elastography for the evaluation of liver stiffness? Hepatitis Monthly. 2011;**11**(7):532-538

[46] Takahashi H, Ono N, Eguchi Y, Eguchi T, Kitajima Y, Kawaguchi Y, et al. Evaluation of acoustic radiation force impulse elastography for fibrosis staging of chronic liver disease: A pilot study. Liver International. 2010;**30**(4):538-545

[47] Goertz RS, Zopf Y, Jugl V, Heide R, Janson C, Strobel D, et al. Measurement of liver elasticity with acoustic radiation force impulse (ARFI) technology: An alternative noninvasive method for staging liver fibrosis in viral hepatitis. Ultraschall in der Medizin. 2010;**31**(2):151-155

[48] Ebinuma H, Saito H, Komuta M, Ojiro K, Wakabayashi K, Usui S, et al. Evaluation of liver fibrosis by transient elastography using acoustic radiation force impulse: Comparison with Fibroscan ((R)). Journal of Gastroenterology. 2011;**46**(10):1238-1248

[49] Colombo S, Buonocore M, Del Poggio A, Jamoletti C, Elia S, Mattiello M, et al. Head-to-head comparison of transient elastography (TE), real-time tissue elastography (RTE), and acoustic radiation force impulse (ARFI) imaging in the diagnosis of liver fibrosis. Journal of Gastroenterology. 2012;**47**(4):461-469

[50] Cassinotto C, Lapuyade B, Mouries A, Hiriart JB, Vergniol J, Gaye D, et al. Non-invasive assessment of liver fibrosis with impulse elastography: Comparison of supersonic shear imaging with ARFI and FibroScan(R). Journal of Hepatology. 2014;**61**(3):550-557

[51] Friedrich-Rust M, Nierhoff J, Lupsor M, Sporea I, Fierbinteanu-Braticevici C, Strobel D, et al. Performance of acoustic radiation force impulse imaging for the staging of liver fibrosis: A pooled

meta-analysis. Journal of Viral Hepatitis. 2012;**19**(2):e212-e219

[52] Bota S, Herkner H, Sporea I, Salzl P, Sirli R, Neghina AM, et al. Meta-analysis: ARFI elastography versus transient elastography for the evaluation of liver fibrosis. Liver International. 2013;**33**(8):1138-1147

[53] Nierhoff J, Chavez Ortiz AA, Herrmann E, Zeuzem S, Friedrich-Rust M. The efficiency of acoustic radiation force impulse imaging for the staging of liver fibrosis: A meta-analysis. European Radiology. 2013;**23**(11):3040-3053

[54] Hu X, Qiu L, Liu D, Qian L. Acoustic radiation force impulse (ARFI) Elastography for noninvasive evaluation of hepatic fibrosis in chronic hepatitis B and C patients: A systematic review and meta-analysis. Medical Ultrasonography. 2017;**19**(1):23-31

[55] Sporea I, Sirli R, Bota S, Fierbinteanu-Braticevici C, Petrisor A, Badea R, et al. Is ARFI elastography reliable for predicting fibrosis severity in chronic HCV hepatitis? World Journal of Radiology. 2011;**3**(7):188-193

[56] Sporea I, Bota S, Peck-Radosavljevic M, Sirli R, Tanaka H, Iijima H, et al. Acoustic radiation force impulse elastography for fibrosis evaluation in patients with chronic hepatitis C: An international multicenter study. European Journal of Radiology. 2012;**81**(12):4112-4118

[57] Rizzo L, Calvaruso V, Cacopardo B, Alessi N, Attanasio M, Petta S, et al. Comparison of transient elastography and acoustic radiation force impulse for non-invasive staging of liver fibrosis in patitts with chronic hepatitis C. The American Journal of Gastroenterology. 2011;**106**(12):2112-2120

[58] Chen SH, Li YF, Lai HC, Kao JT, Peng CY, Chuang PH, et al. Effects of

patient factors on noninvasive liver stiffness measurement using acoustic radiation force impulse elastography in patients with chronic hepatitis C. BMC Gastroenterology. 2012;**12**:105

[59] Li SM, Li GX, Fu DM, Wang Y, Dang LQ. Liver fibrosis evaluation by ARFI and APRI in chronic hepatitis C. World Journal of Gastroenterology. 2014;**20**(28):9528-9533

[60] Conti F, Serra C, Vukotic R, Fiorini E, Felicani C, Mazzotta E, et al. Accuracy of elastography point quantification and steatosis influence on assessing liver fibrosis in patients with chronic hepatitis C. Liver International. 2017;**37**(2):187-195

[61] Goertz RS, Sturm J, Zopf S, Wildner D, Neurath MF, Strobel D. Outcome analysis of liver stiffness by ARFI (acoustic radiation force impulse) elastometry in patients with chronic viral hepatitis B and C. Clinical Radiology. 2014;**69**(3):275-279

[62] Friedrich-Rust M, Buggisch P, de Knegt RJ, Dries V, Shi Y, Matschenz K, et al. Acoustic radiation force impulse imaging for non-invasive assessment of liver fibrosis in chronic hepatitis B. Journal of Viral Hepatitis. 2013;**20**(4):240-247

[63] Zhang D, Chen M, Wang R, Liu Y, Zhang D, Liu L, et al. Comparison of acoustic radiation force impulse imaging and transient elastography for non-invasive assessment of liver fibrosis in patients with chronic hepatitis B. Ultrasound in Medicine & Biology. 2015;**41**(1):7-14

[64] Dong DR, Hao MN, Li C, Peng Z, Liu X, Wang GP, et al. Acoustic radiation force impulse elastography, FibroScan(R), Forns' index and their combination in the assessment of liver fibrosis in patients with chronic hepatitis B, and the impact of inflammatory activity and steatosis on

these diagnostic methods. Molecular Medicine Reports. 2015;**11**(6):4174-4182

[65] Yoneda M, Suzuki K, Kato S, Fujita K, Nozaki Y, Hosono K, et al. Nonalcoholic fatty liver disease: US-based acoustic radiation force impulse elastography. Radiology. 2010;**256**(2):640-647

[66] Friedrich-Rust M, Romen D, Vermehren J, Kriener S, Sadet D, Herrmann E, et al. Acoustic radiation force impulse-imaging and transient elastography for non-invasive assessment of liver fibrosis and steatosis in NAFLD. European Journal of Radiology. 2012;**81**(3):e325-e331

[67] Fierbinteanu Braticevici C, Sporea I, Panaitescu E, Tribus L. Value of acoustic radiation force impulse imaging elastography for non-invasive evaluation of patients with nonalcoholic fatty liver disease. Ultrasound in Medicine & Biology. 2013;**39**(11):1942-1950

[68] Liu H, Fu J, Hong R, Liu L, Li F. Acoustic radiation force impulse Elastography for the non-invasive evaluation of hepatic fibrosis in non-alcoholic fatty liver disease patients: A Systematic Review & Meta-Analysis. PLoS One. 2015;**10**(7):e0127782

[69] Bosch J, Garcia-Pagan JC, Berzigotti A, Abraldes JG. Measurement of portal pressure and its role in the management of chronic liver disease. Seminars in Liver Disease. 2006;**26**(4):348-362

[70] Salzl P, Reiberger T, Ferlitsch M, Payer BA, Schwengerer B, Trauner M, et al. Evaluation of portal hypertension and varices by acoustic radiation force impulse imaging of the liver compared to transient elastography and AST to platelet ratio index. Ultraschall in der Medizin. 2014;**35**(6):528-533

[71] Bota S, Sporea I, Sirli R, Focsa M, Popescu A, Danila M, et al. Can ARFI

elastography predict the presence of significant esophageal varices in newly diagnosed cirrhotic patients? Annals of Hepatology. 2012;**11**(4):519-525

[72] Rifai K, Cornberg J, Bahr M, Mederacke I, Potthoff A, Wedemeyer H, et al. ARFI elastography of the spleen is inferior to liver elastography for the detection of portal hypertension. Ultraschall in der Medizin. 2011;**32**(Suppl 2):E24-E30

[73] Vermehren J, Polta A, Zimmermann O, Herrmann E, Poynard T, Hofmann WP, et al. Comparison of acoustic radiation force impulse imaging with transient elastography for the detection of complications in patients with cirrhosis. Liver International. 2012;**32**(5):852-858

[74] Takuma Y, Nouso K, Morimoto Y, Tomokuni J, Sahara A, Toshikuni N, et al. Measurement of spleen stiffness by acoustic radiation force impulse imaging identifies cirrhotic patients with esophageal varices. Gastroenterology. 2013;**144**(1):92-101 e2

[75] Ferraioli G, Maiocchi L, Lissandrin R, Tinelli C, De Silvestri A, Filice C. Ruling-in and ruling-out significant fibrosis and cirrhosis in patients with chronic hepatitis C using a shear wave measurement method. Journal of Gastrointestinal and Liver Diseases. 2017;**26**(2):139-143

[76] Yada N, Tamaki N, Koizumi Y, Hirooka M, Nakashima O, Hiasa Y, et al. Diagnosis of fibrosis and activity by a combined use of strain and shear wave imaging in patients with liver disease. Digestive Diseases. 2017;**35**(6):515-520