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● *Original Contribution*

# INTRA-INDIVIDUAL COMPARISON BETWEEN 2-D SHEAR WAVE ELASTOGRAPHY (GE SYSTEM) AND VIRTUAL TOUCH TISSUE QUANTIFICATION (SIEMENS SYSTEM) IN GRADING LIVER FIBROSIS

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**Abstract—Ultrasound-based shear wave elastography (SWE) has recently gained substantial attention for non-invasive assessment of liver fibrosis. The purpose of this study was to perform an intra-individual comparison between 2-D shear wave elastography (2-D-SWE with a GE system) and Virtual Touch Tissue Quantification (VTTQ with a Siemens system) to assess whether these can be used interchangeably to grade fibrosis. Ninety-three patients (51 men, 42 women; mean age, 54 y) with liver disease of various etiologies (hepatitis B virus = 47, hepatitis C virus = 22; alcohol = 6, non-alcoholic steatohepatitis = 5, other = 13) were included. Using published system-specific shear wave speed cutoff values, liver fibrosis was classified into clinically non-significant (F0/F1) and significant (≥F2) fibrosis. Results indicated that intra-modality repeatability was excellent for both techniques (GE 2-D-SWE: intra-class correlation coefficient = 0.89 [0.84–0.93]; VTTQ: intra-class correlation coefficient = 0.90 [0.86–0.93]). Intra-modality classification agreement for fibrosis grading was good to excellent (GE 2-D-SWE: $\kappa = 0.65$, VTTQ: $\kappa = 0.82$). However, inter-modality agreement for fibrosis grading was only fair ($\kappa = 0.31$) using published system-specific shear wave speed cutoff values of fibrosis. In conclusion, although both GE 2-D-SWE and Siemens VTTQ exhibit good to excellent intra-modality repeatability, inter-modality agreement is only fair, suggesting that these should not be used interchangeably. (E-mail: willmann@stanford.edu)** **© 2017 World Federation for Ultrasound in Medicine & Biology. All rights reserved.**

*Key Words:* **Ultrasound elastography, GE 2-D shear wave elastography, Virtual Touch Tissue Quantification, Liver, Fibrosis.**

## INTRODUCTION

Liver fibrosis is a wound-healing response to chronic liver injuries, which result mainly from viral hepatitis and chronic alcohol abuse, among other conditions (Pellicoro et al. 2014). This process can eventually lead to cirrhosis, increasing the risk for portal hypertension, hepatic insufficiency and development of hepatocellular carcinoma (Pellicoro et al. 2014). Histology after liver biopsy is the standard of care for evaluating and grading liver fibrosis, which is invasive and can result in procedural complications, such as pain, bleeding, sepsis, pneumothorax and even death (Kose et al. 2015). Also, biopsy-based assessments are vulnerable to sampling errors because only a very small fraction of the liver is evaluated (approximately a 50,000th of the volume) (Barr 2014; Cosgrove et al. 2013), and substantial variability among pathologies has been reported when grading liver fibrosis using the METAVIR scoring system (Ratziu et al. 2005; Regev et al. 2002; Standish et al. 2006). All these limitations led to the development of non-invasive methods for staging liver fibrosis such as serum biomarkers and ultrasound measurement of liver stiffness (Barr et al. 2015; European Association for Study of Liver 2012; European Association for Study of Liver and Asociacion Latinoamericana para el Estudio del Higado 2015), which have already been accepted by clinical guidelines, replacing liver biopsy in several clinical settings.

Ultrasound elastography (USE) is a family of ultrasound-based imaging techniques that can measure liver stiffness, quantifying mechanical properties of tissues, and has exhibited potential in detecting, grading and monitoring liver fibrosis in patients. Of specific interest are the recently introduced ultrasound shear wave elastography (SWE) techniques, which have enabled quantitative

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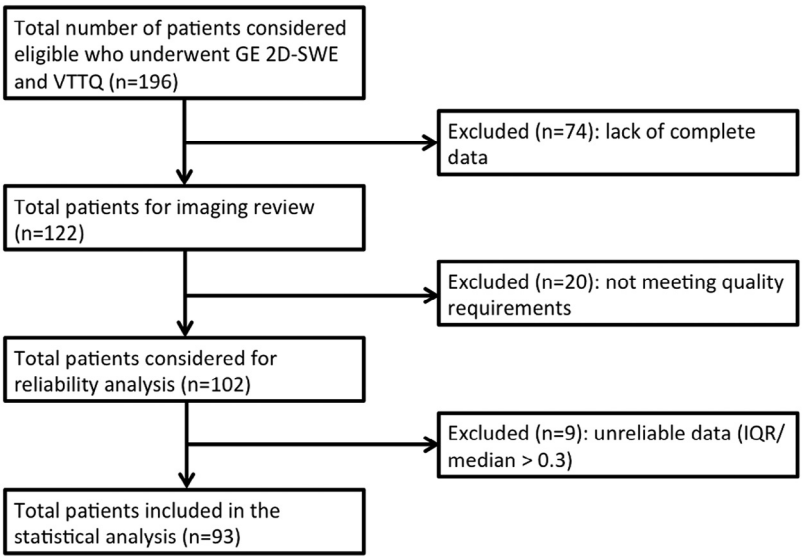


Fig. 1. Flow diagram outlining patient inclusion in this study. IQR = interquartile range; SWE = shear wave elastography; VTTQ = Virtual Touch tissue quantification.

evaluation and grading of liver fibrosis (Garra 2015). SWE techniques rely on ultrasound-based acoustic radiation force impulses (ARFIs) to generate a controlled mechanical stress on the tissue of interest (*i.e.,* liver) and use proprietary ultrasound methods to measure tissue response to these stimuli in the form of shear wave speed (SWS) (Garra 2015). In 2-D SWE (2-D-SWE) approaches, a series of shear waves are generated with ARFI using system-specific proprietary methods, and multiple focal zones are then interrogated (Song et al. 2014). In point SWE (pSWE), ARFI is used to induce tissue displacement in the normal direction at a single focal location, and single point measurements are taken at a perpendicular location (Palmeri et al. 2008). Different implementations of both 2-D-SWE and pSWE exist, but ultimately, 2-D-SWE results in image mapping of SWS measurements at various locations within a user-selected region of interest (ROI), and pSWE results in a point measurement centered in a small ROI custom-placed by the user.

With the advent of various manufacturer-specific SWE methods recently introduced into clinical practice, the challenge is that patients are likely to undergo fibrosis assessment and grading at different sites or clinics using different SWE platforms. However, although individual methods have been validated using biopsy as the reference standard, little information is available on how different commercial implementations of SWE compare with each other in grading fibrosis (Barr et al. 2015). Hence, inter-modality comparison studies in the same patients are critical to assess whether currently available SWE techniques provided by different ultrasound manufacturers can be used interchangeably in routine clinical practice.

Therefore, the purpose of this study was to perform an intra-individual comparison between GE's 2-D-SWE system and a pSWE system and Siemens' Virtual Touch Tissue Quantification (VTTQ) to assess whether these can be used interchangeably to grade clinically non-significant (F0/F1) versus significant (≥F2) liver fibrosis.

## METHODS

*Patient population*

This was a retrospective single-center study approved by the institutional review board and was Health Insurance Portability and Accountability Act compliant; requirements for an informed consent were waived. A total of 196 consecutive patients who underwent clinically indicated fibrosis screening between November 2015 and March 2016 and who were imaged with both GE 2-D-SWE and VTTQ on the same day as part of an internal attempt to evaluate the interchangeability of the two technologies in our clinical practice were retrospectively enrolled. Inclusion criteria were the presence of chronic liver disease or elevated liver enzymes and clinical referral for a routine liver ultrasound with Doppler and USE. Patients were excluded for the following reasons (Fig. 1): (i) lack of two complete sets of 10 SWS measurements (total n = 74 patients) each for both GE 2-D-SWE (n = 55/74) and VTTQ (n = 19/74); (ii) images judged as not meeting quality requirements (total n = 20; images with rib shadows (n = 3/20); measurements not obtained at 4–5 cm of depth from the transducer [n = 12/20] and within 1–2 cm of Glisson's capsule [n = 5/20]); and (iii) presence of unreliable data sets defined as an interquartile range

(IQR) divided by the median value (IQR/median) obtained from each of the 10 measurements ≥0.3 (Barr et al. 2015) (total n = 9 patients; GE 2-D-SWE [n = 2]; VTTQ [n = 7]). The IQR is a measure of the statistical dispersion, equal to the difference between the upper and lower quartiles.

A total of 93 patients were included in the analysis component of the study (51 men with a mean age of 51 ± 15 y; range: 22–86 y; and 42 women with a mean age of 57 ± 13 y, range: 27–86 y). Etiologies of liver disease included chronic hepatitis B in 47 of 93 patients (51%), chronic hepatitis C in 22 of 93 patients (24%), alcoholic liver disease in 6 of 93 patients (6%), non-alcoholic steatohepatitis in 5 of 93 patients (5%), primary biliary cirrhosis in 3 of 93 patients (3%) and elevated liver enzymes in 10 of 93 patients (11%).

*Ultrasound elastography image acquisition*

All patients were asked to fast for at least 8 h before scans. A routine liver ultrasound examination was performed first, including B-mode and Doppler mode imaging of the vasculature in all patients. All elastography measurements of the liver were then performed according to the Consensus Conference statements of the Society of Radiologist in Ultrasound (Barr et al. 2015) by 1 of 11 sonographers (with a minimum of 18 mo of experience in clinical USE). In brief, all patients were placed in either the supine or left lateral decubitus position at ≤30°, whichever provided the best acoustic window, with the right arm elevated above the shoulder to increase the intercostal spaces. The transducer was placed in an intercostal position and was kept still during acquisition. The imaging window was optimized to ensure the best possible B-mode image quality without rib shadows before starting USE acquisition. All parameters were kept consistent in our study, and care was taken to ensure that the ROIs for both SWE methods were at the exact same location. Sonographers were asked to take measurements with both methods at the level of the right portal vein bifurcation, which served as an anatomic landmark, and patients were asked to maintain breath holding at a neutral position. All ROIs were placed in the liver parenchyma at a 4–5-cm depth from the transducer, within 1–2 cm of Glisson's capsule, and perpendicular to the liver capsule, without including large vessels or dilated bile ducts (Fig. 2). Note that none of the patients in this study had intrahepatic ductal dilation. To statistically compensate for small deviations in locations of measurements, two sets of 10 repeated measurements (in m/s) were taken for both SWE techniques, resulting in a total of 40 measurements for each patient. The method used first to acquire the images was chosen randomly, depending on the availability of the system in clinics. Both sets of SWS measurements were taken consecutively for each modality.

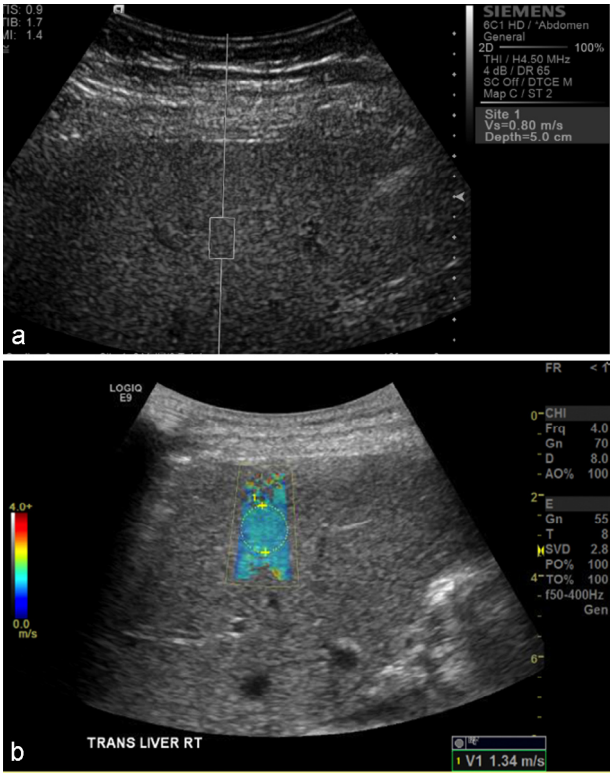


Fig. 2. Representative B-mode images with region-of-interest overlay used to obtained shear wave speed measurements at same anatomic location in 67-y-old man with chronic hepatitis B who underwent elastography measurements with (a) VTTQ and (b) GE 2-D-SWE. Note that regions of interest were placed at 4–6 cm of depth from the transducer and perpendicular to the liver capsule, without including large vessels or dilated bile duct. SWE = shear wave elastography; VTTQ = Virtual Touch tissue quantification.

*2-D shear wave elastography*

GE 2-D-SWE was performed using a LOGIQ E9 (LE9) system coupled to a curved array C1.6 transducer (GE Healthcare, Waukesha, WI, USA) with a frequency range of 4–6 MHz. To generate 2-D maps of SWS at different locations in the probed tissue, this technique generates shear waves based on a comb-push excitation method that results in multiple shear waves at different depths in the tissue (Song et al. 2012). These are then detected using a time-aligned sequential tracking method (Song et al. 2014). SWS maps were generated within user-defined 2-D ROIs, and measurements of SWS were obtained using a customizable circular sub-region that was placed at a user-defined location within the 2-D SWS maps. The diameter of the circular ROIs was 7 mm (39 $mm^2$) in 84 of 93 (90%) of patients (similar to VTTQ ROI) and 13 mm diameter (132 $mm^2$) in 9 of 93 (10%) patients. All SWS measurements were obtained in meters per second (Fig. 2).

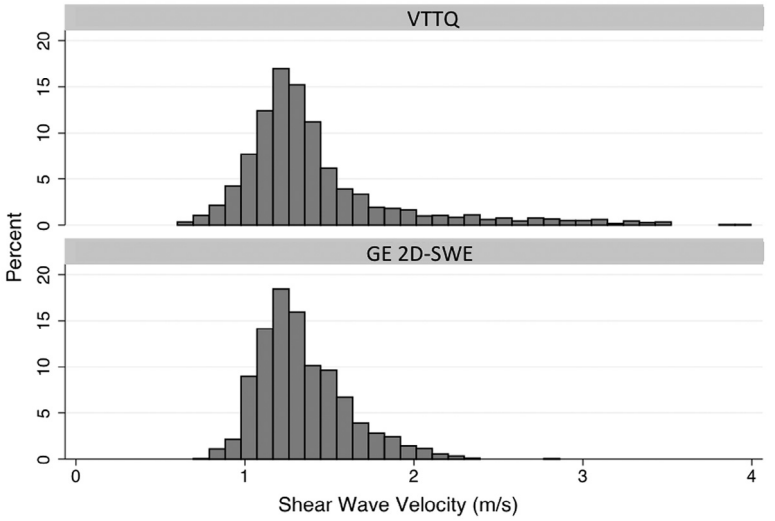


Fig. 3. Bar charts of VTTQ and GE 2-D-SWE distribution of SWS measurements in m/s. Bars show the percent of shear wave speed measurements. Overall, VTTQ and GE 2-D-SWE had similar distributions, both skewed to the left. However, the dispersion of SWS measurements was wider for VTTQ, ranging from 0.67 to 3.90 m/s, whereas for GE 2-D-SWE, it ranged from 0.74 to 2.86 m/s. SWE = shear wave elastography; VTTQ = Virtual Touch tissue quantification.

*Point shear wave elastography*

Point SWE was performed on an Acuson S2000 (Siemens Medical Solutions, Mountain View, CA, USA) equipped with the Virtual Touch Tissue Quantification (VTTQ) mode (Fig. 2). VTTQ uses short-duration acoustic radiation force impulses (ARFIs) to stimulate tissues and generate tissue displacement at a single point in the center of an ROI, ultimately resulting in traveling shear waves that propagate through the tissue (Palmeri et al. 2008). The SWS measurements were made using a method for cross-correlation of radiofrequency data to detect liver tissue displacements caused by the traveling shear wave (Palmeri et al. 2008). The ROI was fixed at 10 mm axial × 6 mm lateral (roughly equivalent to 2-D-SWE ROI), and the VTTQ measurements were obtained within the ROI. All SWS measurements using VTTQ were obtained in meters per second using the Acuson S2000 coupled to a 6 C1 curved array transducer (Siemens Medical Solutions).

*Statistical analysis*

For all patients, SWS measurements for both GE 2-D-SWE and VTTQ were obtained from the picture archiving and communication system (PACS, Centricity, GE) of the Department of Radiology by one blinded reader (5 y of experience in ultrasound reading), and the mean, median, standard deviation and IQR/median for all sets of 10 measurements were recorded. Differences between measurements obtained with GE 2-D-SWE and VTTQ regarding the number of unreliable examinations (defined as IQR/median ≥0.3) were tested with Fisher's exact test. All SWS measurements were log-transformed to achieve normality. The intra-modality measurement repeatability, which is the repeatability of the raw SWS measurements, was assessed with the intra-class correlation coefficient (ICC). An ICC of 0–0.20 suggested no agreement; 0.21–0.40, poor agreement; 0.41–0.60, moderate agreement; 0.61–0.80, good agreement; and >0.80, excellent agreement (Bartko and Carpenter 1976).

Liver fibrosis was classified into clinically nonsignificant (F0/F1) and significant (≥F2) fibrosis based on the following cutoff values: 1.34 m/s for VTTQ and 1.66 m/s for GE 2-D-SWE. The VTTQ cutoff value is based on a meta-analysis using liver biopsy and histology as the reference standard (Friedrich-Rust et al. 2012); the GE 2-D-SWE cutoff values were provided by the manufacturer, and are based on data in 85 patients using biopsy and histology as the reference standard. Intra-modality and inter-modality classification concordance between GE 2-D-SWE and VTTQ with respect to fibrosis grading was expressed as both the κ statistic and percentage agreement. A κ value of 0.01–0.2 suggested slight agreement, 0.21–0.40, fair agreement; 0.41–0.60, moderate agreement; 0.61–0.80, good agreement; and 0.81–1.0, excellent agreement (McHugh 2012). All data analyses and statistical tests were performed with Stata Release 14.1 (StataCorp LP, College Station, TX, USA). Statistical significance was based on a $p$ value < 0.05.

## RESULTS

*Overall data distribution*

The overall distributions of SWS measurements from GE 2-D-SWE and VTTQ for the 93 patients are

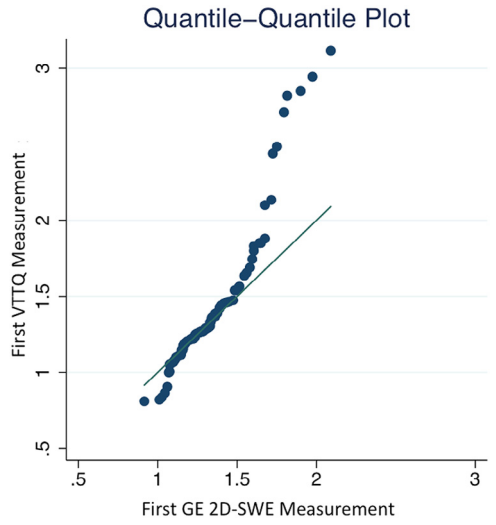


Fig. 4. Quantile–quantile plot between GE 2-D-SWE and VTTQ measurements (only first sets of 10 measurements each were plotted). Note linearity of the points within the interval 1.1 to 1.6 m/s, suggesting that SWE measurements were similar within this interval. SWE = shear wave elastography; VTTQ = Virtual Touch tissue quantification.

illustrated in Figure 3. GE 2-D-SWE measurements exhibited a narrower SWS distribution than did the VTTQ measurements, with the minimum SWS measurement higher and the maximum SWS measurement lower than those obtained with VTTQ. Measurements ranged from 0.74 to 2.86 m/s for GE 2-D-SWE and from 0.67 to 3.90 m/s for VTTQ, with a distribution skewed to the left (GE 2-D-SWE skewness: 1.14; VTTQ skewness: 2.26) (Fig. 3). The overall average SWS ± standard deviation measured with GE 2-D-SWE (1.34 ± 0.26 m/s) was significantly smaller ($p < 0.001$) than the average SWS measurements obtained with VTTQ (1.42 ± 0.48 m/s).

Within the interval 1.1 to 1.6 m/s, both GE 2-D-SWE and VTTQ SWE measurements were similar, as illustrated by the quantile–quantile plot in Figure 4.

*Reliability of SWS measurements*

For GE 2-D-SWE, 2% (2/102) of the patients had SWS measurements that were considered unreliable (based on an IQR/median value ≥ 0.3) and for VTTQ, 7% (7/102) of the patients had SWS measurements that were unreliable; therefore, these were excluded from the quantitative analysis. This difference was not statistically significantly different ($p = 0.38$).

*Intra-modality measurement repeatability*

The average ± standard deviation and median values of GE 2-D-SWE measurements were 1.34 ± 0.25 and 1.30 m/s for set 1 and 1.35 ± 0.27 and 1.29 m/s for set 2, respectively. The average ± standard deviation and median values of VTTQ measurements were 1.43 ± 0.49 and 1.30 m/s for set 1 and 1.42 ± 0.47 and 1.28 m/s for set 2, respectively (Fig. 5). The intra-modality repeatability for both GE 2-D-SWE and VTTQ was excellent (GE 2-D-SWE: ICC = 0.89 [95% confidence interval (CI): 0.84–0.93]; VTTQ: ICC = 0.90 [95% CI: 0.86–0.93]).

*Intra- and inter-modality classification agreement*

The intra-modality agreement for differentiating between clinically non-significant (F0/F1) and significant (F ≥ 2) fibrosis was good ($\kappa = 0.65$) for GE 2-D-SWE, with an excellent percentage agreement of 0.92 (95% CI: 0.85–0.97). For VTTQ, the intra-modality agreement was excellent ($\kappa = 0.82$), with an excellent percentage agreement of 0.91 (95% CI: 0.84–0.96). However, the inter-modality agreement between GE 2-D-SWE and VTTQ for differentiating clinically non-significant from significant fibrosis was only fair ($\kappa = 0.31$) with a percentage agreement of 0.71 (95% CI: 0.61–0.80).

## DISCUSSION

Our results suggest that quantitative GE 2-D-SWE and VTTQ cannot be used interchangeably to grade liver fibrosis in the same patient longitudinally. Although intra-modality repeatability was excellent and intra-modality classification concordance was good to excellent, inter-modality agreement was only fair using the two state-of-the-art USE techniques from GE and Siemens along with currently used cutoff values to differentiate clinically non-significant from significant fibrosis.

Numerous studies have reported on VTTQ's potential to grade liver fibrosis (Bota et al. 2013; Friedrich-Rust et al. 2012; Nierhoff et al. 2013). A systematic review and meta-analysis of 8 studies including 518 patients and using liver biopsy as a reference method found good to excellent diagnostic accuracy for grading fibrosis with area under the receiver operating characteristic (AUROC) values of 0.87, 0.91, 0.93 for diagnosing F ≥ 2, F ≥ 3 and F = 4, respectively, compared with histology (Friedrich-Rust et al. 2012). Another meta-analysis of 3951 patients from 36 studies confirmed good diagnostic accuracy of VTTQ for liver fibrosis grading (Nierhoff et al. 2013). Therefore, VTTQ has been implemented in routine clinical practice in many clinical departments in recent years. In contrast, 2-D-SWE was recently introduced by GE along with a set of cutoff values determined using liver biopsy data obtained in 85 patients as reference standard. In our study, we used the cutoff value of 1.66 m/s to differentiate clinically significant from non-significant fibrosis. Although magnetic resonance elastography (MRE) has been used as the "silver standard" to validate GE's cutoff values in grading fibrosis in 47 patients (Song et al. 2016), larger

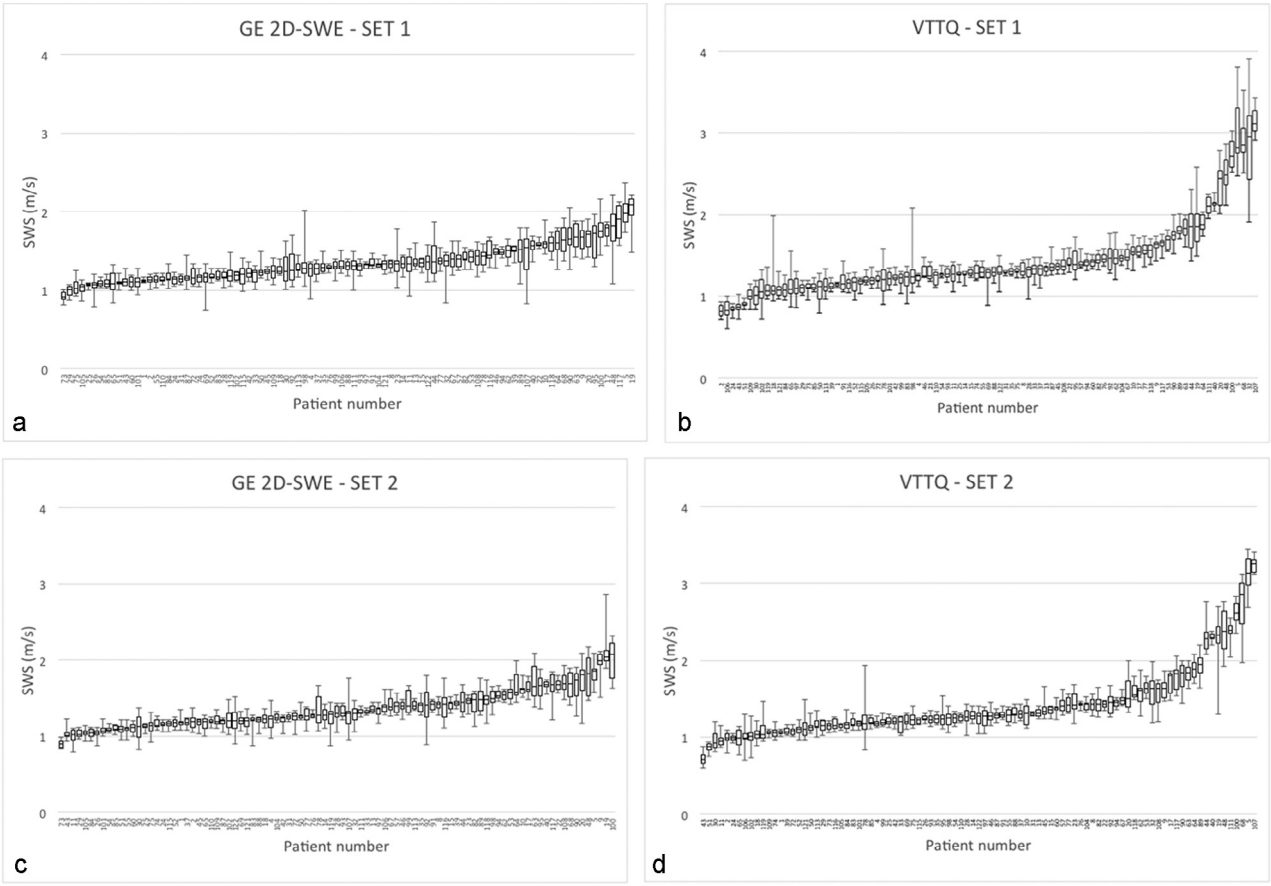


Fig. 5. Box-and-whisker plots of all SWS measurements (m/s) for the first and second sets of GE 2-D-SWE (a, c) and VTTQ (b,d) for each of the 93 patients. Each box in the plot represents the 25th and 75th quartiles, the line inside each box identifies the median and the whiskers indicate the minimum and maximum SWS measurement. SWE = shear wave elastography; SWS = shear wave speed; VTTQ = Virtual Touch tissue quantification.

studies using histology as reference standard are still warranted for further confirmation.

Although various elastography methods have been assessed independently, only a few studies have directly compared the diagnostic capabilities of different SWE techniques/implementations for grading liver fibrosis within the same patient contemporaneously (Belei et al. 2016; Cassinotto et al. 2014; Gerber et al. 2015; Sporea et al. 2013, 2014; Woo et al. 2015). Such studies are critical from a practical clinical point of view to allow interchangeable use of various ultrasound machines for quantitative SWE measurements in a clinical practice. To address this issue and to enable comparisons of the various SWE technologies from various vendors, the ultrasound SWS technical committee of the Radiologic Society of North America Quantitative Imaging Biomarker Alliance initiated an inter-laboratory study of SWS estimations in a variety of phantoms with different stiffness values, but generally classified as relatively stiff or soft compared with the liver. Dynamic mechanical tests of phantom materials were used to quantitatively characterize the differences between commercial SWE systems (Hall et al. 2013). Measurements were taken at three depths on research and clinically available commercial SWS-capable systems (Fibroscan, Philips, Siemens S2000, SSI Aixplorer, Verasonics SWE research implementation 1 at Duke and Verasonics SWE research implementation 2 at Mayo Clinic) as well as on experimental systems. Although system-specific intra-site SWS comparisons were found to agree well, intra-system SWS comparisons as a function of imaging depth were overall statistically significantly different from one manufacturer/implementation to another. More specifically, mean SWS estimates across all sites for each of the systems used ranged from 0.86 to 0.98 m/s, with min/max SWS estimates of 0.78 to 1.06 for the soft phantoms, and 2.05 to 2.18 m/s with min/max SWS estimates of 1.87 to 2.84 m/s for the stiff phantoms. A statistically significant difference in SWS estimates between systems and as a function of depth within phantom was found (Hall et al. 2013). Our clinical results in patients

are in general consensus with these phantom findings; there is a critical need for further *in vivo* and clinical studies to characterize sources of errors in living patients that cannot be accounted for in phantoms (*i.e.,* breathing, physiology), with the ultimate goal of interchangeable use of different systems in patients.

Comparison studies between different SWE systems have been performed in patients with mixed results. In an intra-individual prospective comparison study in 349 patients with liver biopsy and histology used as reference standard, Supersonic Imaging (SSI) 2-D-SWE had substantially higher diagnostic accuracy compared with Siemens VTTQ for the diagnosis of clinically significant fibrosis (AUROC of 0.88 vs. 0.81) (Cassinotto et al. 2014). Also, a study in 54 children and adolescents with different chronic liver diseases assessed with Fibroscan, VTTQ and SSI 2-D-SWE used Fibroscan as a reference method and found that compared with VTTQ, SSI 2-D-SWE correlates better with Fibroscan in children (Belei et al. 2016). Conversely, another study found a higher diagnostic performance for Siemens' VTTQ than for SSI 2-D-SWE (AUROC for $F \geq 2$: 0.92 vs. 0.87) (Gerber et al. 2015). Another study compared Siemens' VTTQ and SSI 2-D-SWE in 79 patients. Contrary to our study using GE 2-D-SWE, the average SWS values measured with SSI 2-D-SWE were 0.24 m/s higher than the values obtained with VTTQ (Woo et al. 2015). This may be due to a different patient population and the GE 2-D-SWE implementation, which uses a lower frame rate that is influenced by the acquisition time (on the order of 100 ms) and cooling time (2–3 s), both dominant factors in limiting the frame-rate according to the manufacturer. Conversely, SSI 2-D-SWE uses ultra-high frame rates to detect traveling shear waves. Although GE and SSI 2-D-SWE use different technologies to detect shear waves, a recent study reported comparable results using GE 2-D-SWE and Aixplorer SSI 2-D-SWE in phantoms (Song et al. 2014).

To the best of our knowledge, our study indicates for the first time in an intra-individual comparison study that measurements of SWS obtained in the same patient with GE 2-D-SWE and VTTQ differed substantially different from each other, with higher intra-modality classification agreement for VTTQ than for GE 2-D-SWE. The reason for this difference may be that less operator involvement is needed for SWS measurements with a software-defined fixed box for selecting ROIs in VTTQ. We also observed that the inter-modality agreement between GE 2-D-SWE and VTTQ was only fair. Taken together, our findings suggest that GE 2-D-SWE cutoff values should be re-evaluated in a study with larger patient populations and using biopsy as the reference standard, in conjunction with VTTQ, with the aim of enabling interchangeable use of technologies through improved concordance between the two methods.

Future investigations of the interchangeability of SWE techniques should address several limitations to our study. First, no gold standard (*i.e.,* histology after liver biopsy) or "silver standard" (*i.e.,* MRE) was used to validate the accuracy of liver fibrosis grading with the two SWE methods in our study. The use of such standards could further validate results and provide confirmatory grading for each of the modalities to identify which of the two is superior in its current state. However, because both 2-D-SWE and VTTQ have been validated in previous studies using either histology or MRE as the reference standard, our goal was not to add additional validation data, but rather to focus on comparing the two validated and clinically introduced USE technologies with the goal of using them interchangeably in our clinical practice.

Second, system settings and parameters (*i.e.,* ultrasound frequency, sampling rate, ROI size and location, gains, depths) can result in biased results if not maintained the same when comparing measurements from different groups of patients or when USE is used in longitudinal applications. Imaging parameters were kept consistent in our study for all patients; however, although the ROI size was fixed for VTTQ, it was freely adjustable for GE 2-D-SWE and sonographers increased the ROI size in 10% of cases. This may have added to the variability in GE 2-D-SWE data.

Third, both 2-D-SWE and VTTQ can result in precise measurements under conditions in which the tissue is homogeneous and where there is negligible dispersion and a fixed direction of SW propagation. However, in the context of live tissues, kernel size (the region[s] of tissue where each SWS measurement is made, assumed to be homogeneous for stiffness measurements) can have a significant effect on SWS measurement precision and spatial resolution because tissues are effectively not homogeneous (Lipman et al. 2016; Palmeri et al. 2010; Rouze et al. 2012; Wang et al. 2013). Here, we aimed to determine whether both SWE methods could be used interchangeably by measuring the stiffness in the same region of the liver. To that end, the kernels necessary for spatial mapping in GE's 2-D-SWE were likely different from those in VTTQ, resulting in errors when comparing VTTQ and GE measurements, especially at higher fibrosis grades where adjacent structures (*i.e.,* fibrosis) and general heterogeneity could affect the precision of the measurement through excessive heterogeneity. Currently, GE recommends assessing the quality of a 2-D stiffness map by optimizing the B-mode imaging window, placing the ROI near the center of imaging, and choosing the region when >50% of ROI has uniform color fill with a default gain of 55 before taking an average measurement; those recommendations were followed in our study. In the future, manufacturers may opt to include a quality indicator to provide real-time feedback to optimize placement of the transducer and ROIs (Lipman et al. 2016; Palmeri et al. 2010; Rouze et al. 2012; Wang et al. 2013)].

Fourth, given the retrospective design, inter-observer variability in measuring fibrosis could not be assessed in this study. However, to minimize variability among and between sonographers, sonographers were asked to always obtain measurements at the exact same anatomic location with both systems, using the bifurcation of the right portal vein as anatomic landmark.

Finally, because of the retrospective study design with strict quality criteria (*e.g.,* requirement of a minimum of 10 measurements and two sets each for each elastography technique) to assess both intra-modality and inter-modality agreement, a substantial number of examinations were excluded, reducing the total number of patients included to 93. Prospective studies with larger patient numbers are warranted to confirm our findings.

## CONCLUSIONS

In summary, GE 2-D-SWE and VTTQ exhibit high repeatability, but only fair inter-modality agreement for differentiating clinically non-significant from significant liver fibrosis, suggesting that these two methods cannot be used interchangeably at this time. Adjustments of cutoff values and additional technical developments with more transparency in currently proprietary USE technologies of different vendors may make it possible to use the various technologies interchangeably in clinical practice.

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