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The Clinical Practice Review

In vitro quantification of tissue elasticity: S-Shearwave Elastography

RS80A with Prestige

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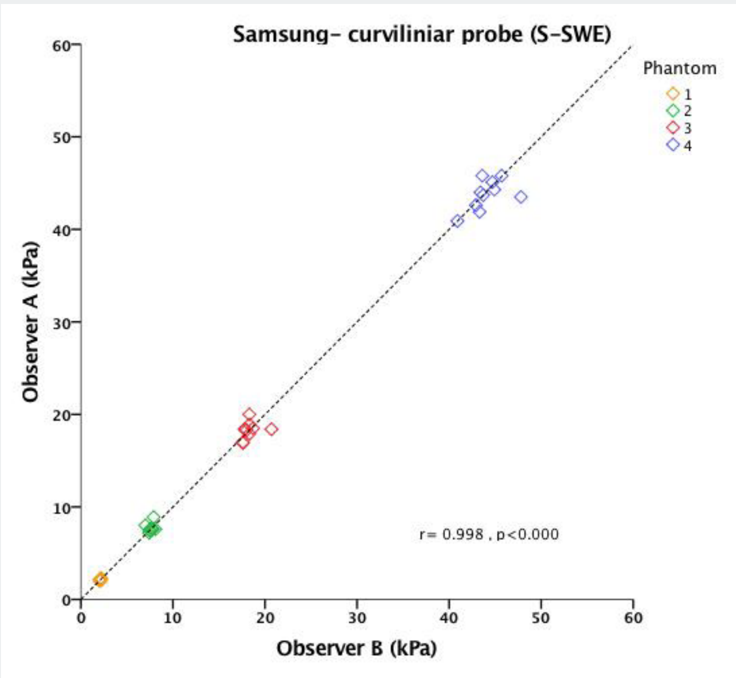

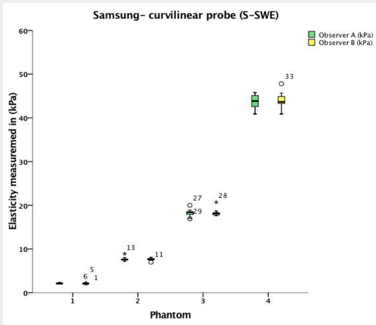

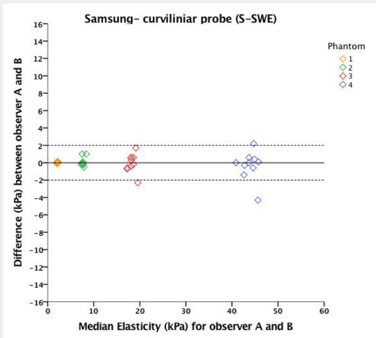

"The reproducibility of elasticity measurements was excellent for S-Shearwave Elastography."

Introduction

Elastography is an imaging technique aiming to assess human tissue elasticity through quantitative or semi-quantitative measurements. In this in vitro study, we have investigated the performance of a quantitative elastography platform using the S-Shearwave Elastography installed in RS80A with Prestige ultrasound equipment (Samsung Medison Co. Ltd., Seoul, Korea). The evaluation was performed using a curvilinear probe on a liver fibrosis phantom. We investigated the intra and interobserver agreement by intraclass correlation analysis (ICC) and coefficient of variation (CV) by correlation and limits of agreement.

Basics of shear wave elastography

Shear wave elastography is a non-invasive ultrasound method used to quantitatively measure tissue elasticity (tissue stiffness) in the evaluation of tissue pathology (e.g. fibrosis or cancer) based on the generation and analysis of shear waves[1]. The method has been proved useful in the diagnostic of tissue pathology in several organs[6,9-10]. Elastography in the form of Transient elastography (TE) has been widely validated for the detection of severe fibrosis or cirrhosis and the exclusion of significant fibrosis[3-5,11].

The tissue stiffness is measured by Young's modulus and expressed as pressure in Pascals (Pa), or more commonly, kilopascals (kPa). The relationship between the local stress and the resulting strain is defined by Young's modulus (E), quantifying tissue stiffness:

$$E = \frac{\Delta\ strain}{\Delta\ stress}$$

This means that the harder the tissue, the higher the Young's modulus. The link between Young's modulus (elasticity E) and shear wave propagation speed is shown in this formula:

$$E = 3\rho(c)2$$

Where ρ is the density of tissue expressed in kg/m3, which in human tissue is very close to the density of water (1 kg/dm3), and shear wave propagation speed is c. Shear wave elastography systems measure the velocity of the propagating shear waves, and these travel faster in harder than softer tissue. When applying S-Shearwave, the elasticity may be expressed as either shear wave velocity (m/s) or as Young's Modulus (E) in kPa using the equation above.

The "Reliability Measurement Index (RMI)" is a quality control parameter integrated into the system, and is calculated by the weighted sum of two factors: the residual of the wave equation and the magnitude of the shear wave. In practice, high values of RMI are strongly correlated with reproducible measurements. The proposed index can be utilized to filter out unreliable measurements, possibly improving performance of shear wave elastography, and could be used as a criterion to assess the quality of the data.

Material and method

The objects of examination were liver fibrosis phantoms (CIRS Model 039, CIRS Inc. Virginia, USA). The model 039 consists of four separate phantoms of varying stiffness. Each phantom is 10 cm deep and made with Zerdine®, a patented synthetic polymer, housed in a cylinder with a Saran-based scan surface and a scanning well that can be filled with fluid when using curvilinear probes. The phantom is compatible with the main ultrasound shear wave modalities. It has standard configuration with the following nominal acoustic properties: Material density: 1.03g/cc, Speed of sound: 1540m/s, Attenuation: 0.5dB/cm/MHz, Contrast: 0 dB with respect to CIRS liver reference. The actual acoustic and mechanical properties were batch tested and the measured values are provided in Table 1.

Table 1: Phantom Acoustic Properties

Phantom	Young's modulus	Spdde of sound	Attenuation
1	2.7 kPa (+/-5%)	1533 m/s	0.46 dB/cm/MHz
2	11.5 kPa (+/- 5%)	1536 m/s	0.46 dB/cm/MHz
3	24.8 kPa (+/- 5%)	1531 m/s	0.46 dB/cm/MHz
4	46.3 kPa (+/- 5%)	1530 m/s	0.46 dB/cm/MHz

Table 1. The actual acoustic and mechanical properties of the phantoms that were batch tested.

Statistical Analysis

Intraobserver variability was assessed by the coefficient of variation (CV), which is the standard deviation (SD) divided by the mean elasticity value. A low CV is equivalent to high measurement repeatability. Interobserver reliability is presented as the interclass correlation coefficients (ICC). High interobserver reliability is indicated by an ICC near 1.00. Interobserver agreement was further assessed by correlation plot analysis using Pearson's correlation coefficient (r). Differences between individual measurements and a common mean value for the two observers were reported as Limits-of-agreement for the system used[2]. Statistical analysis was performed with Statistical Package for the Social Sciences (SPSS).

Result

Range of measurements

Table 2: Phantom Median Elasticity Measurements

Observer	Phantom 1 2.7 kPa +/- 5% (min-max)	Phantom 2 11.5kPa +/- 5% (min-max)	Phantom 3 24.8 kPa +/- 5% (min-max)	Phantom 4 46.3 kPa +/- 5% (min-max)
A	2.1 kPa (2-2.3)	7.60 kPa (7.2-8.9)	18.40 kPa (17-20)	43.85 kPa (40.9-45.8)
B	2.1 kPa (2-2.2)	7.65 kPa (7-8.1)	18.15 kPa (17.6-20.7)	43.65 kPa (40.9-47.8)
A+B	2.1 kPa (2-2.3)	7.60 kPa (7-8.9)	18.30 kPa (17-20.7)	43.70 kPa (40.9-47.8)

Table 2. The median (min-max) elasticity measurements on liver fibrosis phantoms with the reference tissue to real values performed using RS80A with Prestige.

Table 3: Phantom Mean Measurements

Phantom	Mean A	Mean B	CV A	CV B	CV AB	Intraclass coefficient	Intraclass coefficient
1	2.12	2.11	0.04	0.03	0.04	Observer A 0.999 Observer B 0.998	1.0
2	7.71	7.63	0.06	0.04	0.05		
3	18.27	18.31	0.05	0.05	0.05		
4	43.76	44.09	0.04	0.04	0.04		

Table 3. The mean of all measurements for each observer with corresponding coefficients of variation (CV) and the intra and interclass coefficient (ICC) for observer A and B are given as a single value for all phantoms, as well as the interobserver ICC for observers A and B.

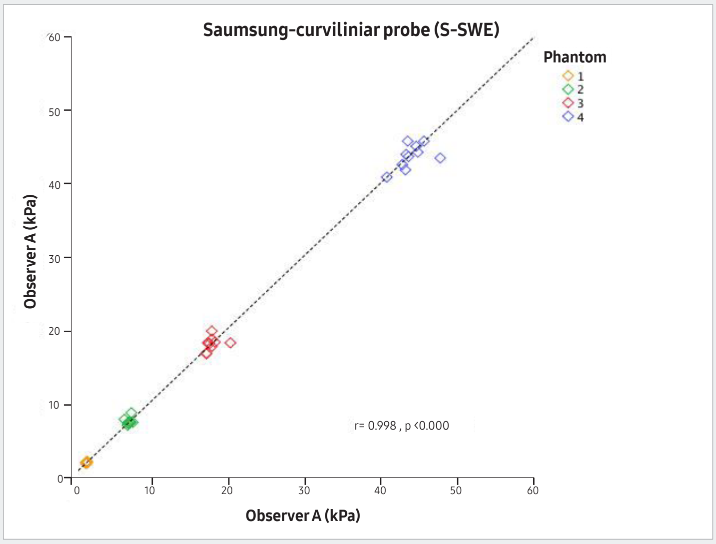

Figure 1. High correlation between the two independent observers when performing elasticity measurements on the liver phantom with a correlation coefficient R=0.998 (figure 1).

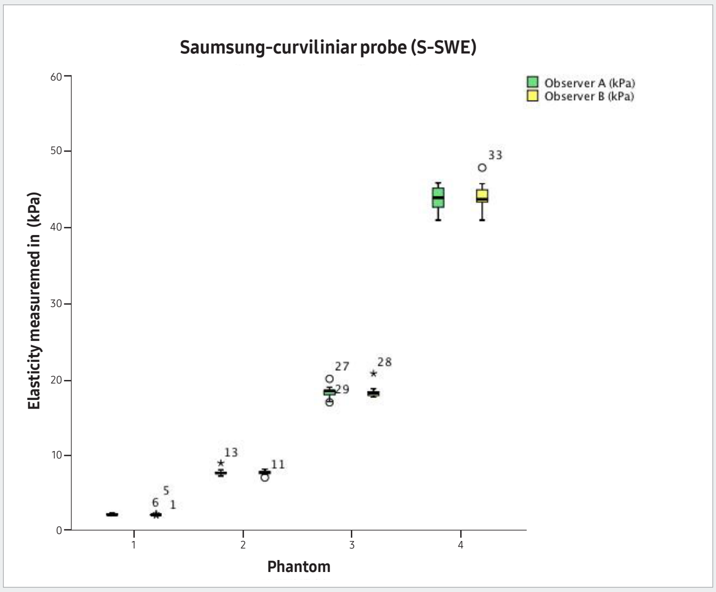

Figure 2. The boxplots for observer A and B for all inclusions show the median values as well as low measurement variability as interquartile range as the height of the box for each inclusion (figure 2).

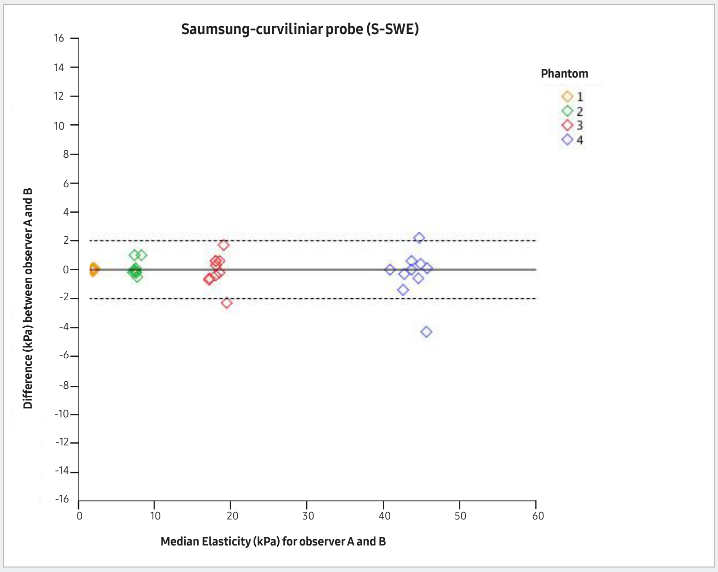

Figure 3. The Bland-Altman plot illustrates the differences in individual measurements to a common mean value for both observers. The deviation from 0 on the vertical axis is very limited for S-Shearwave which represents no systematic bias in measurements between the observers (figure 3).

Discussion

In this study, we have evaluated the use of S-Shearwave on four tissue-mimicking phantoms. We found a high degree of reproducibility, both for individual observers and between two observers, as reported by CV in Table 3 and demonstrated in figures 1-3.

The study represents near “ideal”, but yet simplified, conditions for reproducibility assessment. The phantom material is homogeneous and isotropic when compared to real liver tissue, but it does not have the visco-elastic properties of real liver tissue. The phantom material is contained in a stiff cylinder which also is different from liver tissue. All the measurements were done at similar distance from the transducer surface. These are key issues for repeatability in measurements that will probably be more variable in real liver tissue[7]. However, these results show a very high potential of measurement reproducibility in liver tissue scanning. Most of the phantom elasticity measurements underestimated the value provided by the manufacturer of the phantom. This was equally observed by both examiners in this in vitro study. This may be caused by the in vitro material, but in general, the material density of Zerdine is 1.0-1.05, which is comparable to live soft tissue. If similar underestimation will occur when scanning live tissue is beyond the scope of this paper, and must be further investigated. For phantoms 2-4, the underestimation is quite stable at approximately 4 kPa. Other shearwave elastography systems also tended to underestimate phantom material hardness in a separate study, but less consistently[8].

As for the other systems we have tested, the variability of stiffness measurements increases in variability with increasing values. This is demonstrated in the correlation plot and in the limits-of-agreement plot. The variability of S-Shearwave is also limited for the harder phantoms, and less or similar than we have observed in other systems we have tested[8]. When variability is divided by measurement result, as in the variation coefficient, we find this to be similar for phantom 1+2 (softer) and for 3+4 (harder), with respective CV 0.043 and CV 0.045.

Summary

The reproducibility of elasticity measurements was excellent for S-Shearwave Elastography. We found high correlations for both intraobserver (ICC 0.998-0.999) and interobserver (ICC 1.0) results. All phantoms could be differentiated by quantitative shear wave elastography using S-Shearwave. Further studies must be conveyed in real live soft tissues.

Supported Systems

- RS80A with Prestige
- HS70A with Prime

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