Journal of Ultrasound in Medicine

RSNA/QIBA Shear Wave Speed Bias Quantification in Elastic and Viscoelastic Phantoms

Journal:	*Journal of Ultrasound in Medicine*
Manuscript ID	JUM-2020-06-0914.R2
Wiley - Manuscript type:	Original Research
Date Submitted by the Author:	20-Nov-2020
Complete List of Authors:	Palmeri, Mark; Duke University, Biomedical Engineering Milkowski, Andy; Siemens Healthineers USA Inc, Ultrasound Barr, Richard; Northeastern Ohio Medical University Carson, Paul; University of Michigan Medical Center, Basic Radiology Sci Div Couade, Mathieu; SuperSonic Imagine Chen, Jun; Mayo Clinic Chen, Shigao; Mayo Clinic, Dhyani, Manish; Lahey Health System Inc Ehman, Richard L.; Mayo Clinic Garra, Brian; Medical Imaging Ministries of the Americas Gee, Albert; Mindray Medical International Ltd Guenette, Gilles; Siemens Healthineers USA Inc Hah, Zaegyoo; Samsung Medison Co Ltd Lynch, John; CIRS Inc MacDonald, Micahel; General Electric Company Managuli, Ravi; Hitachi Aloka Miette, Veronique; Echosens SA Nightingale, Kathy; Duke University, Biomedical Engineering Obuchowski, Nancy; ObuchoN@ccf.org Rouze, Ned; Duke University Morris, Cody; Duke University Fielding, Shana; Duke University Deng, Yufeng; Duke University Chan, Derek; Duke University Choudhury, Kingshuk; Duke University Yang, Siyun; Duke University Samir, Anthony; Massachusetts General Hospital, Radiology Shamdasani, Vijay; Philips Healthcare US Urban, Matthew; Mayo Clinic, Department of Physiology and Biomedical Engineering Wear, Keith; FDA Xie, Hua; Philips Healthcare US Ozturk, Arinc; Massachusetts General Hospital, Radiology Qiang, Bo; Mayo Clinic Song, Pengfei; Mayo Clinic College of Medicine, Department of Radiology McAleavey, Stephen; University of Rochester Rosenzweig, Stephen; Siemens Healthineers USA Inc Wang, Michael; General Electric Company

This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1002/jum.15609

Okamura, Yoko; Canon Inc
McLaughlin, Glen; Mindray Medical International Ltd
Chen, Yuling; Mindray Medical International Ltd
Napolitano, David; Mindray Medical International Ltd
Carlson, Lindsey; University of Wisconsin-Madison
Erpelding, Todd; Canon Inc
Hall, Timothy; Wisconsin Institutes for Med Research, Medical Physics Dept

Section: Basic Science (Instrumentation), Elastography

Keywords: Shear Wave, Acoustic Radiation Force, QIBA, Phantom, Elasticity, Viscoelasticity

Abstract: **OBJECTIVE:** To quantify the bias of shear wave speed (SWS) measurements between different commercial ultrasonic shear elasticity systems and a magnetic resonance elastography (MRE) system in elastic and viscoelastic phantoms. **METHODS:** Two elastic phantoms, representing healthy through fibrotic liver tissue, were measured with 5 different ultrasound platforms, and three viscoelastic phantoms, were measured with 12 different ultrasound platforms. Measurements were performed with different systems at different sites, at 3 focal depths and with different appraisers. SWS bias across the systems was quantified as a function of system, site, focal depth and appraiser. A single MRE research system was also used to characterize these phantoms using discrete frequencies from 60-500 Hz. **RESULTS:** SWS from different systems had a mean difference 95% CI of ±0.145 m/s (±9.6%) across both elastic phantoms and ±0.340 m/s (±15.3%) across the viscoelastic phantoms. Focal depth and appraiser were less significant sources of SWS variability than system and site. MRE best matched ultrasonic SWS in the viscoelastic phantoms using a 140 Hz source, but had a -0.27±0.027 m/s (-12.2±1.2%) bias when using the clinically-implemented 60 Hz vibration source. **CONCLUSION:** SWS reconstruction across different manufacturer systems is more consistent in elastic than viscoelastic phantoms, with a mean difference bias of ±10% in all cases. MRE measurements in the elastic and viscoelastic phantoms best match the ultrasonic systems with a 140 Hz excitation, but have a significant negative bias operating at 60 Hz. This study establishes a foundation for meaningful comparison of SWS measurements made with different platforms.

RSNA/QIBA Shear Wave Speed Bias Quantification in Elastic and Viscoelastic Phantoms

Mark L. Palmeri, M.D., Ph.D.[1], Andy Milkowski, M.S.[2], Richard Barr, M.D., Ph.D.[3], Paul Carson, Ph.D.[4], Mathieu Couade, Ph.D.[5], Jun Chen, Ph.D.[6], Shigao Chen, Ph.D.[6], Manish Dhyani, M.D.[7], Richard Ehman, Ph.D.[6], Brian Garra, M.D.[8], Albert Gee, Ph.D.[9], Gilles Guenette[10], Zaegyoo Hah, Ph.D.[11], Ted Lynch, Ph.D.[12], Michael Macdonald, Ph.D.[13], Ravi Managuli, Ph.D.[14], Veronique Miette, Ph.D.[15], Kathryn R. Nightingale, Ph.D.[1], Nancy Obuchowski, Ph.D.[17], Ned C. Rouze, Ph.D.[1], D. Cody Morris[1], Shana Fielding[1], Yufeng Deng, Ph.D.[1], Derek Chan[1], Kingshuk Choudhury, Ph.D.[1], Siyun Yang, Ph.D.[1], Anthony E. Samir, M.D.[7], Vijay Shamdasani, Ph.D.[16], Matthew Urban, Ph.D.[6], Keith Wear, Ph.D.[8], Hua Xie, Ph.D.[16], Arinc Ozturk, M.D.[7], Bo Qiang, M.S.[6], Pengfei Song, Ph.D.[6], Steve McAleavey, Ph.D.[18], Stephen Rosenzweig, Ph.D.[2], Michael Wang, Ph.D.[13], Yoko Okamura, M.S.[19], Glen McLaughlin, Ph.D.[9], Yuling Chen, Ph.D.[9], David Napolitano, Ph.D.[9], Lindsey Carlson, Ph.D.[20], Todd Erpelding, Ph.D.[19], and Timothy J. Hall, Ph.D.[20]

[1]*Duke University, Durham, NC, USA*

[2]*Siemens Ultrasound, Issaquah, WA, USA*

[3]*The Surgical Hospital at Southwoods, Boardman, OH, USA*

[4]*University of Michigan, Ann Arbor, MI, USA*

[5]*SuperSonic Imagine, Aix-en-Provence, France*

[6]*Mayo Clinic, Rochester, MN, USA*

[7]*Massachusetts General Hospital, Boston, MA, USA*

[8]*Food and Drug Administration, Silver Spring, MD, USA*

[9]*Zonare Medical Systems, Mountain View, CA, USA*

[10]*Toshiba Medical Research Institute, Redmond, WA, USA*

[11]*Samsung Medison, Seoul, South Korea*

[12]*CIRS, Norfolk, VA, USA*

[13]*General Electric, Milwaukee, WI, USA*

[14]*Hitachi Healthcare, Twinsburg, OH, USA*
[15]*Echosens, Paris, France*
[16]*Philips Research, Cambridge, MA, USA*
[17]*The Cleveland Clinic, Cleveland, OH, USA*
[18]*University of Rochester, Rochester, NY, USA*
[19]*Canon Medical Systems Corp., Otawara, Japan*
[20]*University of Wisconsin, Madison, WI, USA*

Short Running Title: QIBA SWS Bias in Elastic and Viscoelastic Phantoms

Corresponding Author: Mark L. Palmeri, M.D., Ph.D. (mark.palmeri@duke.edu)

Abstract

OBJECTIVE: To quantify the bias of shear wave speed (SWS) measurements between different commercial ultrasonic shear elasticity systems and a magnetic resonance elastography (MRE) system in elastic and viscoelastic phantoms.

METHODS: Two elastic phantoms, representing healthy through fibrotic liver, were measured with 5 different ultrasound platforms, and three viscoelastic phantoms, representing healthy through fibrotic liver tissue, were measured with 12 different ultrasound platforms. Measurements were performed with different systems at different sites, at 3 focal depths and with different appraisers. SWS bias across the systems was quantified as a function of system, site, focal depth and appraiser. A single MRE research system was also used to characterize these phantoms using discrete frequencies from 60-500 Hz.

RESULTS: SWS from different systems had a mean difference 95% CI of ±0.145 m/s (±9.6%) across both elastic phantoms and ±0.340 m/s (±15.3%) across the viscoelastic phantoms. Focal depth and appraiser were less significant sources of SWS variability than system and site. MRE best matched ultrasonic SWS in the viscoelastic phantoms using a 140 Hz source, but had a -0.27±0.027 m/s (-12.2±1.2%) bias when using the clinically-implemented 60 Hz vibration source.

CONCLUSION: SWS reconstruction across different manufacturer systems is more consistent in elastic than viscoelastic phantoms, with a mean difference bias of $< \pm 10\%$ in all cases. MRE measurements in the elastic and viscoelastic phantoms best match the ultrasonic systems with a 140 Hz excitation, but have a significant negative bias operating at 60 Hz. This study establishes a foundation for meaningful comparison of SWS measurements made with different platforms.

1 Introduction

The Radiological Society of North America (RSNA) created the Quantitative Imaging Biomarker Alliance (QIBA) with imaging system manufacturers, academics, clinicians and representatives from the USA federal government (e.g., Food and Drug Administration (FDA), National Institutes of Health (NIH), and National Institute of Standards and Technology (NIST)) to advance the concept of converting "imaging systems" to "measurement systems." QIBA profiles are developed for each measurement system that provide specific claims of what biomarker performance is possible when following the QIBA protocol, with the ultimate intent being to validate the profile across imaging systems with phantoms. The ultrasound shear wave speed (SWS) biomarker committee was formed in 2012, with the purpose of developing a protocol and data analysis methods to allow direct comparison of SWS measurements made with different commercial systems with the current clinical application being to estimate liver fibrosis. Several systems that measure SWS in the liver are commercially available, and many articles report that these measurements can differentiate fibrosis stages [1, 2]. Shear Wave Elasticity Imaging (SWEI) [3] methods implemented by several manufacturers, including both point SWS measurements and 2D-Shear Wave Elastography [4], have been cleared by the FDA, and the technology has already reduced the number of liver biopsy procedures performed in Asia and Europe, as reflected in the National Institute of Health and Care Excellence (NICE) guidelines for the management of viral hepatitis and the role of SWEI in diagnosing and following disease progression in these patient populations [5].

Literature suggests SWS measurements depend on measurement system [1, 2, 6, 7, 8]. These system differences cause clinical uncertainty and slow the adoption of this technology by the clinical community. Given the need for serial assessment of liver fibrosis and the impracticality of serial liver biopsy, providing a consistent SWS measurement that is system-agnostic would improve the impact of this technology to noninvasively stage liver fibrosis.

A crucial step towards understanding sources of bias in SWS estimates is performing parametric studies in calibrated phantoms across all of the different manufacturer systems to study potential confounding factors, including focal depth, material stiffness and viscosity, and appraiser. Phantoms may be elastic, which are relatively easy to fabricate, or viscoelastic, which are more difficult to fabricate, but more closely mimic human liver. SWS is independent of shear wave frequency content in elastic media, but it depends on frequency in viscoelastic media. Viscosity causes dispersion in the propagating shear waves, which means that the resultant shear wave speed is dependent on frequency content of the shear wave, with higher frequency components of the shear wave propagating faster than the lower frequency components [9]. The frequency content of the generated shear wave can be impacted by the spatial and temporal acoustic radiation force focal configurations used to generate the shear waves, the stiffness of the tissue, and is also dependent on the how the shear wave displacements are estimated using echoes from tracking beams [10]. Some commercial systems use tissue displacement data acquired from a single reference in the tissue before the acoustic radiation force is applied, while other systems estimate tissue velocity data using a progressive referencing sequence after the acoustic radiation force generates the shear wave [4]. Velocity data represent the first time derivative of the displacement data, and therefore inherently have higher appreciable frequency content than the displacement data, making it a potential source of SWS difference between systems in viscoelastic media [9]. In these studies, we have calculated both group SWS, which refers to the speed of a broadband pulse containing many frequencies, and phase SWS, which refers to the speed of monochromatic waves as a function of frequency.

We first conducted an elastic phantom study (Phase I) to evaluate first-order, inter-system measurement differences in the absence of material viscosity [11]. We then conducted the viscoelastic phantom study (Phase II) to evaluate how systems performed in materials with viscosity, which more realistically match the material properties of human liver tissue. For both Phase I and Phase II studies, comparative measurements were made with a research Magnetic Resonance Elastography (MRE) system as a non-ultrasonic modality that can also independently characterize stiffness and dispersion and is used clinically to characterize liver fibrosis [12]. Additionally, MRE allows for multiple, discrete, excitation frequencies to be used to generate shear waves in the phantoms, which is not possible with the clinical ultrasound systems and allows for more direct characterization of the dispersive properties of these phantoms.

The Phase I and Phase II studies allowed us to quantify the bias of SWS measurements between different commercial ultrasonic shear wave elasticity imaging systems and an MRE system in elastic and viscoelastic phantoms. These analyses serve as a foundation for the claims and protocols in the first QIBA Ultrasound SWS profile [13].

2 Methods

2.1 Phantom Calibration

2.1.1 Elastic Phantoms (Phase I)

Phase I studies were conduced from January 2012 - December 2013. Eleven pairs of elastic phantoms (E178*, Table 1) with nominal SWS of 1.0 and 2.0 m/s, herein referred to as the "soft" and "stiff" elastic phantoms, respectively, were fabricated by Computerized Imaging Reference Systems (CIRS), Inc. (Norfolk, VA, USA). These two nominal speeds were chosen based on the speeds associated with normal and fibrotic livers in the literature, where accurate resolution of speed is important for clinical diagnosis [2]. The phantoms were homogeneous cylinders that were 100 mm in diameter and height, except for a pair of phantoms designed for MRE measurements (E1788) that were 200 mm in diameter and 120 mm in height to reduce standing wave reflections off the phantom walls.

The SWS in all of the phantoms were measured at Duke University using a Verasonics Vantage™ research scanner (Verasonics, Inc., Kirkland, WA, USA) sequence (Table 2) following the procedure outlined in Appendix I [14]. A grand mean was calculated across all of the phantom measurements and used as a normalization factor to compensate for SWS bias due to fabrication variability among the phantoms. Ten replicate measurements were made across 10 different speckle realizations (transducer positions) with 3 different focal depths (40, 60 and 80 mm) in each phantom, where each speckle realization was obtained by rotating the phantom about a common location using a rotation platform. Group and phase SWS measurements were made using the methods described in [9] and are available for download.[1]

2.1.2 Viscoelastic Phantoms (Phase II)

Phase II studies were conducted from January 2014 - March 2016. Three viscoelastic (Phase II) phantoms (E2297, Table 1), were characterized at Duke University using a Verasonics research scanner following the procedure outlined in Appendix I [14]. In contrast to the Phase I studies: (a) 16 replicate measurements, instead of 10, were performed in each phantom; and (b) 3 different stiffness phantoms, instead of 2, were measured with a given system at each imaging site.

Viscoelastic phantoms (Phase II) can be susceptible to more fabrication replication variability, so for

[1] https://github.com/RSNA-QIBA-US-SWS/VerasonicsPhantomSequences

the Phase II study, a single set of phantoms were shipped to each of the different measurement sites. The stiffnesses and viscosities chosen for the Phase II phantoms represent different degrees of normal through fibrotic livers (supporting data presented in the Results section).

To characterize how the phantom dispersion represents that of the human liver, we compared the group speeds derived from displacement and velocity data in these phantoms to group speeds derived from displacement and velocity data in healthy and diseased human livers. All human data were acquired in an IRB-approved study that has already been published [15, 16]. While the data acquisitions in the human data were done with a system and sequence not used to image the Phase II phantoms, we were not interested in the absolute agreement of speeds between the different systems. We instead evaluated the ratio of the group speeds estimated with each type of data, where a non-unity ratio indicates dispersion, which should be relatively independent of bias between the different systems.

2.2 Site Measurement Protocol

The phantoms were distributed among 12 sites for measurements on commercial clinical SWS-capable systems, including FibroScan®(Echosens, Paris, France), Philips EPIQ 5 (Philips Healthcare, Amsterdam, Netherlands), Siemens ACUSON S2000/S3000™ (Siemens Healthineers, Munich, Germany), Supersonic Imagine (SSI) Aixplorer (Aix-en-Provence, France), Hitachi HiVision Ascendus (Hitachi Healthcare, Tokyo, Japan), GE LOGIQ E9 (GE Healthcare, Chicago, IL, USA), Samsung RS80 (Samsung Healthcare, Seoul, South Korea), Canon (formerly Toshiba) Aplio 500 (Canon Medical Systems Corp., Otawara, Japan), and Mindray (formerly Zonare) ZS3 (Mindray, Shenzhen, China) as well as Verasonics research systems at Duke University and the Mayo Clinic. It should be noted that in the Phase I study (2012-2013), only 5 of the systems were available at the time for phantom measurements, while all of the systems were available for the Phase II phantom measurements (2014-2016). The systems and sites in our analysis have been assigned arbitrary letter designations (A-K) to maintain their anonymity throughout the study, and there is no correlation between the letter designations between the Phase I and II studies (i.e., System A in Phase I is not necessarily System A in Phase II).

For the Phase I study, each site had at least three appraisers scan each phantom 10 times at each focal depth (30, 45 and 70 mm, which differed from the Phase I calibration measurements described in Section 2.1.1) with a handheld transducer, with each combination of appraiser and focal depth repeated for 3 trials in random order relative to the other appraisers. A single appraiser at each site was used in the Phase

II study, and 16 replicate measures were made in these phantoms.

The order of data acquisition was randomized for phantoms, appraisers, depths, and imaging systems (if more than one was used) to allow for accurate statistical investigation of results. Participants were all blinded to the intermediate results of others measurement sites. All of these data were then analyzed to estimate the bias in SWS estimates across different systems, measurement sites, focal depths and appraisers. If a system did not report SWS (c_T) directly, but instead reported Young's modulus (E) or shear modulus (μ), those moduli were converted to SWS assuming an isotropic, incompressible, elastic material assumption:

$$c_T = \sqrt{\frac{\mu}{\rho}} = \sqrt{\frac{E}{3\rho}}, \tag{1}$$

where ρ represents the density of the phantom material (as quoted on the phantom label or assumed to be 1000 kg/m^3).

Since curvilinear arrays were used to image phantoms with flat surfaces, a coupling solution was used to match the sound speed of the phantom material to minimize index of refraction mismatch that could bias SWS estimates [17, 18].

Statistical ANOVA analysis was performed to evaluate which variables in our study (phantom, system, site, appraiser, focal depth) led to significant differences ($p<0.01$) between reported shear wave speeds. Tukey mean difference analysis was also performed to evaluate trends in bias among systems and sites. Linear regression was used to evaluate for bias as a function of focal depth for each system. All statistical analysis was performed using the `statsmodels` and `SciPy` packages in `Python (v3.8)` [19, 20].

2.3 Magnetic Resonance Elastography (MRE)

MRE on the Phase I and Phase II phantoms was performed at a single research site. To generate shear wave propagation in the phantoms, a square MRE electromechanical shear driver (64 mm × 64 mm × 3.0 mm) was placed on top of the phantom with a light compression to maintain mechanical coupling. The driver frequency ranged from 60-500 Hz, with MRE performed at each discrete frequency. To better match the bandwidth of ultrasound SWS systems, the shear wave frequencies used in the MRE measurements were expanded to included higher values than those used in clinical MRE of the liver (typically 60 Hz) [12].

Shear wave propagation images were acquired using a 3D MRE wave imaging sequence on a single-channel coil and a 1.5 T GE Signa scanner (Waukesha, WI, USA). The following major parameters were used in the study: FOV = 216 mm, matrix = 128×128, TR = 1600-2314 ms, TE = 62.7-119 ms, slice thickness/spacing = 3.5/0 mm, 16 slices, motion sensitivity (MENC) = 4.5-25.2 μm/π radians, motion sensitivity direction = $x/y/z$, axial imaging plane.

A 3D MRE direct inversion (DI) algorithm was used to process wave images and compute elastograms [21]. The model-free DI algorithm provides calculated images depicting the magnitude, real part, and imaginary part of the complex shear modulus. Region-of-interest measurements were obtained from each of the images over a large area of each phantom.

The complex shear modulus ($G^*(\omega)$) was calculated as $G^*(\omega) = G_r(\omega) + i\, G_i(\omega)$, where G_r and G_i are the real and imaginary parts of the complex shear modulus as a function of angular frequency (ω). Using this complex shear modulus, the phase velocity (v_s) can be expressed as:

$$v_s(\omega) = \sqrt{\frac{2}{\rho}\frac{|G^*(\omega)|^2}{G_r(\omega) + |G^*(\omega)|}}. \tag{2}$$

Prior to the MRE exams, the phantoms were allowed to equilibrate to 20°C for at least 8 hours before measurements were made.

3 Results

3.1 Elastic Phantoms (Phase I)

Figure 1 shows the calibration measurements made on all of the elastic phantoms. Figures 2 and 3 show the aggregated SWS measurements grouped by unique site and system, respectively. There were statistically significant differences in SWS measured between soft and stiff phantoms ($p < 0.01$), between different systems ($p < 0.01$), at different sites ($p < 0.01$) and as a function of focal depth ($p < 0.01$).

Figure 4 shows a Tukey mean difference plot for aggregate systems and sites, using the normalization data (Figure 1) as the reference measurement for each phantom. These data had a mean difference 95% CI of ±0.145 m/s (±9.6%) between the soft and stiff phantoms.

Table 3 shows focal depth bias for each system in each elastic phantom.

At each site, there was not a significant difference in SWS acquisitions between different replicate acquisition procedures ($p > 0.05$). Differences between appraisers were significant ($p < 0.01$), but the variance associated with appraiser differences (0.00176 m/s) was <7% compared to the variance associated with system, site and focal depth (0.0266 m/s).

Figure 5 shows the group and phase SWS estimates made in a pair of the Phase I elastic phantoms, along with MRE estimates of phase SWS in a customized set of elastic MRE phantoms. As summarized in Table 5, the soft phantom (E1786-1) had a statistically significant ($p < 0.001$) (0.85/0.77) 10.4% increase in group SWS using velocity instead of displacement data, and a 0.30 (m/s)/kHz linear increase ($R^2 = 0.87$) in phase velocity. The stiff phantom did not have a statistically significant difference in group SWS ($p > 0.05$), with only a 0.03 (m/s)/kHz linear increase ($R^2 = 0.43$) in phase velocity.

3.2 Viscoelastic Phantoms (Phase II)

Figure 6 shows the comparison of different systems measuring the group SWS in the Phase II phantoms. There was a statistically significant difference in SWS measured between each of the 3 Phase II phantoms ($p < 0.01$), along with a statistically significant difference between SWS measurements as a function of system ($p < 0.01$), site ($p < 0.01$), and focal depth ($p < 0.01$).

Figure 7 shows a Tukey mean difference plot for different systems using the normalization data from the Verasonics calibrations as the reference measurements for each phantom. This figure shows a mean difference 95% CI of ±0.340 m/s (±15.3%) across all three phantoms.

Figure 8 shows the displacement- and velocity-based group SWS reconstructions in the three viscoelastic phantoms, along with their corresponding phase velocity curves. As summarized in Table 5, the E2291-A1 phantom had a (2.17/1.61) 35% increase in velocity group SWS compared with displacement group SWS, with a 0.61 (m/s)/kHz linear increase in phase velocity ($R^2 = 0.92$) with frequency; the E2297-B3 phantom had (2.77/2.12) 31% increase in velocity:displacement group SWS with a 0.78 (m/s)/kHz linear increase in phase velocity ($R^2 = 0.96$) with frequency; the E2297-C1 phantom had a (3.33/2.55) 31% increase in velocity:displacement group SWS with a 0.78 (m/s)/kHz linear increase in phase velocity ($R^2 = 0.92$) with frequency. Figure 9 shows the group SWS calculated displacement and velocity shear wave data in both the Phase I (elastic) and Phase II (viscoelastic) phantoms compared to *in vivo* human data from [15, 16]. The human data had a increase in velocity:displacement group SWS of (2.26/1.78) 27±5.6% across all fibrosis stages.

Table 4 shows focal depth bias for each system in each viscoelastic phantom.

Matched MRE measurements made at discrete excitation frequencies ranging from 60-200 Hz are shown in Figure 10. The MRE data represent the mean measurements (with negligible error bars), superimposed on the aggregate ultrasound SWS data for all systems and sites at a focal depth of 45 mm. The corresponding dispersion slopes are summarized in Table 5. The 140 Hz MRE excitation frequency matched the mean of the ultrasound SWS measurements, but the clinically-implemented 60 Hz excitation had a -0.27±0.027 m/s (-12.2±1.2%) bias.

Figure 11 shows the SWS measured in the Phase II phantoms at 4 times points ranging from Aug 2014 - Sept 2015 to evaluate their temporal stability.

4 Discussion

The Phase I elastic study revealed several interesting findings. We found that the mean difference between systems had a 95% CI of ±9.6%. It can be noted that one system (B) reported values with coarser quantization (0.1 m/s) compared to the other systems. In addition to system variability, site variability was also appreciable, even when the same system was being used at difference sites. While there were biases associated with each system and site, those biases were not necessarily consistent in both the soft and stiff phantoms (e.g., a system that had a negative bias in the soft phantom, may have had a positive bias in the stiff phantom).

Focal depth bias was, in general, a less significant confounding factor than system and site variability. There was one outlier case (System C in the stiff elastic phantom) that did have an appreciable -0.132 m/s bias across the 30 - 70 mm focal depth range (R^2 = 0.95), though that system did not exhibit such bias in the soft elastic phantom or the viscoelastic phantoms.

While the Phase I studies did demonstrate a statistically-significant difference in SWS measured between different appraisers at a given measurement site, it was much less of a confounding factor compared to system and site differences. That being said, these studies were conducted in phantoms and do not capture the challenges of imaging livers in patients, where differences in appraisers could be significant.

System and site differences were also present in the Phase II viscoelastic phantoms and the mean difference 95% CI (±7.8%) was greater than that in the elastic phantoms. These viscoelastic phantoms match the distribution of group SWS displacement:velocity ratios that we observe in human data, indicating similar amounts of dispersive characteristics in these phantoms. Both of the elastic phantoms exhibited minimal dispersion using these group SWS ratios. It should be noted, however, that MRE yielded significantly greater linear dispersion slopes than the ultrasonic system phase velocity analysis for these Phase II phantoms. The source of this discrepancy has not been resolved and will be a focus of future studies.

The best agreement between MRE and the aggregated ultrasound SWS measurements in the viscoelastic phantoms occurred at an excitation frequency of 140 Hz, but the lower 60 Hz excitation used in clinical MRE could lead to lower MRE values for liver stiffness in the literature than ultrasonic systems [22, 12].

The ultrasound system SWS distribution for the softest viscoelastic phantom (E2297-A1) in Figure 10 demonstrates a bimodal distribution. Such a distribution may be indicative that some systems are reconstructing group shear wave speeds using displacement data (leading to the lower distribution), while others may be using velocity data (leading to the higher distribution). Such separation of these populations could be lost in the stiffer phantoms as the variability of the reconstruction using either displacement or velocity data increases. It should be noted that this bimodal distribution explanation is simply a hypothesis as each manufacturer did not reveal how they calculate their group SWS metrics. If the data type (displacement / velocity) is a source of this variability, then manufacturer consensus on what data to use in calculating group SWS, or implementation of a bias-reduction factor, could help provide better consistency of reported SWS between systems.

Because proprietary processing algorithms and scanner sequencing could not be disclosed by manufacturers in this study, we cannot conclude what the sources of inter-system bias were in these studies. To allow researchers in academics, industry and clinical practice to have a common platform to perform ultrasonic SWS measurements, we have created standardized shear wave acquisition sequences on a Verasonics research scanner [14] that can be used to test tissue-mimicking phantoms, along with post-processing code to estimate the group SWS using displacement and velocity as the raw input data into the reconstruction algorithms [9], as presented in this study. In addition to estimating the group speeds, the reconstruction code also estimates phase velocity over the more energetic bandwidth of the shear wave signal. These sequences and post-processing software are openly available on GitHub[2] and will be incorporated in the first-generation of the QIBA profile for ultrasound SWS[3]. In addition to these phantom studies and associated experimental sequences and post-processing code, elastic and viscoelastic digital phantoms based on finite element methods have been developed and released to the community to use for algorithm development and validation [23].

The work presented in this manuscript represents the culmination of several years of effort with evolving methodology between the two phases of the study, and in turn has some limitations. The use of a grand mean

[2] https://github.com/RSNA-QIBA-US-SWS/VerasonicsPhantomSequences
[3] http://qibawiki.rsna.org/index.php/Profiles

normalization across all of the phantom pairs fabricated for the Phase I study allowed all of the phantoms to be compared to a nominal reference value, but complicated studies that involved relative measurements made on any singleton pair of phantoms. Circulating the same sets of phantoms, as was done in Phase II, placed the comparative burden on the longitudinal stability of these phantoms, which did appear relatively consistent across the duration of the study.

The collection of data over several years may have led to different software versions being installed on systems that were deemed the same in our analysis. All of of the system software and models used in this study may be older than the latest generation system SWS elasticity tools and algorithms. The recording of specific scanner software version is considered to be just as important as recording system and transducer models in the proposed QIBA profile.

These studies have not evaluated the differences that exist between different ultrasound systems in the presence of *in vivo* confounding factors, such as physiologic motion and challenging imaging artifacts, such as clutter and finding good acoustic windows. Additionally, while the range of stiffnesses and viscosities in the Phase I and Phase II phantoms represent realistic values that have been measured in healthy and fibrotic livers, they do not represent the full range of material parameters that may be encountered when estimating SWS in liver.

The results of these elastic and viscoelastic phantom studies have been incorporated into the measurement protocols described in the QIBA Ultrasound SWS profile to minimize inter-institutional and inter-system variability, and the inclusion of future, standardized phantom and clinical SWS measurements will allow the profile to be refined in future revisions [13].

5 Conclusions

Elastic phantom measurements made across different manufacturer systems and different measurement sites had a mean difference 95% CI of ± 0.145 m/s (±9.6%) across both phantoms, while viscoelastic phantoms had a mean difference 95% CI of ±0.340 m/s (±15.3%). Focal depth and appraiser were not appreciable sources of variability compared to system and site. The best agreement between ultrasound systems and MRE in the elastic and viscoelastic phantoms was with an MRE excitation frequency of 140 Hz; the clinically-implemented excitation frequency of 60 Hz had a -12.2% bias, which could be a source of discrepancy in the literature between MRE and ultrasonic systems characterizing liver fibrosis with SWS. This study establishes a foundation for meaningful comparison of diagnostic SWS measurements made with different platforms.

Acknowledgments

We gratefully acknowledge the support of CIRS, Inc. for providing the phantoms used in this study. We are also grateful to the RSNA for covering the costs of shipping the phantoms to the individual sites. Funding for these studies has been provided by the RSNA, NIH NIBIB contracts HHSN268201500021C & HHSN268201000050C, NIH NIDDKD grants R01DK092255 and R01DK106957, and NIH NIBIB grants R01EB002132 and R01EB001981. The mention of commercial products, their sources, or their use in connection with material reported herein is not to be construed as either an actual or implied endorsement of such products by the FDA. Additional thanks to the RSNA QIBA staff for their help in coordinating group teleconferences, phantom shipping and data exchange, and Julian Lee for assistance in data collection. Special thanks to Dr. Daniel Sullivan for fostering the QIBA vision and providing an infrastructure for these studies and collaborations between academics and industry.

Appendix I: Verasonics Data Acquisition Procedure

The following steps outline the procedure used to acquire phantom data:

1. Place the phantom on an optical isolation table to reduce room vibration artifacts. To aid in acquiring multiple independent speckle realizations at the same location in the phantom, the phantom can be placed on a rotating platform to avoid having to lift the transducer between acquisitions.

2. Remove cover of phantom and pour enough saline solution to ensure adequate acoustic coupling with the transducer at a matched sound speed.

3. Secure the C5–2 transducer in a ring stand and lower it onto the phantom.

4. Connect the transducer to the Verasonics scanner.

5. Initialize the Vantage Verasonics software (switch into the Verasonics directory in MATLAB™ (The Mathworks, Inc., Natick, MA) and type `activate` in the Command Window. Run the C5–2 shear

wave MTL set-up script[4].

6. The set-up script will save the acquisition structures to a MATLAB output file and display a VSX command in the Command Window.

7. Run this command in MATLAB to launch the Verasonics imaging graphical user interface (GUI). This GUI will display live B-mode.

8. Change the push voltage to 60 V (or adjust as necessary depending on the stiffness of the phantom to the voltage required for shear wave data with adequate displacement).

9. Click on the live B-mode image to acquire in-phase/quadrature (IQ) shear-wave data. This will save two IQ data files (real and imaginary components of the data), as well as a parameters file in the indicated directory.

10. In the directory containing the IQ data, run the displacement processing using `genDispMTL.m`, which will generate an output file `[timestamp]_fromIQ_arfidata.mat`.

11. Rotate the phantom to obtain a different speckle realization. Ensure that the transducer is appropriately coupled to the phantom and repeat the acquisition until there are an adequate number of replicate displacement data.

Verasonics sequences and post-processing code for the generated data are available for download[5] [14].

References

[1] Ferraioli G., Filice C., Castera L., et al. WFUMB guidelines and recommendations for clinical use of ultrasound elastography: Part 3: Liver *Ultrasound in Medicine and Biology.* 2015;41:1161-1179.

[2] Barr Richard G., Ferraioli Giovanna, Palmeri Mark L., et al. Elastography Assessment of Liver Fibrosis: Society of Radiologists in Ultrasound Consensus Conference Statement *Radiology.* 2015;276:845-861. PMID: 26079489.

[4] `https://github.com/RSNA-QIBA-US-SWS/VerasonicsPhantomSequences/blob/master/SetUpC5_2Shear_wave_MTL.m`

[5] `https://github.com/RSNA-QIBA-US-SWS/VerasonicsPhantomSequences`

[3] Arvazyan A Rmen P S, Udenko O L E G V R, Wanson S Cott D S, et al. Shear Wave Elasticity Imaging: A New Ultrasonic Technology of Medical Diagnostics *Ultrasound Med. Biol.*. 1998;24:1419–1435.

[4] Doherty Joshua R., Trahey Gregg E., Nightingale Kathryn R., Palmeri Mark L.. Acoustic radiation force elasticity imaging in diagnostic ultrasound *IEEE Trans. Ultrason. Ferroelectr. Freq. Control.* 2013.

[5] Health & Care Excellence (NICE) National Institute. Hepatitis B (chronic): diagnosis and management *Guidance and guidelines [NICE] (accessed Feb. 2018).* 2017.

[6] Ferraioli Giovanna, De Silvestri Annalisa, Lissandrin Raffaella, et al. Evaluation of Inter-System Variability in Liver Stiffness Measurements *Ultraschall in Med.* 2019;40:64-75.

[7] Nadebaum David P., Sood Siddharth, Gibson Robert N.. Variability of Liver Shear Wave Measurements Using a New Ultrasound Elastographic Technique *J Ultrasound Med.* 2017;37:647–656.

[8] Long Zaiyang, Tradup Donald J., Song Pengfei, et al. Clinical acceptance testing and scanner comparison of ultrasound shear wave elastography *Journal of Applied Clinical Medical Physics.* 2018;0.

[9] Rouze N. C., Deng Y., Trutna C. A., Palmeri M. L., Nightingale K. R.. Characterization of Viscoelastic Materials using Group Shear Wave Speeds *IEEE Transactions on Ultrasonics, Ferroelectrics, and Frequency Control.* 2018;65:780-794.

[10] Palmeri Mark L., Deng Yufeng, Rouze Ned C., Nightingale Kathryn R.. Dependence of shear wave spectral content on acoustic radiation force excitation duration and spatial beamwidth in *IEEE Int. Ultrason. Symp. IUS* 2014.

[11] Hall Timothy J., Milkowski Andy, Garra Brian, et al. RSNA/QIBA: Shear wave speed as a biomarker for liver fibrosis staging in *IEEE Int. Ultrason. Symp. IUS* 2013.

[12] Venkatesh SK, Yin M, Ehman RL. Magnetic resonance elastography of liver: technique, analysis, and clinical applications *J Magn Reson Imaging.* 2013;37:544–555.

[13] QIBA Profile: Ultrasound Measurement of Shear Wave Speed for Estimation of Liver Fibrosis *Quantitative Imaging Biomarker Alliance. Profile Stage: Public Comment.* (accessed on October 21, 2019); `http://qibawiki.rsna.org/index.php/Profiles`.

[14] Deng Y., Rouze N. C., Palmeri M. L., Nightingale K. R.. Ultrasonic Shear Wave Elasticity Imaging Sequencing and Data Processing Using a Verasonics Research Scanner *IEEE Transactions on Ultrasonics, Ferroelectrics, and Frequency Control.* 2017;64:164-176.

[15] Palmeri Mark L., Wang Michael H., Rouze Ned C., et al. Noninvasive evaluation of hepatic fibrosis using acoustic radiation force-based shear stiffness in patients with nonalcoholic fatty liver disease *Journal of Hepatology.* 2011;55:666–672.

[16] Morris D.C., Rouze N.C., Palmeri M.L., Nightingale K.R.. Group shear wave based viscoelastic parameter estimation in SWEI: Analysis of sources of bias *Proceedings of the 2017 IEEE International Ultrasonics Symposium.* 2017.

[17] Zhao Heng, Song Pengfei, Urban Matthew W., et al. Bias Observed in Time-of-Flight Shear Wave Speed Measurements Using Radiation Force of a Focused Ultrasound Beam *Ultrasound in Medicine & Biology.* 2011;37:1884 - 1892.

[18] Deng Y., Rouze N. C., Palmeri M. L., Nightingale K. R.. On System-Dependent Sources of Uncertainty and Bias in Ultrasonic Quantitative Shear-Wave Imaging *IEEE Transactions on Ultrasonics, Ferroelectrics, and Frequency Control.* 2016;63:381-393.

[19] Seabold Skipper, Perktold Josef. Statsmodels: Econometric and statistical modeling with python in *9th Python in Science Conference* 2010.

[20] Virtanen Pauli, Gommers Ralf, Oliphant Travis E., et al. SciPy 1.0: Fundamental Algorithms for Scientific Computing in Python *Nature Methods.* 2020;17:261–272.

[21] Oliphant T.E., Manduca A., Ehman R.L., Greenleaf J.F.. Complex-valued stiffness reconstruction for magnetic resonance elastography by algebraic inversion of the differential equation *Magnetic resonance in medicine.* 2001;45:299-310.

[22] Manduca A., Oliphant T.E., Dresner M.A., et al. Magnetic resonance elastography: Non-invasive mapping of tissue elasticity *Medical Image Analysis.* 2001;5:237 - 254.

[23] Palmeri M. L., Qiang B., Chen S., Urban M. W.. Guidelines for Finite-Element Modeling of Acoustic Radiation Force-Induced Shear Wave Propagation in Tissue-Mimicking Media *IEEE Transactions on Ultrasonics, Ferroelectrics, and Frequency Control.* 2017;64:78-92.

Tables

Table 1: Phantoms fabricated by CIRS, Inc. and measured as part of these Phase I and Phase II studies, including their designated usage in these studies.

Phantom Label	Elastic / Viscoelastic	Phase I/II	Purpose
E1786-[1-10]	Elastic	Phase I	Inter-system Comparison
E1787-[1-10]	Elastic	Phase I	Inter-system Comparison
E1788-[1,2]	Elastic	Phase I	US:MRE Comparison
E2297-[A1, B3, C1]	Viscoelastic	Phase II	Inter-system & US:MRE Comparison

Table 2: Acoustic radiation force excitation and displacement tracking parameters used on a Verasonics research scanner with a Philips C5–2 curvilinear array to measure all the Phase I elastic phantoms before distribution to individual measurement sites.

Excitation Parameters		Tracking Parameters	
Frequency	2.4 MHz	Frequency	3.2 MHz
Focal Depths	40, 60, 80 mm	Transmit F-number	Plane-wave
F-number	F/2.0	Receive F-number	F/2.0
Duration	400 μs (960 cycles)	Pulse Repetition Frequency	5 kHz

Table 3: Focal depth bias as a function of different systems in the Phase I phantoms, calculated using simple linear regression. Entries in **bold** text indicate non-negligible bias with moderate-to-good linear regression coefficients.

System	Phantom	Focal Depth Slope ((m/s)/mm)	R^2
A	Soft	-0.00063	0.01
	Stiff	-0.0035	0.14
B	Soft	0.000032	3.0e-06
	Stiff	-0.00091	0.06
C	Soft	0.00046	0.002
	Stiff	**-0.0033**	**0.95**
D	Soft	-0.00091	0.46
	Stiff	**-0.0037**	**0.75**
E	Soft	**0.0011**	**0.76**
	Stiff	-0.0028	0.40
F	Soft	-0.012	0.47
	Stiff	-0.0021	0.08

Table 4: Focal depth bias as a function of different systems in the Phase II phantoms, calculated using simple linear regression. Entries in **bold** text indicate non-negligible bias with moderate-to-good linear regression coefficients.

System	Phantom	Focal Depth Slope ((m/s)/mm)	R^2
A	E2297-A1	-0.0019	0.08
	E2297-B3	-0.0042	0.14
	E2297-C1	-0.0070	0.16
B	E2297-A1	-0.0047	0.095
	E2297-B3	-0.0096	0.11
	E2297-C1	-0.0073	0.019
C	E2297-A1	-0.00095	0.13
	E2297-B3	**-0.0031**	**0.76**
	E2297-C1	-0.00054	0.029
D	E2297-A1	0.0064	0.14
	E2297-B3	0.0055	0.10
	E2297-C1	0.016	0.21
E	E2297-A1	0.0034	0.14
	E2297-B3	0.00084	0.0039
	E2297-C1	-0.0025	0.038
F	E2297-A1	0.0046	0.25
	E2297-B3	0.0065	0.24
	E2297-C1	0.0051	0.085
G	E2297-A1	-0.0039	0.34
	E2297-B3	-0.0063	0.32
	E2297-C1	-0.0073	0.24
H	E2297-A1	-0.0027	0.11
	E2297-B3	-0.0047	0.21
	E2297-C1	0.00066	0.0012
I	E2297-A1	-0.0017	0.047
	E2297-B3	-0.0070	0.40
	E2297-C1	-0.0075	0.36
J	E2297-A1	-0.0052	0.26
	E2297-B3	-0.0046	0.37
	E2297-C1	0.0026	0.025
K	E2297-A1	0.0024	0.20
	E2297-B3	0.0024	0.25
	E2297-C1	0.0074	0.47
L	E2297-A1	-0.0026	0.17
	E2297-B3	0.0019	0.027
	E2297-C1	-0.0024	0.038

Table 5: Comparison of the dispersion estimated in the Phase I and II phantoms using the Verasonics ultrasound system and MRE. Linear regression of the phase velocity data was performed using the frequency ranges shown for each phantom in Figures 5 and 8.

	Ultrasound [(m/s)] / kHz]	**MRE** [(m/s) / kHz]
E1786-1	0.30 (R^2 = 0.87)	—
E1787-1	0.03 (R^2 = 0.43)	—
E1788-1	—	0.60 (R^2 = 0.970)
E1788-2	—	0.20 (R^2 = 0.970)
E2297-A1	0.61 (R^2 = 0.92)	3.0 (R^2 = 0.99)
E2297-B3	0.78 (R^2 = 0.96)	3.2 (R^2 = 0.98)
E2297-C1	0.78 (R^2 = 0.92)	3.8 (R^2 = 0.99)

431 # Figures

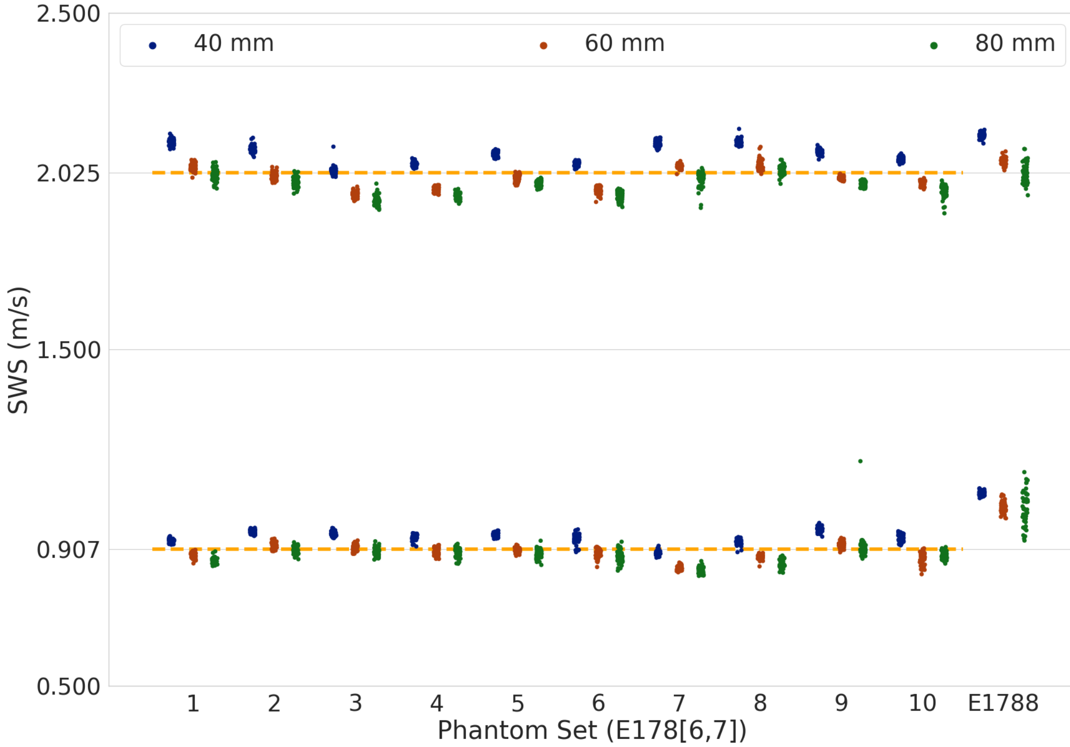


Figure 1: Calibration measurements on all the softer (E1786) and stiffer (E1787) elastic ultrasound phantoms and the phantom set designated for comparison with MRE measurements (E1788) using a research scanner sequence at 3 different focal depths (40 (blue), 60 (red) & 80 (green) mm). The dashed-orange line in each plot represents the grand mean of all measurements made in the ultrasound phantoms for each plot: 0.907 ± 0.033 (3.7%) m/s and 2.025 ± 0.051 (2.5%) m/s for the soft and stiff phantoms, respectively. A given phantom set's mean difference from these grand means was used as a corrective factor to normalize for this fabrication variability between different phantom pairs.

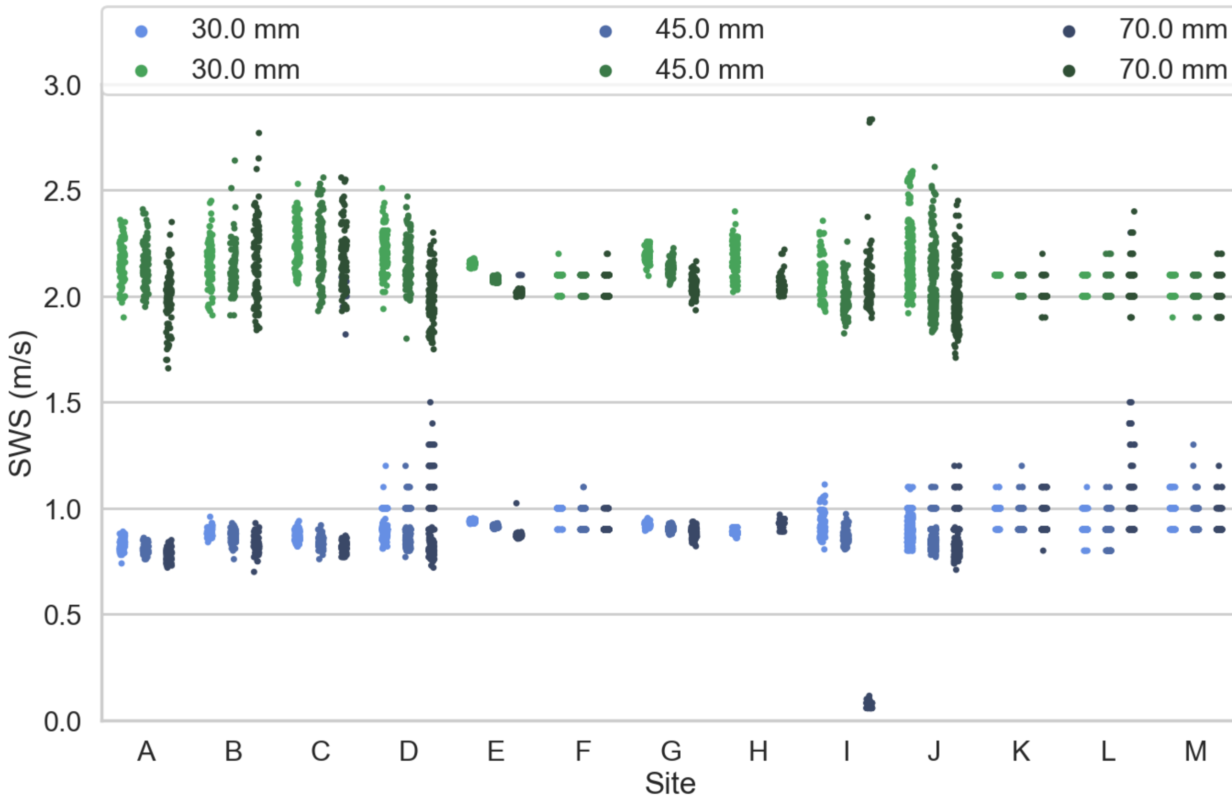


Figure 2: Aggregate SWS data in the soft (blue) and stiff (green) elastic phantoms measured at different sites, where some sites had multiple systems available for measurement. Each system at each site was used by 3 appraisers who made 10 replicate measurements at each of the focal depths (30, 45 and 70 mm) in each phantom. In some cases (Sites D, E, F, J, K, L and M), coarser quantization (rounding to the nearest 0.1 m/s) of the reported SWS by some or all of the site systems is apparent.

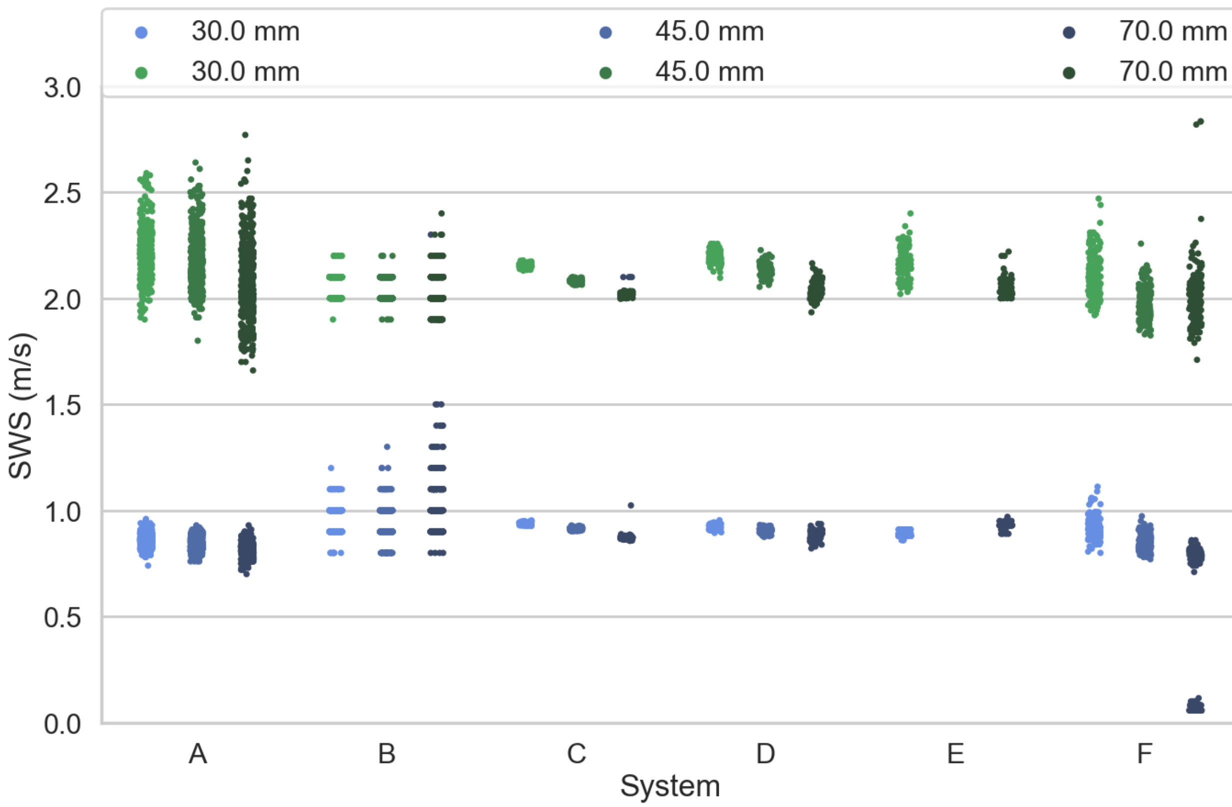


Figure 3: All the elastic phantom data grouped by unique system. Some systems were used at only a single measurement site, while other systems were used at multiple measurement sites. Note that a single system (B) appears to report SWS with coarser quantization (0.1 m/s) compared to the other systems.

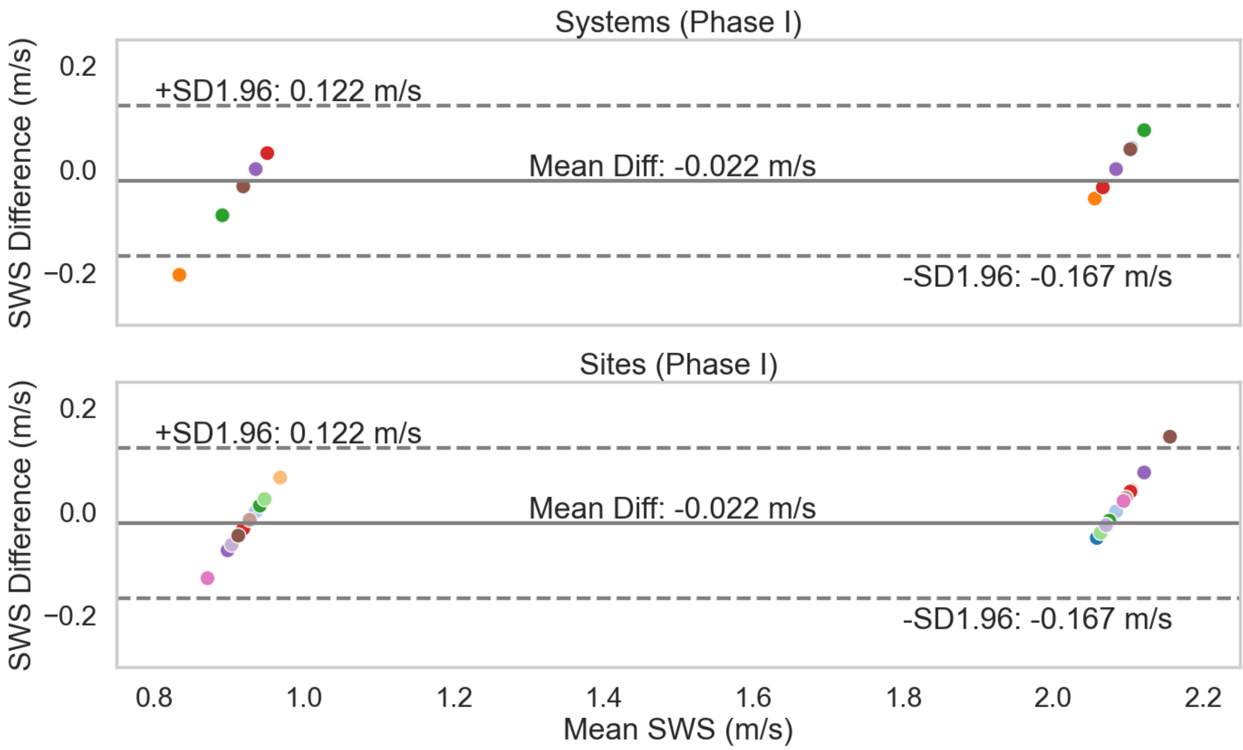


Figure 4: Tukey mean difference plots for the aggregated Phase I systems (top) and sites (bottom), using the normalization data (Figure 1) as the reference measurement for each phantom. The colors in each plot represent the same system/site, respectively. Note that system/site biases are not necessarily consistent across the soft and stiff phantoms (e.g., a system with a negative bias in the soft phantom may have a positive bias in the stiff phantom).

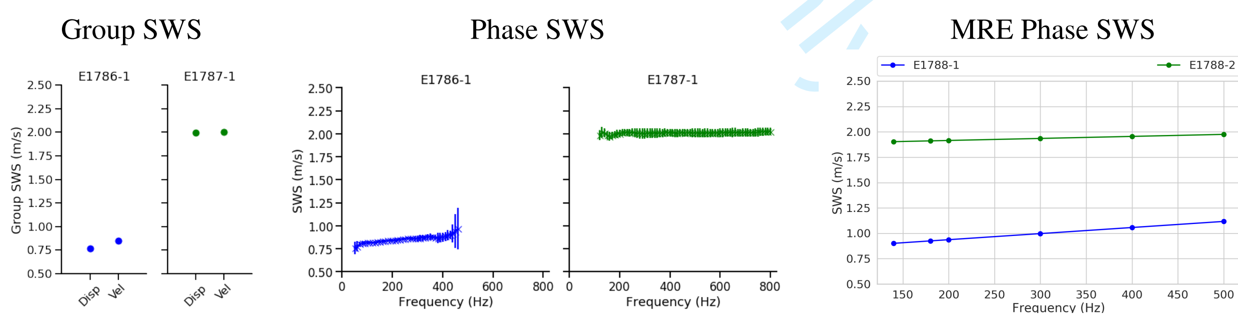


Figure 5: Group and phase SWS measurements in one pair of the Phase I elastic phantoms made using the Verasonics research scanner sequences and processing code at a focal depth of 45 mm, derived from shear wave displacement ("Disp") and from shear wave velocity ("Vel"). The circles in each plot represent the mean of 10 independent acquisitions, while the error bars represent the 95% confidence interval for each measurement. MRE measurements were made at discrete frequencies of 140, 180, 200, 300, 400 and 500 Hz. The slopes of linear fits to these phase velocities, which are indicative of undesired dispersion (frequency-dependent phase velocity) in these elastic phantoms, are summarized in Table5.

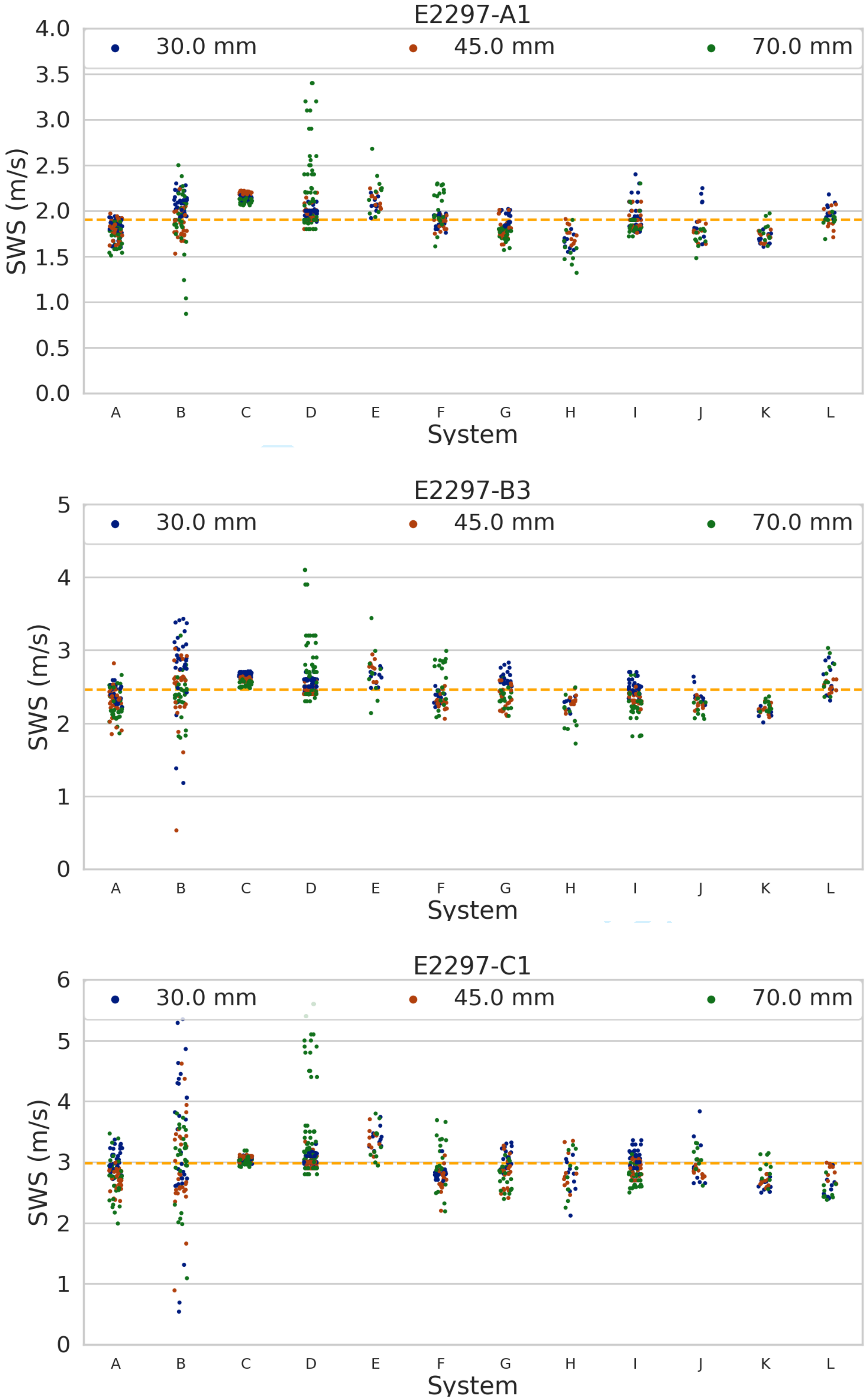


Figure 6: Phase II phantoms measured with different systems with 3 different focal depth configurations (30, 45 and 70 mm). The orange line on each plot represents the grand median value across all systems for each phantom.

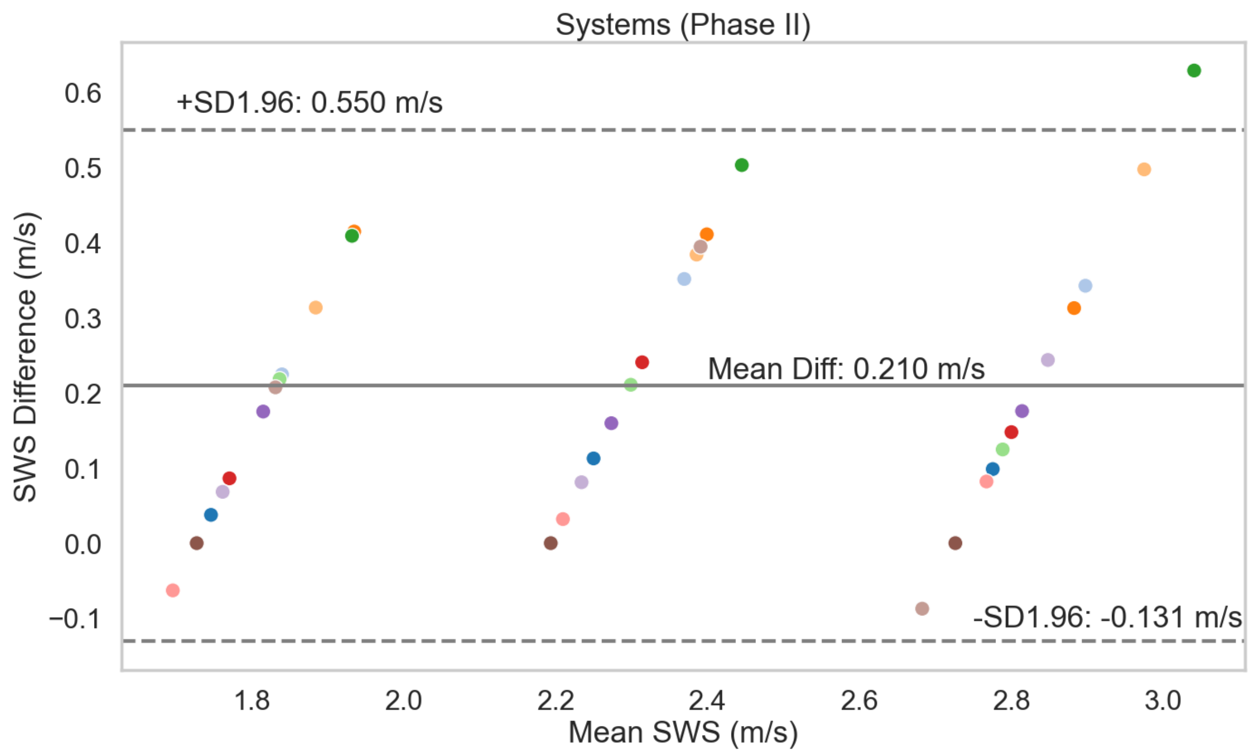


Figure 7: Tukey mean difference plots for the aggregated Phase II systems using the data from the calibration Verasonics system as the reference measurements for each phantom. The colors in each plot represent the same system. Note that system biases are not necessarily consistent across the different phantoms (e.g., a system with a negative bias in one phantom may have a positive bias another phantom).

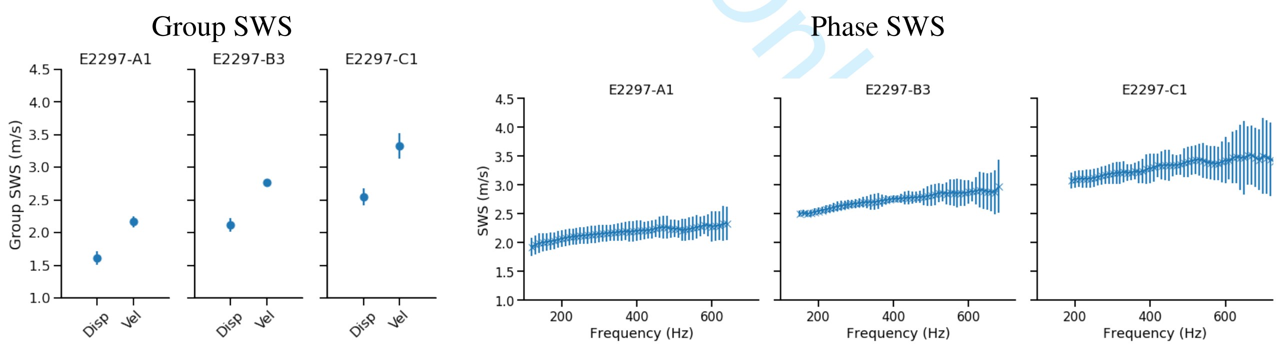


Figure 8: Group and phase velocities calculated in the three Phase II viscoelastic phantoms that were distributed to all of the measurement sites. The error bars represent the 95% confidence interval over 16 independent measurements. As expected, these viscoelastic phantoms have higher group SWS estimated when using velocity (“Vel”) data instead of displacement (“Disp”) data (left plots). This same trend is seen in the positive slope of the corresponding phase velocity curves (right plots). In the phase velocity plots, note that the frequency range of the reconstructed phase velocities increases as a function of increasing stiffness, and the variance of the estimated phase velocity increases at higher frequencies due to the lower SNR at these higher frequencies. The slopes of the linear-fit phase velocity lines are summarized in Table 5.

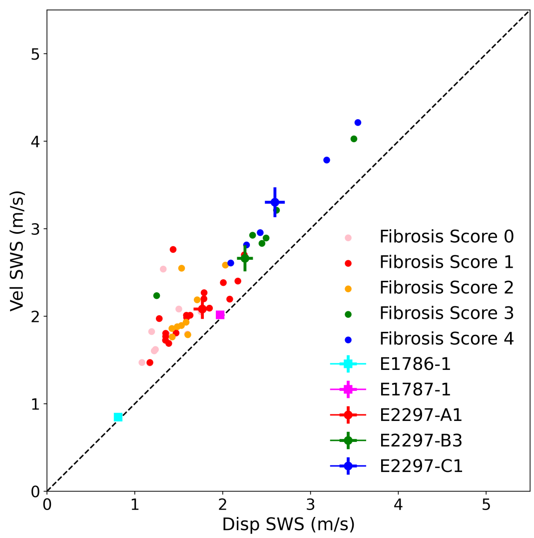


Figure 9: Comparison of group SWS calculated with displacement and velocity data in the Phase I and II phantoms compared with equivalent processing of *in vivo* human data at varying fibrosis stages. The dashed line represents a unity ratio between velocity and displacement-based group SWS that would be indicative of an elastic material, while data points above this line would indicate a dispersive material. In the Phase II phantoms, the group SWS calculated using velocity data was 32±1.9% greater than using displacement data, while in the human data, the velocity-based group SWS was 27±5.6% greater than the displacement-based group SWS across all fibrosis stages.

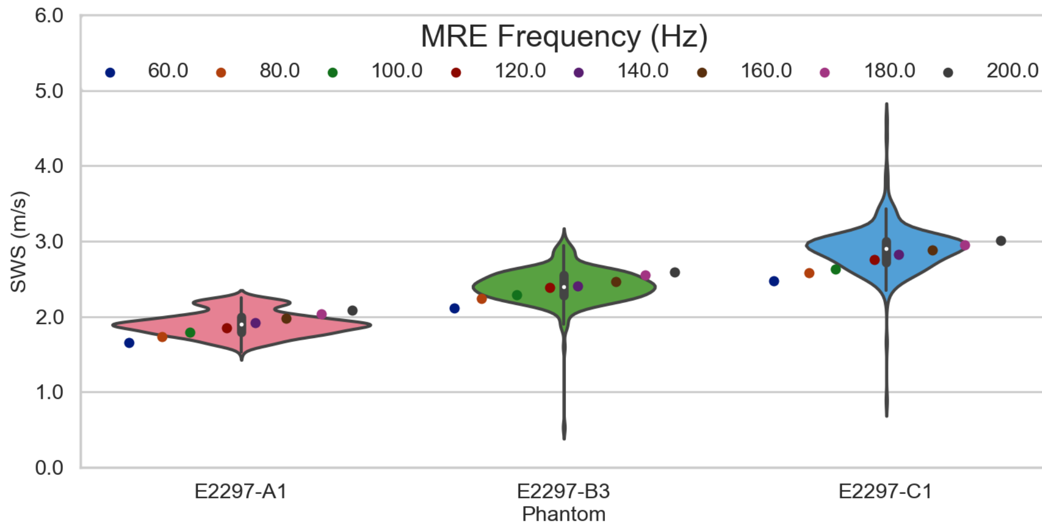


Figure 10: Violin distributions of aggregate ultrasound SWS data across all systems and sites at a focal depth of 45 mm for each Phase II phantom, compared with discrete MRE measurements made at frequencies ranging from 60-200 Hz. The black box within each violin plot represents the interquartile range of the data, with the white circle representing the median value. Vertical lines extend away from each violin distribution to represent 1.5x the standard deviation of the data. The surrounding shape represents the probability density of the data.

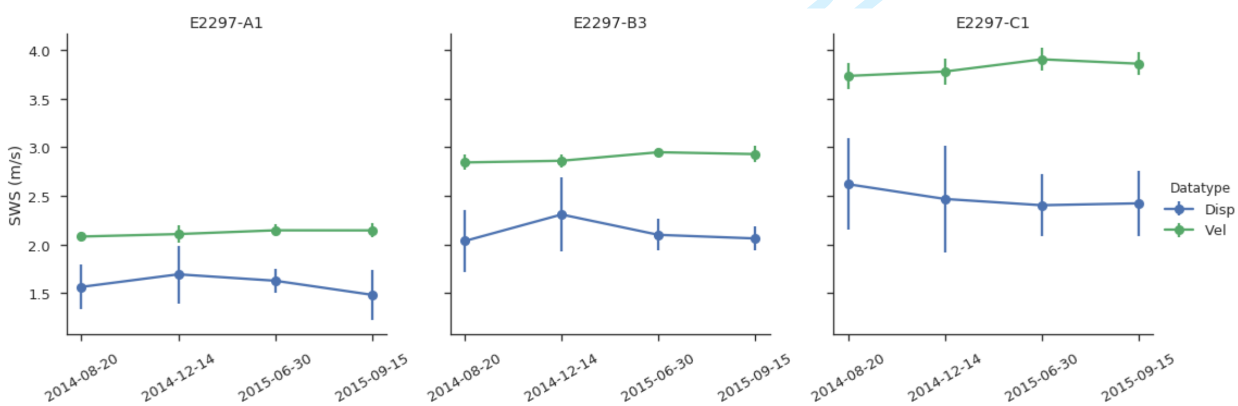
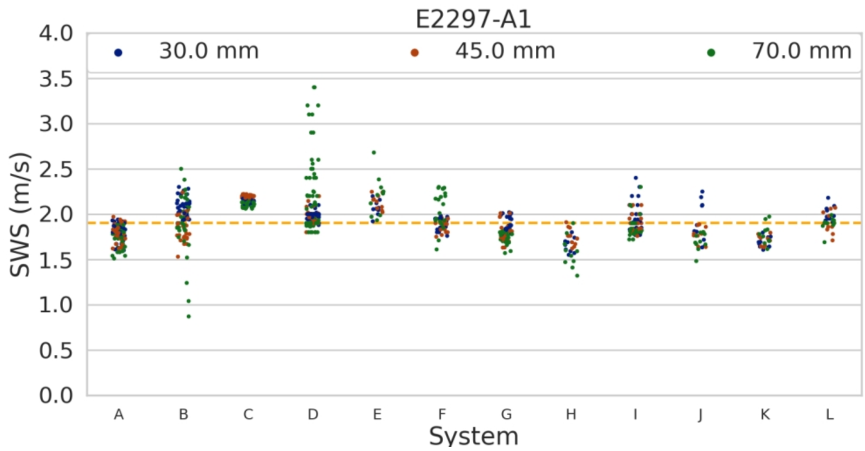
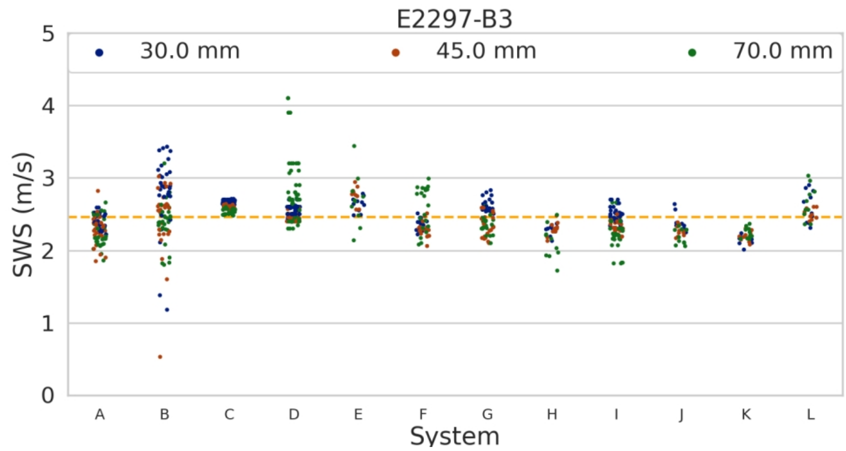
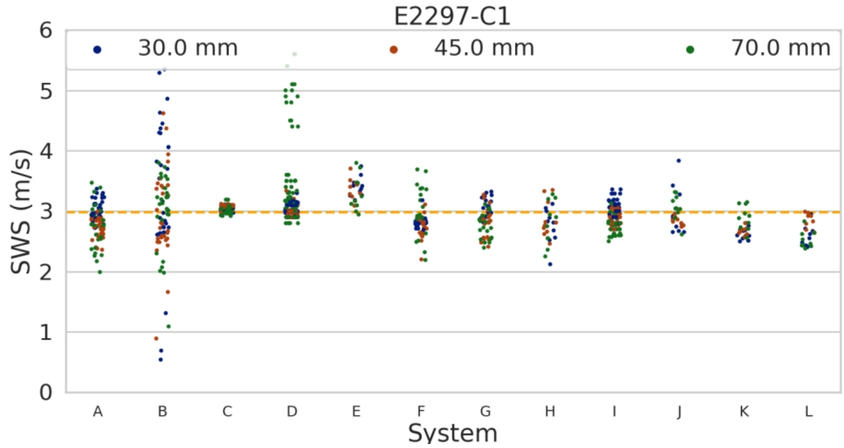


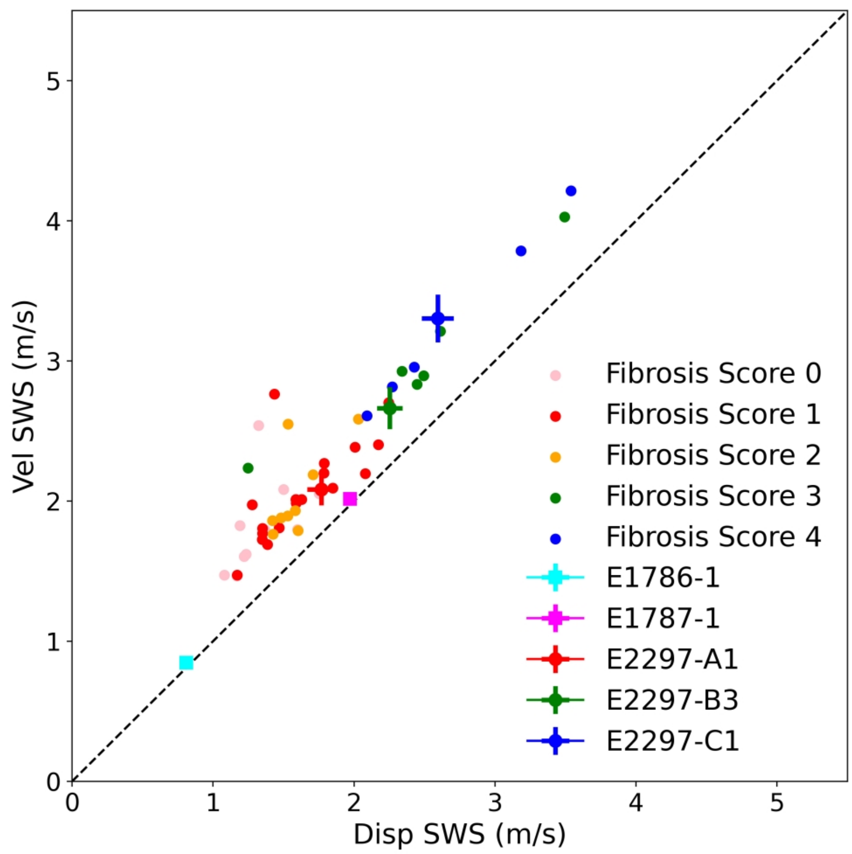
Figure 11: Measurements demonstrating the longitudinal stability of the Phase II phantoms using the group SWS calculated using displacement and velocity data as representative metrics. The error bars represent the standard deviation over 16 independent measurements.


E2297-A1
30.0 mm
45.0 mm
70.0 mm
SWS (m/s)
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
A
B
C
D
E
F
G
H
I
J
K
L
System

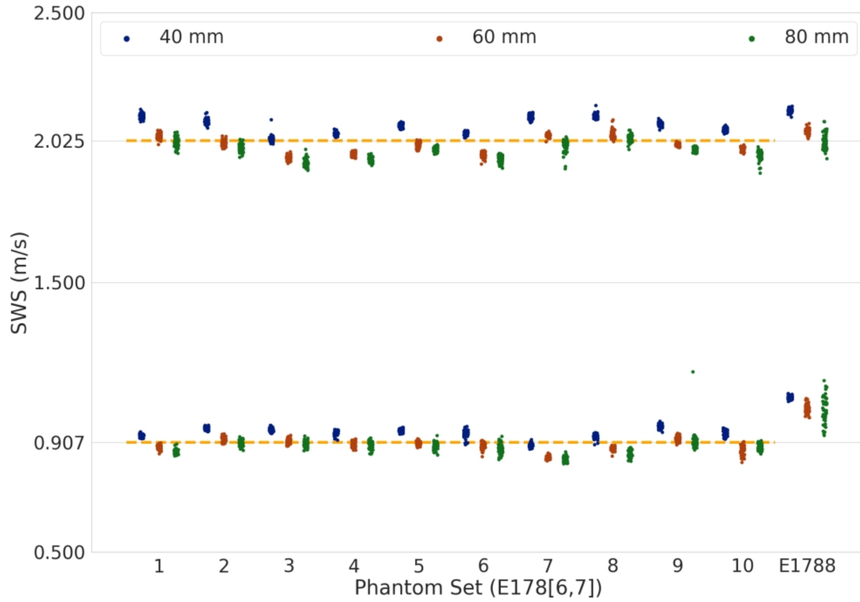


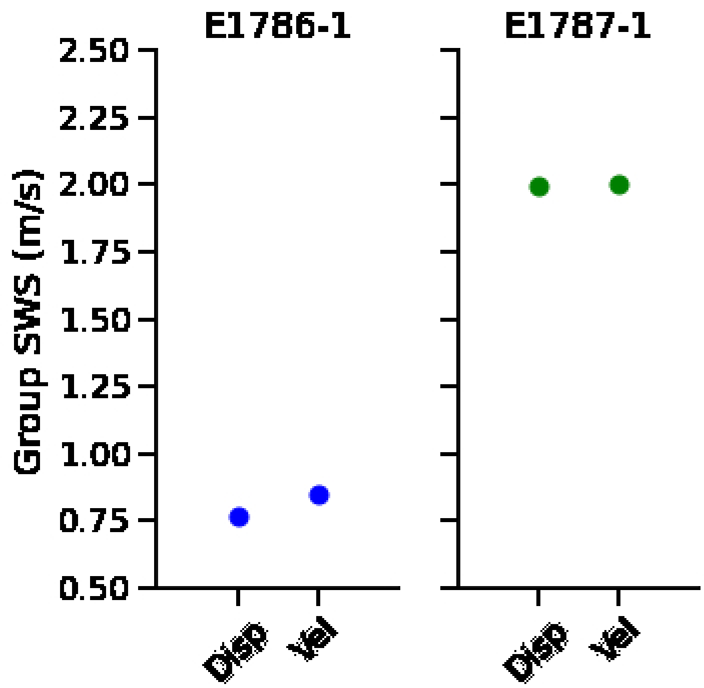
E2297-B3
30.0 mm
45.0 mm
70.0 mm
SWS (m/s)
0
1
2
3
4
5
A
B
C
D
E
F
G
H
I
J
K
L
System

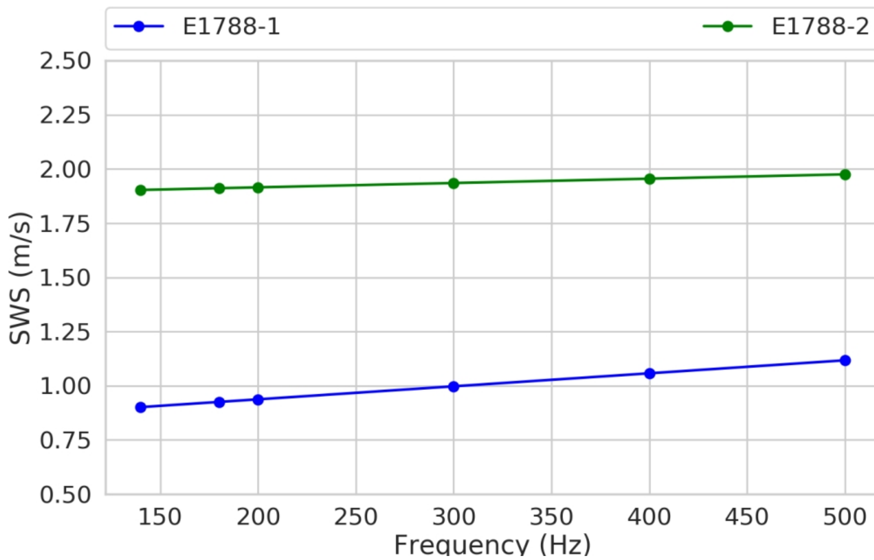

E2297-C1
30.0 mm
45.0 mm
70.0 mm
SWS (m/s)
System
6
5
4
3
2
1
0
A
B
C
D
E
F
G
H
I
J
K
L

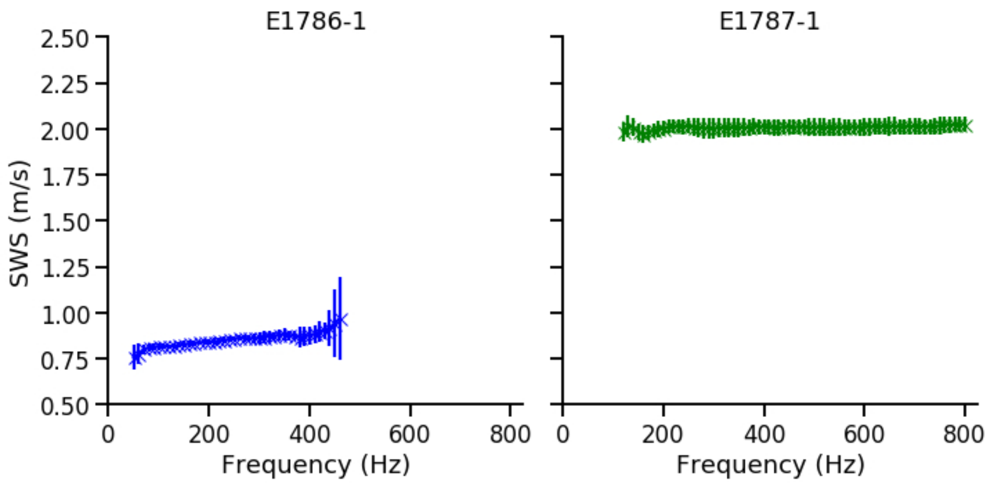


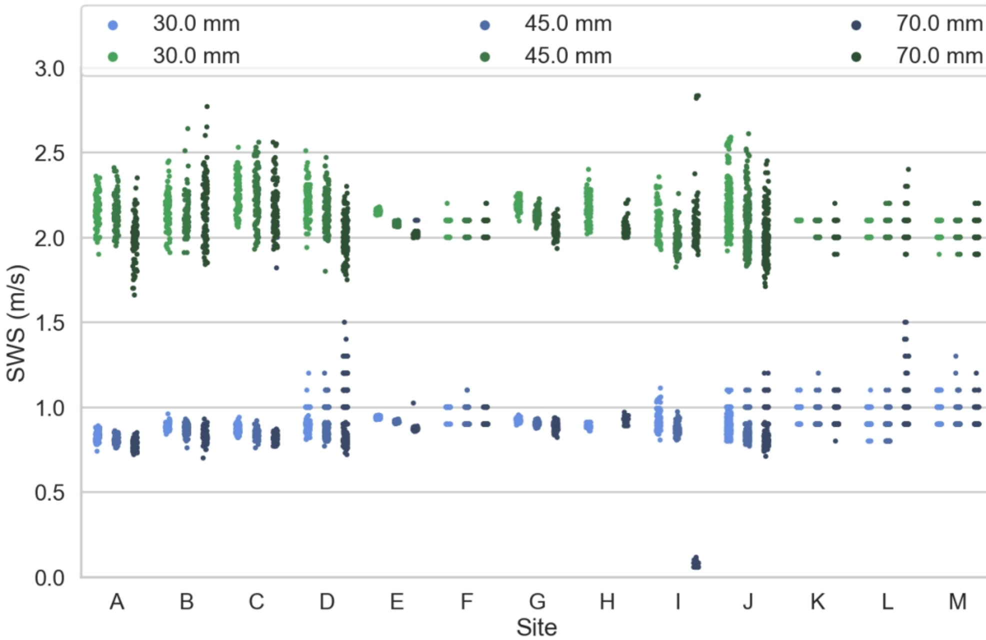
Vel SWS (m/s)
Disp SWS (m/s)
0
1
2
3
4
5
Fibrosis Score 0
Fibrosis Score 1
Fibrosis Score 2
Fibrosis Score 3
Fibrosis Score 4
E1786-1
E1787-1
E2297-A1
E2297-B3
E2297-C1


40 mm
60 mm
80 mm
2.500
2.025
1.500
0.907
0.500
SWS (m/s)
1
2
3
4
5
6
7
8
9
10
E1788
Phantom Set (E178[6,7])

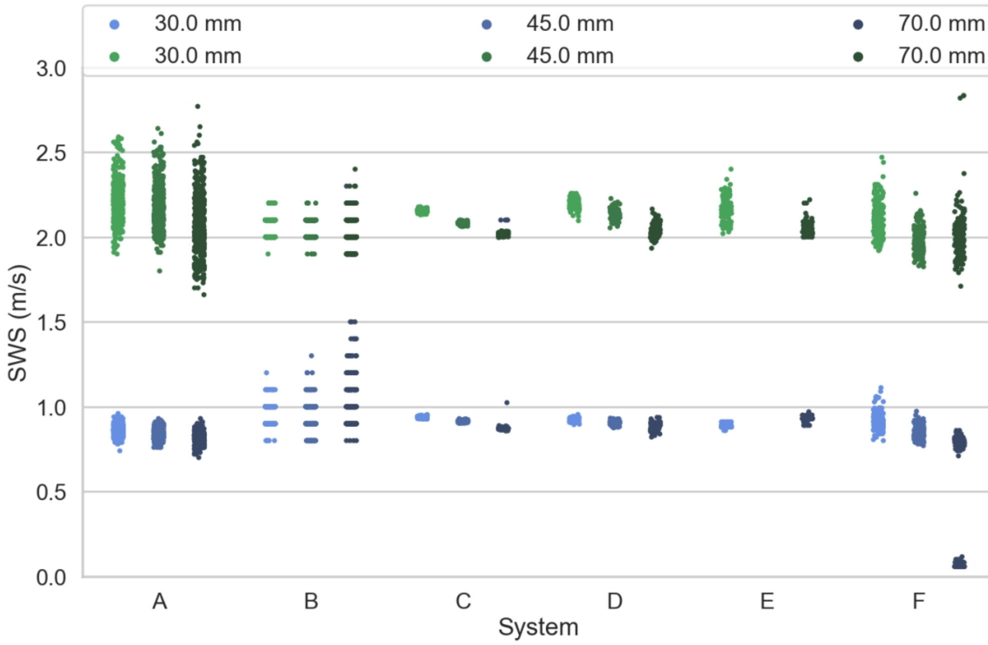

E1786-1
E1787-1
Group SWS (m/s)
2.50
2.25
2.00
1.75
1.50
1.25
1.00
0.75
0.50
Disp
Vel
Disp
Vel

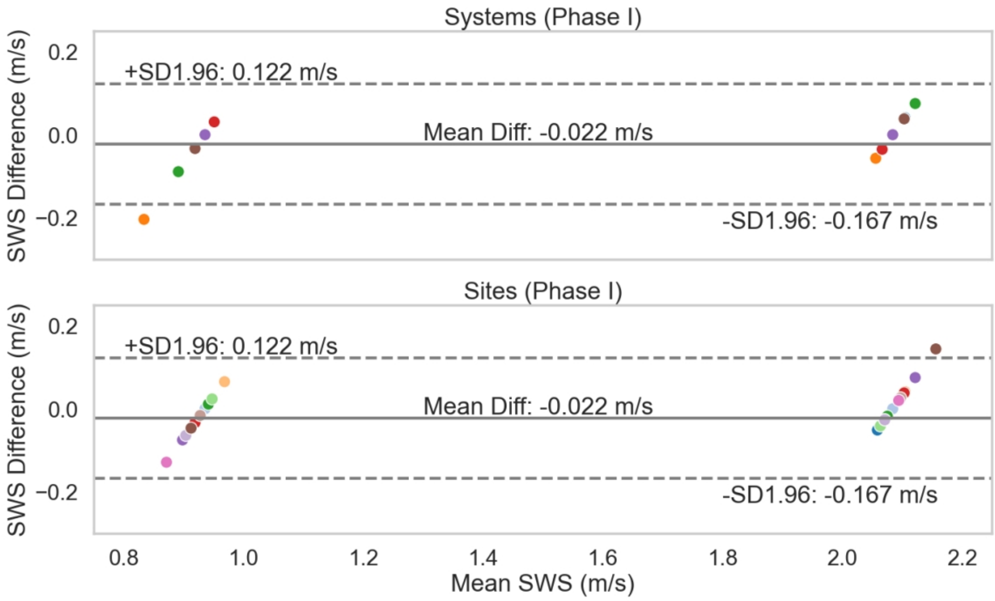

E1788-1
E1788-2
2.50
2.25
2.00
1.75
1.50
1.25
1.00
0.75
0.50
SWS (m/s)
150
200
250
300
350
400
450
500
Frequency (Hz)

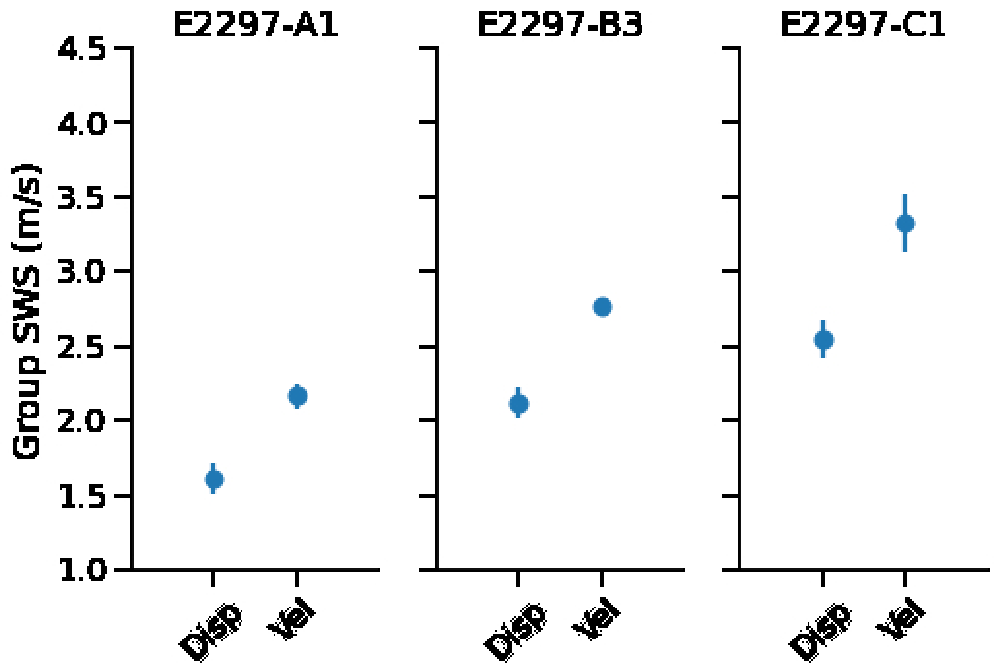

E1786-1
E1787-1
SWS (m/s)
2.50
2.25
2.00
1.75
1.50
1.25
1.00
0.75
0.50
0
200
400
600
800
Frequency (Hz)

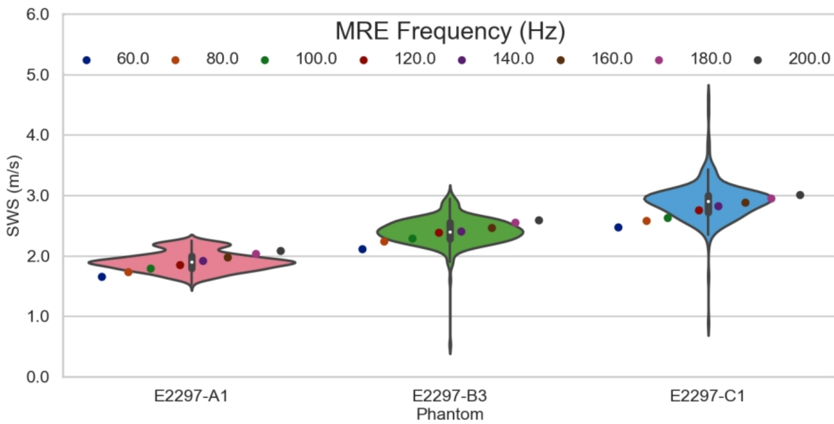


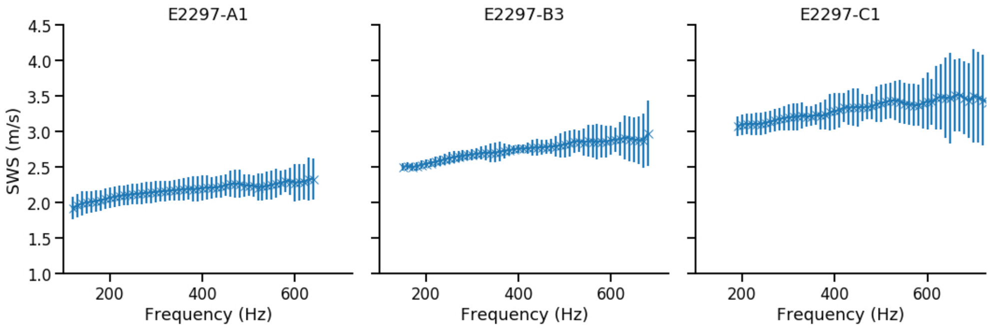
30.0 mm
30.0 mm
45.0 mm
45.0 mm
70.0 mm
70.0 mm
3.0
2.5
2.0
1.5
1.0
0.5
0.0
SWS (m/s)
A
B
C
D
E
F
G
H
I
J
K
L
M
Site


30.0 mm
30.0 mm
45.0 mm
45.0 mm
70.0 mm
70.0 mm
SWS (m/s)
3.0
2.5
2.0
1.5
1.0
0.5
0.0
A
B
C
D
E
F
System

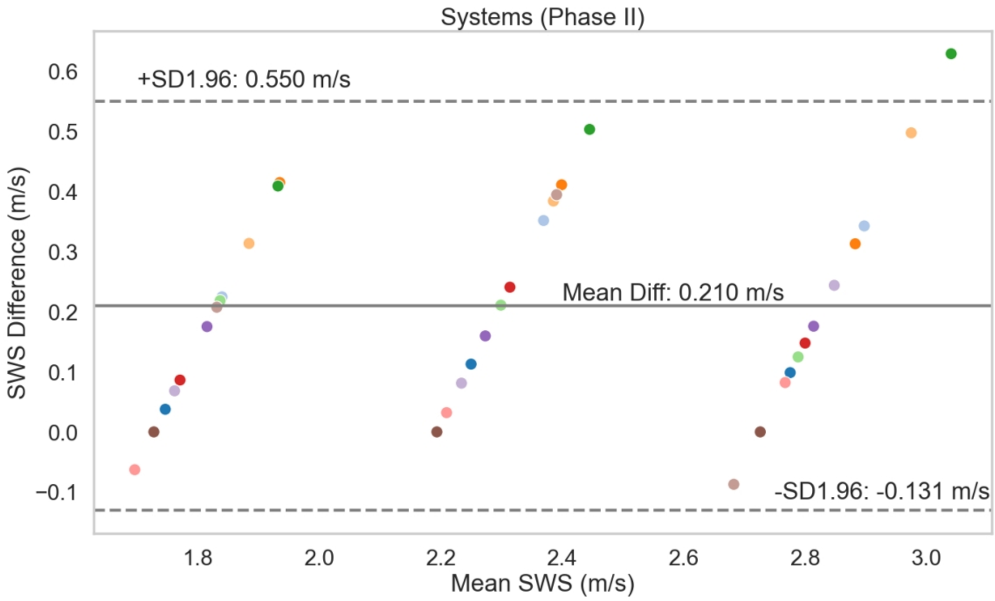

Systems (Phase I)
SWS Difference (m/s)
0.2
0.0
−0.2
+SD1.96: 0.122 m/s
Mean Diff: -0.022 m/s
-SD1.96: -0.167 m/s
Sites (Phase I)
SWS Difference (m/s)
0.2
0.0
−0.2
+SD1.96: 0.122 m/s
Mean Diff: -0.022 m/s
-SD1.96: -0.167 m/s
0.8
1.0
1.2
1.4
1.6
1.8
2.0
2.2
Mean SWS (m/s)

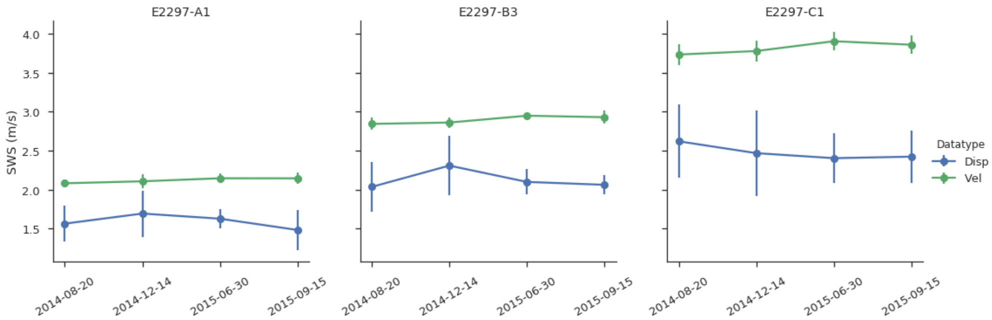

E2297-A1
E2297-B3
E2297-C1
Group SWS (m/s)
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
Disp
Vel
Disp
Vel
Disp
Vel


MRE Frequency (Hz)
60.0
80.0
100.0
120.0
140.0
160.0
180.0
200.0
SWS (m/s)
6.0
5.0
4.0
3.0
2.0
1.0
0.0
E2297-A1
E2297-B3
E2297-C1
Phantom



E2297-A1
E2297-B3
E2297-C1
SWS (m/s)
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
200
400
600
Frequency (Hz)


Systems (Phase II)
+SD1.96: 0.550 m/s
Mean Diff: 0.210 m/s
-SD1.96: -0.131 m/s
SWS Difference (m/s)
Mean SWS (m/s)
0.6
0.5
0.4
0.3
0.2
0.1
0.0
−0.1
1.8
2.0
2.2
2.4
2.6
2.8
3.0


E2297-A1
E2297-B3
E2297-C1
SWS (m/s)
4.0
3.5
3.0
2.5
2.0
1.5
2014-08-20
2014-12-14
2015-06-30
2015-09-15
Datatype
Disp
Vel

Please wait...

If this message is not eventually replaced by the proper contents of the document, your PDF viewer may not be able to display this type of document.

You can upgrade to the latest version of Adobe Reader for Windows®, Mac, or Linux® by visiting http://www.adobe.com/go/reader_download.

For more assistance with Adobe Reader visit http://www.adobe.com/go/acrreader.

INTERNATIONAL COMMITTEE of MEDICAL JOURNAL EDITORS

ICMJE Form for Disclosure of Potential Conflicts of Interest

Instructions

The purpose of this form is to provide readers of your manuscript with information about your other interests that could influence how they receive and understand your work. The form is designed to be completed electronically and stored electronically. It contains programming that allows appropriate data display. Each author should submit a separate form and is responsible for the accuracy and completeness of the submitted information. The form is in six parts.

1. Identifying information.

2. The work under consideration for publication.

This section asks for information about the work that you have submitted for publication. The time frame for this reporting is that of the work itself, from the initial conception and planning to the present. The requested information is about resources that you received, either directly or indirectly (via your institution), to enable you to complete the work. Checking "No" means that you did the work without receiving any financial support from any third party -- that is, the work was supported by funds from the same institution that pays your salary and that institution did not receive third-party funds with which to pay you. If you or your institution received funds from a third party to support the work, such as a government granting agency, charitable foundation or commercial sponsor, check "Yes".

3. Relevant financial activities outside the submitted work.

This section asks about your financial relationships with entities in the bio-medical arena that could be perceived to influence, or that give the appearance of potentially influencing, what you wrote in the submitted work. You should disclose interactions with ANY entity that could be considered broadly relevant to the work. For example, if your article is about testing an epidermal growth factor receptor (EGFR) antagonist in lung cancer, you should report all associations with entities pursuing diagnostic or therapeutic strategies in cancer in general, not just in the area of EGFR or lung cancer.

Report all sources of revenue paid (or promised to be paid) directly to you or your institution on your behalf over the 36 months prior to submission of the work. This should include all monies from sources with relevance to the submitted work, not just monies from the entity that sponsored the research. Please note that your interactions with the work's sponsor that are outside the submitted work should also be listed here. If there is any question, it is usually better to disclose a relationship than not to do so.

For grants you have received for work outside the submitted work, you should disclose support ONLY from entities that could be perceived to be affected financially by the published work, such as drug companies, or foundations supported by entities that could be perceived to have a financial stake in the outcome. Public funding sources, such as government agencies, charitable foundations or academic institutions, need not be disclosed. For example, if a government agency sponsored a study in which you have been involved and drugs were provided by a pharmaceutical company, you need only list the pharmaceutical company.

4. Intellectual Property.

This section asks about patents and copyrights, whether pending, issued, licensed and/or receiving royalties.

5. Relationships not covered above.

Use this section to report other relationships or activities that readers could perceive to have influenced, or that give the appearance of potentially influencing, what you wrote in the submitted work.

Definitions.

Entity: government agency, foundation, commercial sponsor, academic institution, etc.
Grant: A grant from an entity, generally [but not always] paid to your organization
Personal Fees: Monies paid to you for services rendered, generally honoraria, royalties, or fees for consulting , lectures, speakers bureaus, expert testimony, employment, or other affiliations
Non-Financial Support: Examples include drugs/equipment supplied by the entity, travel paid by the entity, writing assistance, administrative support, etc**.**

Other: Anything not covered under the previous three boxes
Pending: The patent has been filed but not issued
Issued: The patent has been issued by the agency
Licensed: The patent has been licensed to an entity, whether earning royalties or not
Royalties: Funds are coming in to you or your institution due to your patent

ICMJE INTERNATIONAL COMMITTEE of MEDICAL JOURNAL EDITORS

ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 1. Identifying Information

1. Given Name (First Name): Mathieu
2. Surname (Last Name): COUADE
3. Date: 23-November-2020

4. Are you the corresponding author? ☐ Yes ☑ No

Corresponding Author's Name: Mark Palmeri

5. Manuscript Title
RSNA/QIBA Shear Wave Speed as a Biomarker for Liver Fibrosis Staging: Elastic and Viscoelastic Phantom Studies

6. Manuscript Identifying Number (if you know it)
ID JUM-2020-06-0914

Section 2. The Work Under Consideration for Publication

Did you or your institution **at any time** receive payment or services from a third party (government, commercial, private foundation, etc.) for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc.)?

Are there any relevant conflicts of interest? ☐ Yes ☑ No

Section 3. Relevant financial activities outside the submitted work.

Place a check in the appropriate boxes in the table to indicate whether you have financial relationships (regardless of amount of compensation) with entities as described in the instructions. Use one line for each entity; add as many lines as you need by clicking the "Add +" box. You should report relationships that were **present during the 36 months prior to publication**.

Are there any relevant conflicts of interest? ☐ Yes ☑ No

Section 4. Intellectual Property -- Patents & Copyrights

Do you have any patents, whether planned, pending or issued, broadly relevant to the work? ☐ Yes ☑ No

ICMJE INTERNATIONAL COMMITTEE of MEDICAL JOURNAL EDITORS

ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 5. Relationships not covered above

Are there other relationships or activities that readers could perceive to have influenced, or that give the appearance of potentially influencing, what you wrote in the submitted work?

☐ Yes, the following relationships/conditions/circumstances are present (explain below):

☑ No other relationships/conditions/circumstances that present a potential conflict of interest

At the time of manuscript acceptance, journals will ask authors to confirm and, if necessary, update their disclosure statements. On occasion, journals may ask authors to disclose further information about reported relationships.

Section 6. Disclosure Statement

Based on the above disclosures, this form will automatically generate a disclosure statement, which will appear in the box below.

Dr. COUADE has nothing to disclose.

Evaluation and Feedback

Please visit http://www.icmje.org/cgi-bin/feedback to provide feedback on your experience with completing this form.

ICMJE Form for Disclosure of Potential Conflicts of Interest

Instructions

The purpose of this form is to provide readers of your manuscript with information about your other interests that could influence how they receive and understand your work. The form is designed to be completed electronically and stored electronically. It contains programming that allows appropriate data display. Each author should submit a separate form and is responsible for the accuracy and completeness of the submitted information. The form is in six parts.

1. Identifying information.

2. The work under consideration for publication.

This section asks for information about the work that you have submitted for publication. The time frame for this reporting is that of the work itself, from the initial conception and planning to the present. The requested information is about resources that you received, either directly or indirectly (via your institution), to enable you to complete the work. Checking "No" means that you did the work without receiving any financial support from any third party -- that is, the work was supported by funds from the same institution that pays your salary and that institution did not receive third-party funds with which to pay you. If you or your institution received funds from a third party to support the work, such as a government granting agency, charitable foundation or commercial sponsor, check "Yes".

3. Relevant financial activities outside the submitted work.

This section asks about your financial relationships with entities in the bio-medical arena that could be perceived to influence, or that give the appearance of potentially influencing, what you wrote in the submitted work. You should disclose interactions with ANY entity that could be considered broadly relevant to the work. For example, if your article is about testing an epidermal growth factor receptor (EGFR) antagonist in lung cancer, you should report all associations with entities pursuing diagnostic or therapeutic strategies in cancer in general, not just in the area of EGFR or lung cancer.

Report all sources of revenue paid (or promised to be paid) directly to you or your institution on your behalf over the 36 months prior to submission of the work. This should include all monies from sources with relevance to the submitted work, not just monies from the entity that sponsored the research. Please note that your interactions with the work's sponsor that are outside the submitted work should also be listed here. If there is any question, it is usually better to disclose a relationship than not to do so.

For grants you have received for work outside the submitted work, you should disclose support ONLY from entities that could be perceived to be affected financially by the published work, such as drug companies, or foundations supported by entities that could be perceived to have a financial stake in the outcome. Public funding sources, such as government agencies, charitable foundations or academic institutions, need not be disclosed. For example, if a government agency sponsored a study in which you have been involved and drugs were provided by a pharmaceutical company, you need only list the pharmaceutical company.

4. Intellectual Property.

This section asks about patents and copyrights, whether pending, issued, licensed and/or receiving royalties.

5. Relationships not covered above.

Use this section to report other relationships or activities that readers could perceive to have influenced, or that give the appearance of potentially influencing, what you wrote in the submitted work.

Definitions.

Entity: government agency, foundation, commercial sponsor, academic institution, etc.
Grant: A grant from an entity, generally [but not always] paid to your organization
Personal Fees: Monies paid to you for services rendered, generally honoraria, royalties, or fees for consulting , lectures, speakers bureaus, expert testimony, employment, or other affiliations
Non-Financial Support: Examples include drugs/equipment supplied by the entity, travel paid by the entity, writing assistance, administrative support, etc**.**

Other: Anything not covered under the previous three boxes
Pending: The patent has been filed but not issued
Issued: The patent has been issued by the agency
Licensed: The patent has been licensed to an entity, whether earning royalties or not
Royalties: Funds are coming in to you or your institution due to your patent

INTERNATIONAL COMMITTEE of MEDICAL JOURNAL EDITORS

ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 1. Identifying Information

1. Given Name (First Name): Yuling
2. Surname (Last Name): Chen
3. Date: 20-November-2020

4. Are you the corresponding author? ☐ Yes ☑ No

Corresponding Author's Name: Mark Palmeri

5. Manuscript Title: RSNA/QIBA Shear Wave Speed Bias Quantification in Elastic and Viscoelastic Phantoms

6. Manuscript Identifying Number (if you know it)

Section 2. The Work Under Consideration for Publication

Did you or your institution **at any time** receive payment or services from a third party (government, commercial, private foundation, etc.) for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc.)?

Are there any relevant conflicts of interest? ☐ Yes ☑ No

Section 3. Relevant financial activities outside the submitted work.

Place a check in the appropriate boxes in the table to indicate whether you have financial relationships (regardless of amount of compensation) with entities as described in the instructions. Use one line for each entity; add as many lines as you need by clicking the "Add +" box. You should report relationships that were **present during the 36 months prior to publication**.

Are there any relevant conflicts of interest? ☐ Yes ☑ No

Section 4. Intellectual Property -- Patents & Copyrights

Do you have any patents, whether planned, pending or issued, broadly relevant to the work? ☐ Yes ☑ No

ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 5. Relationships not covered above

Are there other relationships or activities that readers could perceive to have influenced, or that give the appearance of potentially influencing, what you wrote in the submitted work?

☐ Yes, the following relationships/conditions/circumstances are present (explain below):

☑ No other relationships/conditions/circumstances that present a potential conflict of interest

At the time of manuscript acceptance, journals will ask authors to confirm and, if necessary, update their disclosure statements. On occasion, journals may ask authors to disclose further information about reported relationships.

Section 6. Disclosure Statement

Based on the above disclosures, this form will automatically generate a disclosure statement, which will appear in the box below.

Dr. Chen has nothing to disclose.

Evaluation and Feedback

Please visit http://www.icmje.org/cgi-bin/feedback to provide feedback on your experience with completing this form.

Please wait...

If this message is not eventually replaced by the proper contents of the document, your PDF viewer may not be able to display this type of document.

You can upgrade to the latest version of Adobe Reader for Windows®, Mac, or Linux® by visiting http://www.adobe.com/go/reader_download.

For more assistance with Adobe Reader visit http://www.adobe.com/go/acrreader.

Please wait...

Please wait...

If this message is not eventually replaced by the proper contents of the document, your PDF viewer may not be able to display this type of document.

You can upgrade to the latest version of Adobe Reader for Windows®, Mac, or Linux® by visiting http://www.adobe.com/go/reader_download.

For more assistance with Adobe Reader visit http://www.adobe.com/go/acrreader.

Please wait...

If this message is not eventually replaced by the proper contents of the document, your PDF viewer may not be able to display this type of document.

You can upgrade to the latest version of Adobe Reader for Windows®, Mac, or Linux® by visiting http://www.adobe.com/go/reader_download.

For more assistance with Adobe Reader visit http://www.adobe.com/go/acrreader.

Please wait...

If this message is not eventually replaced by the proper contents of the document, your PDF viewer may not be able to display this type of document.

You can upgrade to the latest version of Adobe Reader for Windows®, Mac, or Linux® by visiting http://www.adobe.com/go/reader_download.

For more assistance with Adobe Reader visit http://www.adobe.com/go/acrreader.

Please wait...

If this message is not eventually replaced by the proper contents of the document, your PDF viewer may not be able to display this type of document.

You can upgrade to the latest version of Adobe Reader for Windows®, Mac, or Linux® by visiting http://www.adobe.com/go/reader_download.

For more assistance with Adobe Reader visit http://www.adobe.com/go/acrreader.

ICMJE INTERNATIONAL COMMITTEE of MEDICAL JOURNAL EDITORS

ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 1. Identifying Information

1. Given Name (First Name): Yoko
2. Surname (Last Name): Okamura
3. Date: 12/15/2020

4. Are you the corresponding author? ☑ Yes ☐ No

5. Manuscript Title: RSNA/QIBA Shave Wave Speed Bias Quantification in Elastic and Viscoelastic Phantoms

6. Manuscript Identifying Number (if you know it): JUM-2020-06-0914.R2

Section 2. The Work Under Consideration for Publication

Did you or your institution **at any time** receive payment or services from a third party (government, commercial, private foundation, etc.) for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc.)?

Are there any relevant conflicts of interest? ☐ Yes ☑ No

Section 3. Relevant financial activities outside the submitted work.

Place a check in the appropriate boxes in the table to indicate whether you have financial relationships (regardless of amount of compensation) with entities as described in the instructions. Use one line for each entity; add as many lines as you need by clicking the "Add +" box. You should report relationships that were **present during the 36 months prior to publication**.

Are there any relevant conflicts of interest? ☐ Yes ☑ No

Section 4. Intellectual Property -- Patents & Copyrights

Do you have any patents, whether planned, pending or issued, broadly relevant to the work? ☐ Yes ☑ No

ICMJE INTERNATIONAL COMMITTEE *of* MEDICAL JOURNAL EDITORS

ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 5. Relationships not covered above

Are there other relationships or activities that readers could perceive to have influenced, or that give the appearance of potentially influencing, what you wrote in the submitted work?

- [ ] Yes, the following relationships/conditions/circumstances are present (explain below):
- [x] No other relationships/conditions/circumstances that present a potential conflict of interest

At the time of manuscript acceptance, journals will ask authors to confirm and, if necessary, update their disclosure statements. On occasion, journals may ask authors to disclose further information about reported relationships.

Section 6. Disclosure Statement

Based on the above disclosures, this form will automatically generate a disclosure statement, which will appear in the box below.

Evaluation and Feedback

Please visit http://www.icmje.org/cgi-bin/feedback to provide feedback on your experience with completing this form.

ICMJE INTERNATIONAL COMMITTEE of MEDICAL JOURNAL EDITORS

SAVE

ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 1. Identifying Information

1. Given Name (First Name): Nancy
2. Surname (Last Name): Obuchowski
3. Date: 27-November-2020

4. Are you the corresponding author? ☐ Yes ☑ No

Corresponding Author's Name: Mark Palmeri

5. Manuscript Title: RSNA/QIBA Shear Wave Speed as a......

6. Manuscript Identifying Number (if you know it): JUM-2020-06-0914

Section 2. The Work Under Consideration for Publication

Did you or your institution **at any time** receive payment or services from a third party (government, commercial, private foundation, etc.) for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc.)?

Are there any relevant conflicts of interest? ☑ Yes ☐ No

If yes, please fill out the appropriate information below. If you have more than one entity press the "ADD" button to add a row. Excess rows can be removed by pressing the "X" button.

Name of Institution/Company	Grant?	Personal Fees?	Non-Financial Support?	Other?	Comments	
RSNA/QIBA	☐	☐	☐	☑	Dr. Obuchowski serves as a statistical consultant to QIBA through a contract between her institution and QIBA	×

ADD

Section 3. Relevant financial activities outside the submitted work.

Place a check in the appropriate boxes in the table to indicate whether you have financial relationships (regardless of amount of compensation) with entities as described in the instructions. Use one line for each entity; add as many lines as you need by clicking the "Add +" box. You should report relationships that were **present during the 36 months prior to publication**.

Are there any relevant conflicts of interest? ☐ Yes ☑ No

ADD

Section 4. Intellectual Property -- Patents & Copyrights

Do you have any patents, whether planned, pending or issued, broadly relevant to the work? ☐ Yes ☑ No

INTERNATIONAL COMMITTEE of MEDICAL JOURNAL EDITORS

SAVE

ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 5. Relationships not covered above

Are there other relationships or activities that readers could perceive to have influenced, or that give the appearance of potentially influencing, what you wrote in the submitted work?

☐ Yes, the following relationships/conditions/circumstances are present (explain below):

☑ No other relationships/conditions/circumstances that present a potential conflict of interest

At the time of manuscript acceptance, journals will ask authors to confirm and, if necessary, update their disclosure statements. On occasion, journals may ask authors to disclose further information about reported relationships.

Section 6. Disclosure Statement

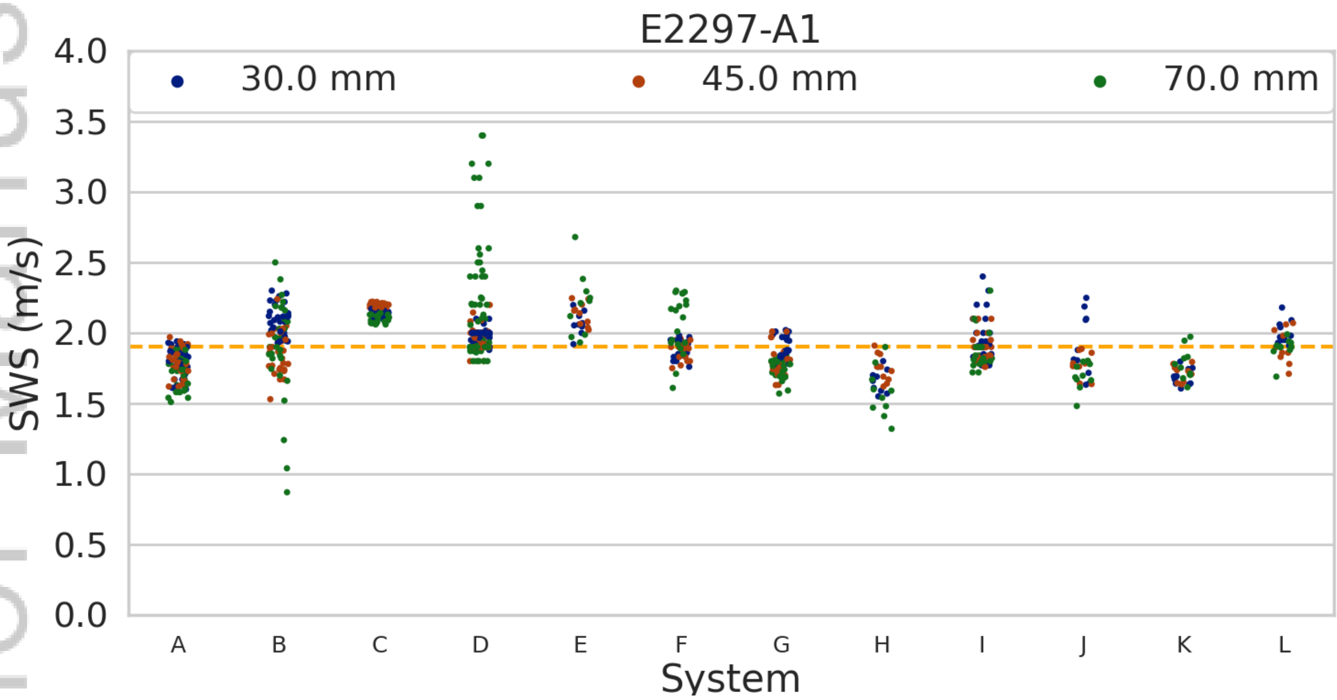
Based on the above disclosures, this form will automatically generate a disclosure statement, which will appear in the box below.

Generate Disclosure Statement

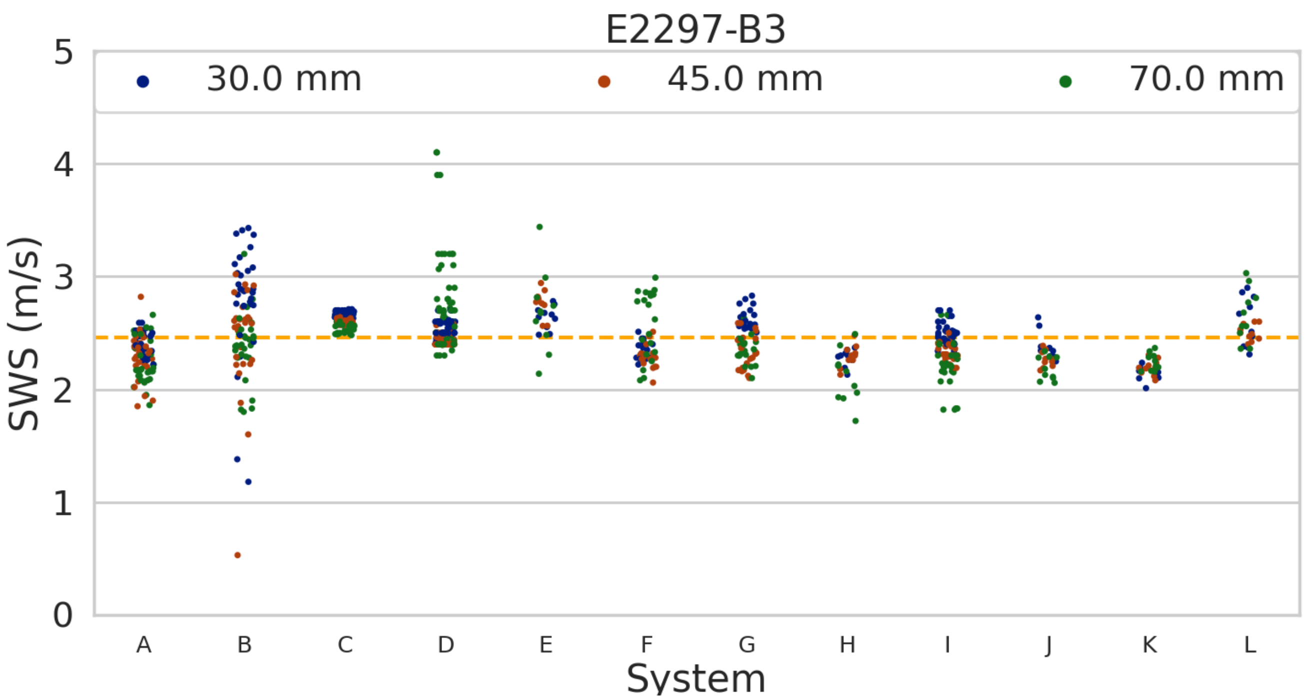
Dr. Obuchowski reports other from RSNA/QIBA, during the conduct of the study .

Evaluation and Feedback

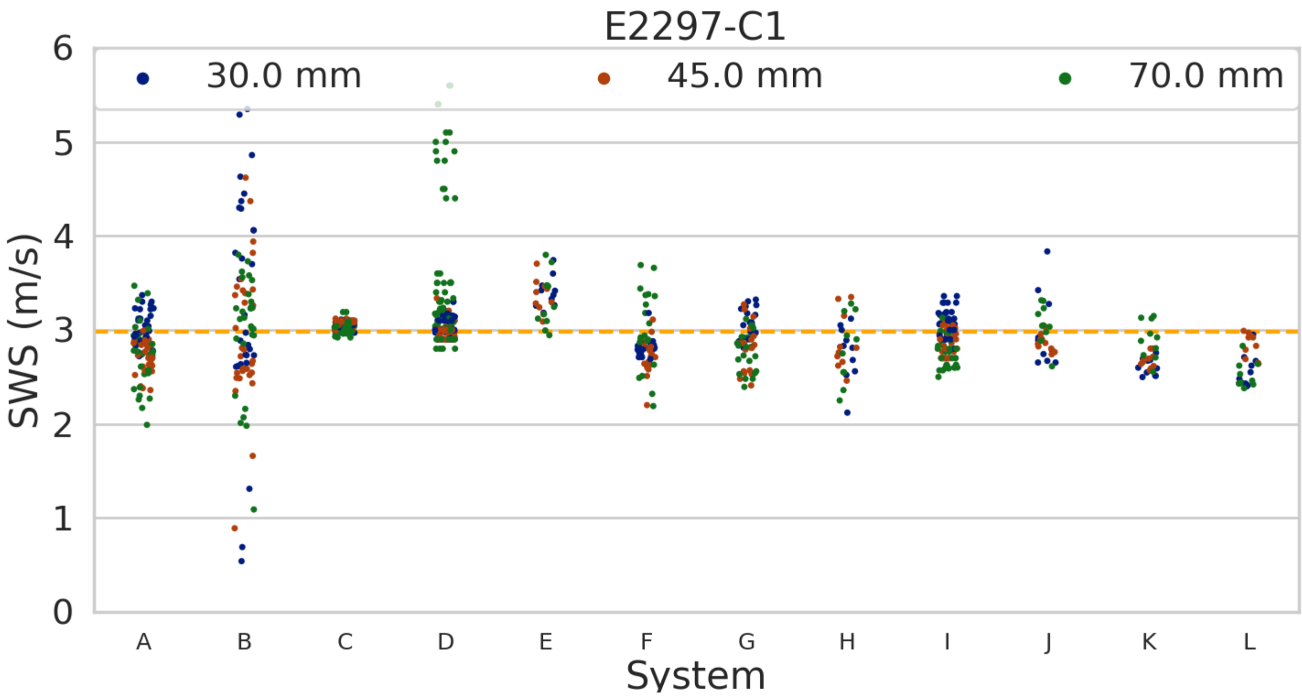
Please visit http://www.icmje.org/cgi-bin/feedback to provide feedback on your experience with completing this form.



JUM_15609_E2297-A1_probe_C.png



JUM_15609_E2297-B3_probe_C.png



JUM_15609_E2297-C1_probe_C.png

Please wait...

If this message is not eventually replaced by the proper contents of the document, your PDF viewer may not be able to display this type of document.

You can upgrade to the latest version of Adobe Reader for Windows®, Mac, or Linux® by visiting http://www.adobe.com/go/reader_download.

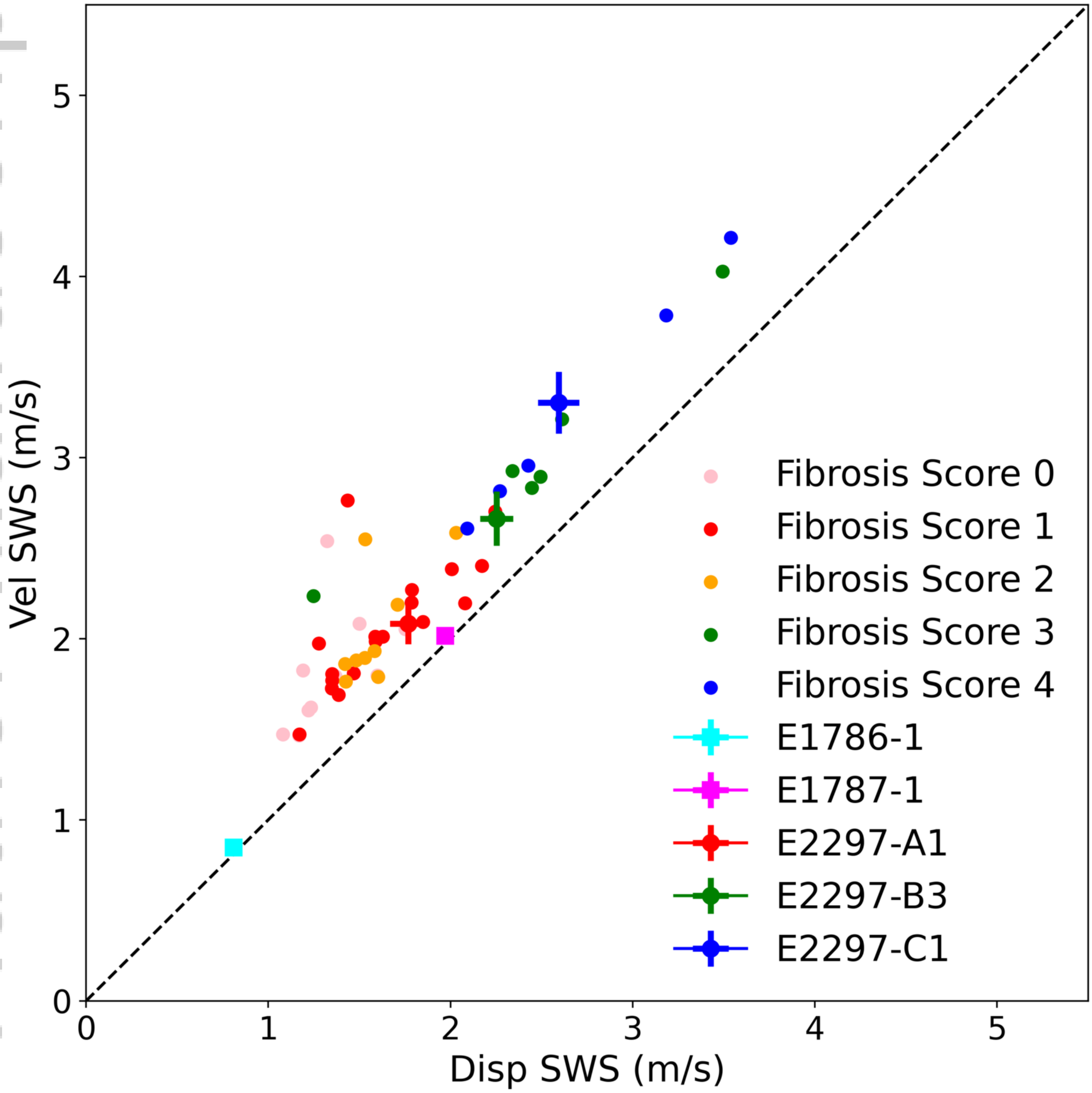
For more assistance with Adobe Reader visit http://www.adobe.com/go/acrreader.

Please wait...

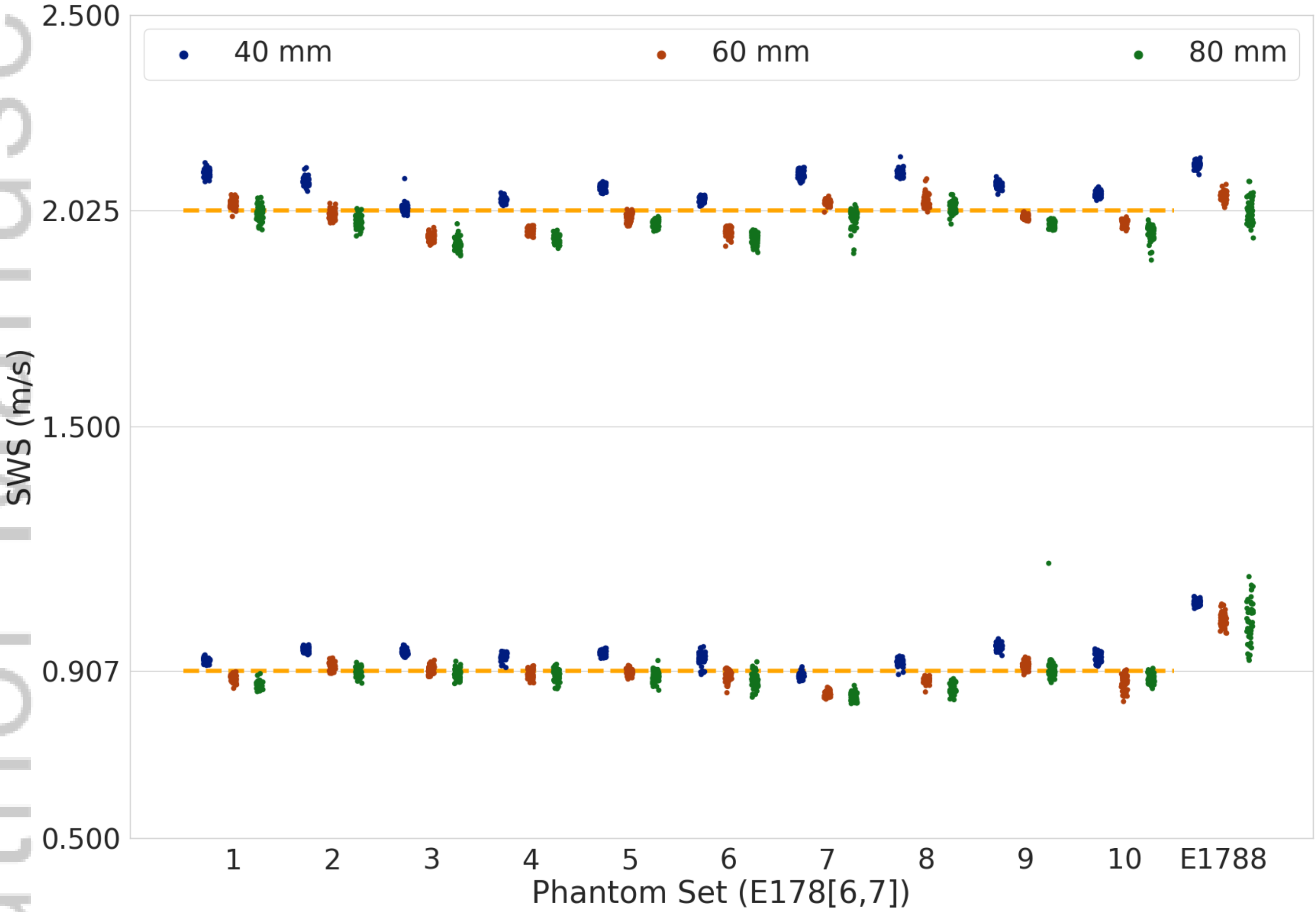
If this message is not eventually replaced by the proper contents of the document, your PDF viewer may not be able to display this type of document.

You can upgrade to the latest version of Adobe Reader for Windows®, Mac, or Linux® by visiting http://www.adobe.com/go/reader_download.

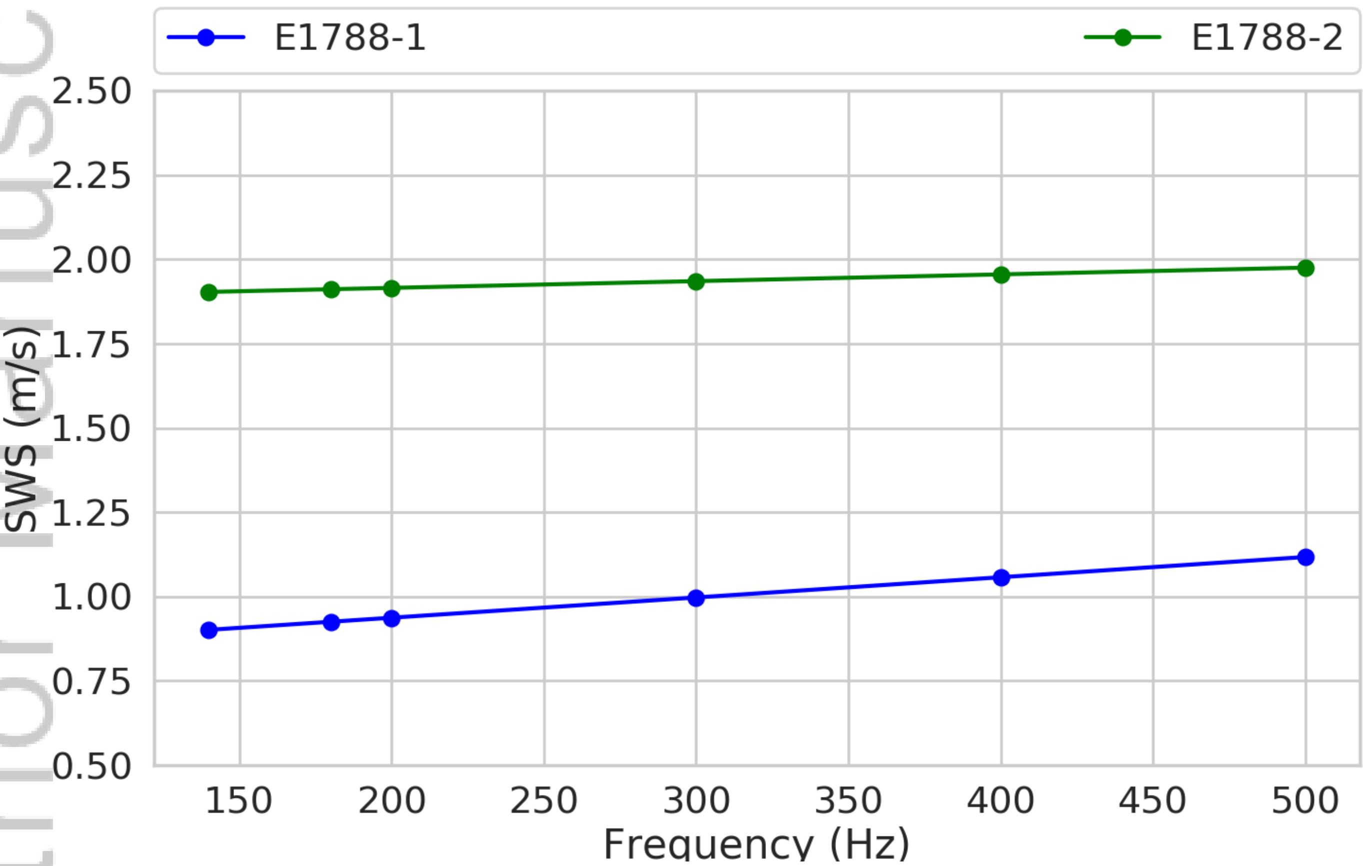
For more assistance with Adobe Reader visit http://www.adobe.com/go/acrreader.



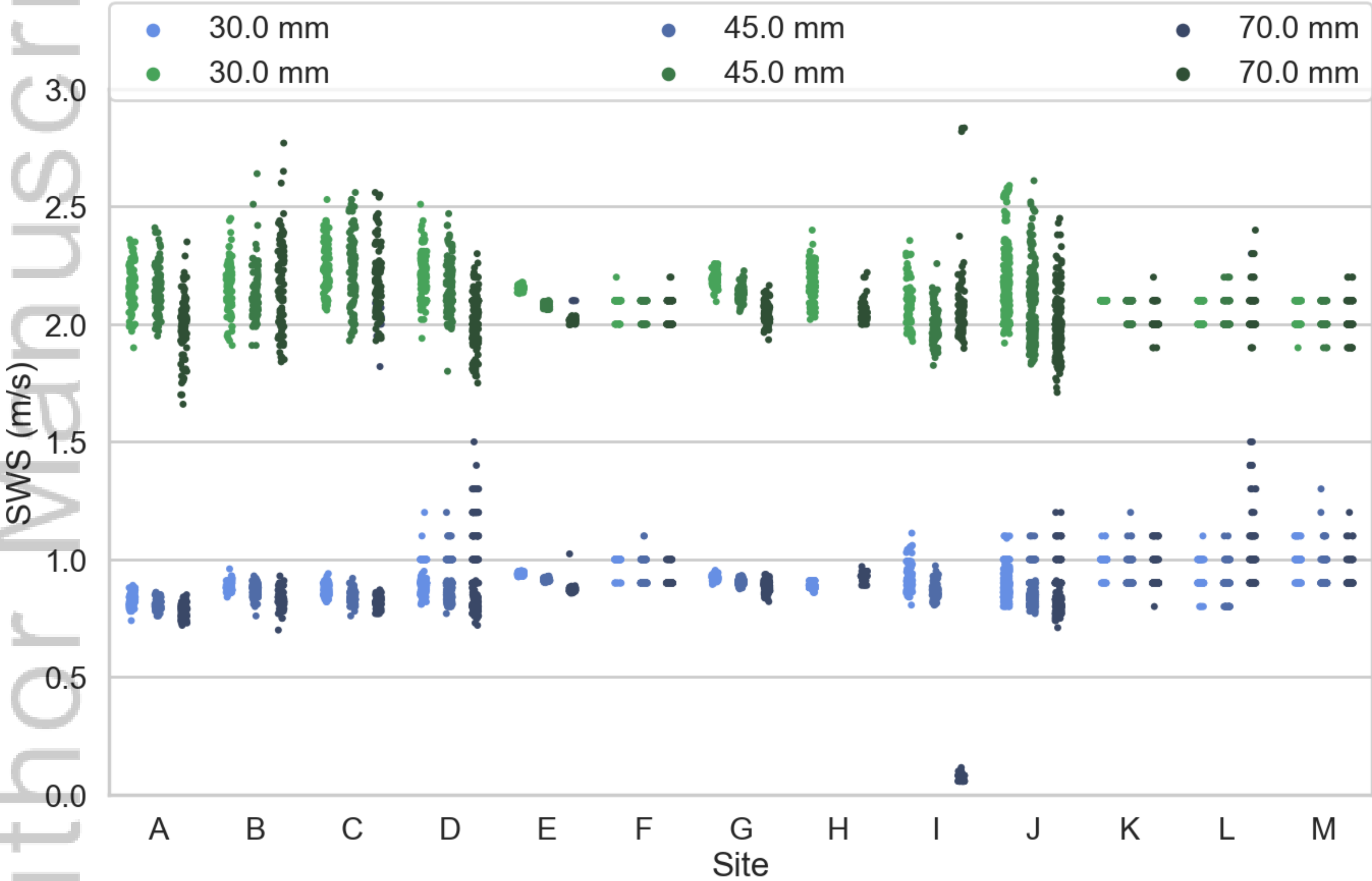
JUM_15609_phantoms_humans.png



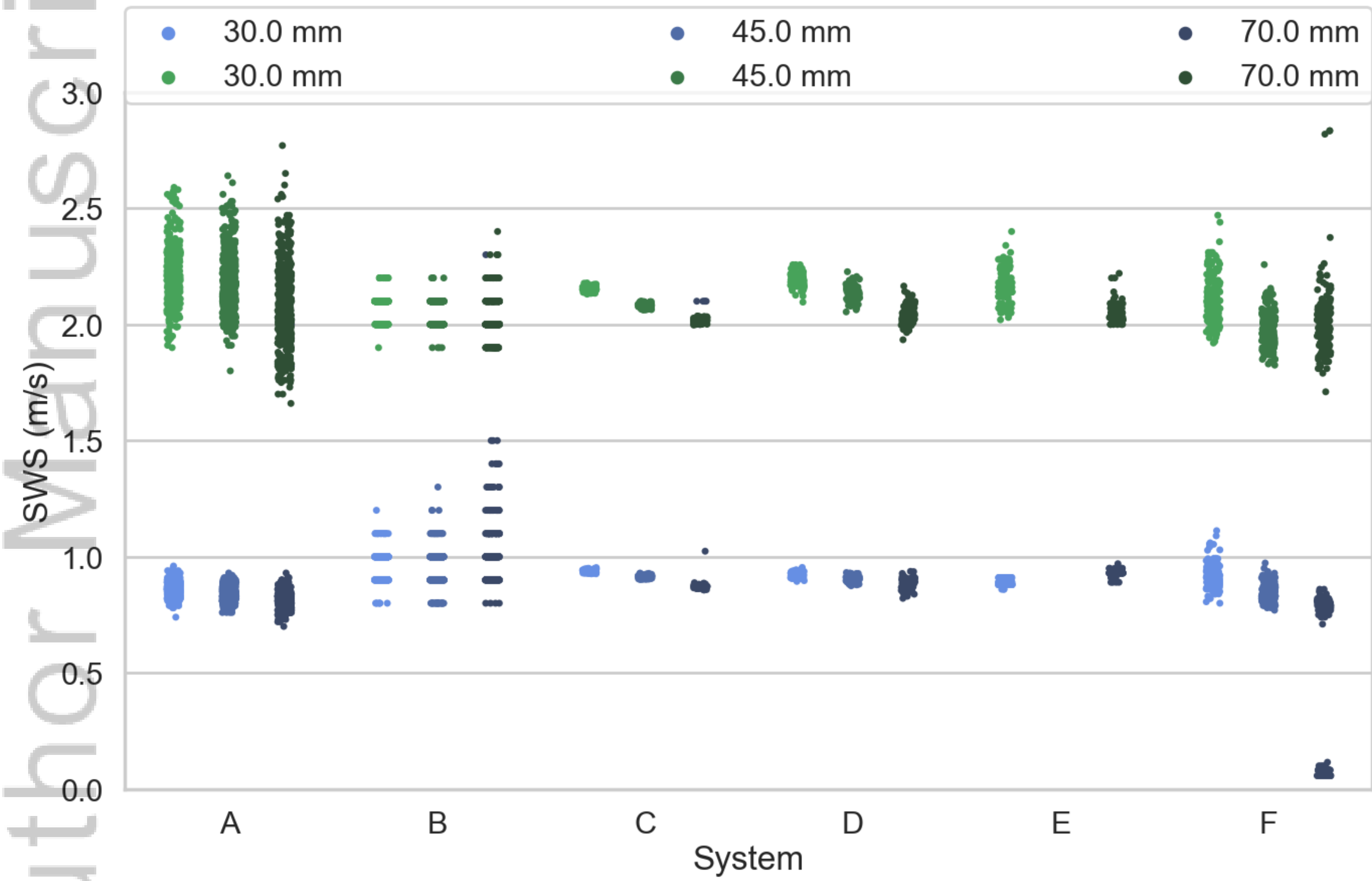
JUM_15609_phase1_duke_all_phantoms.png



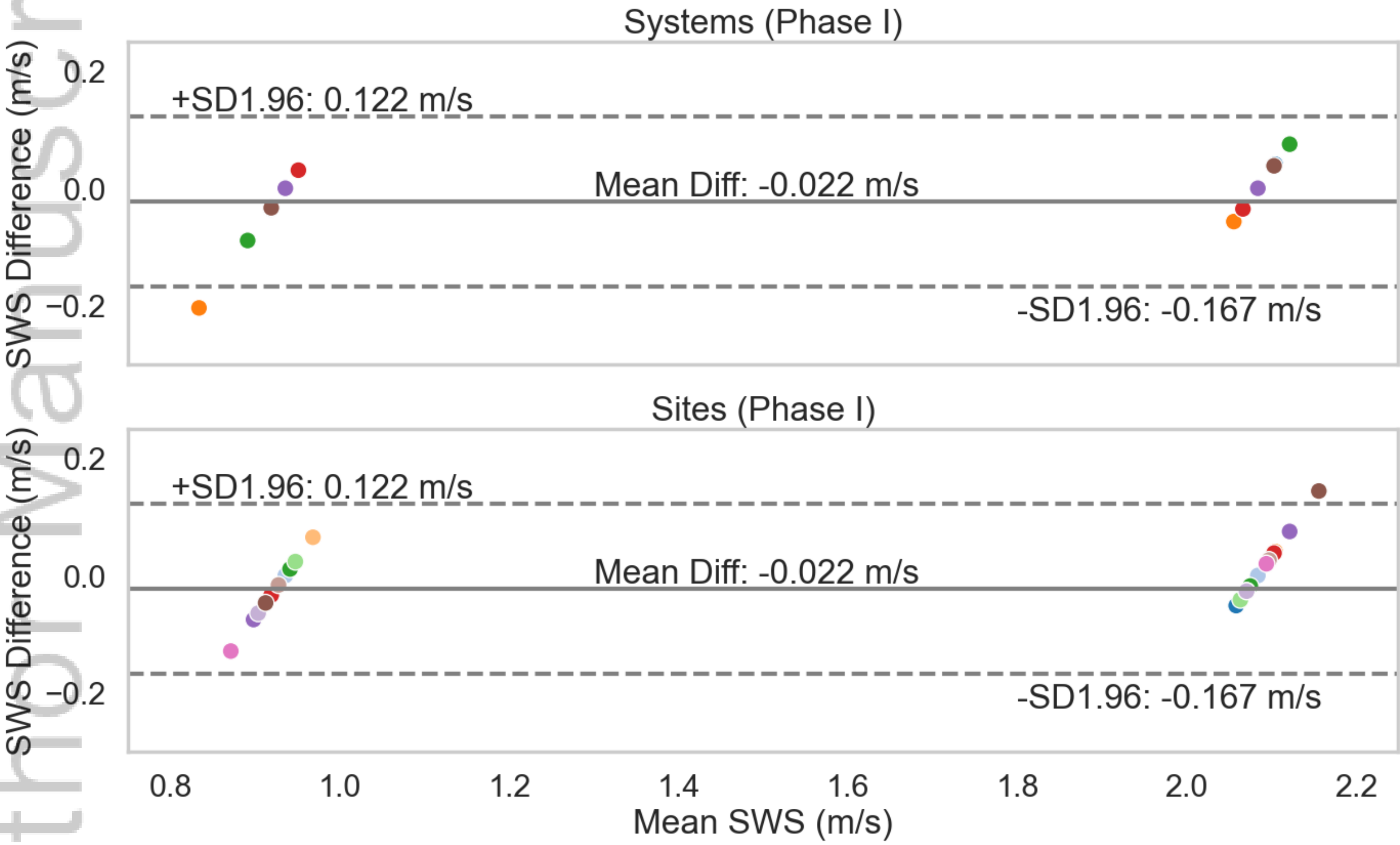
JUM_15609_phase1_mre.png



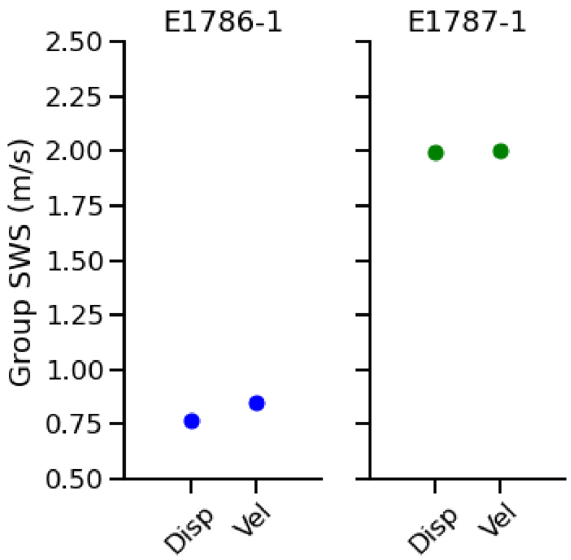
JUM_15609_phase1_sws_site_alldepths.png



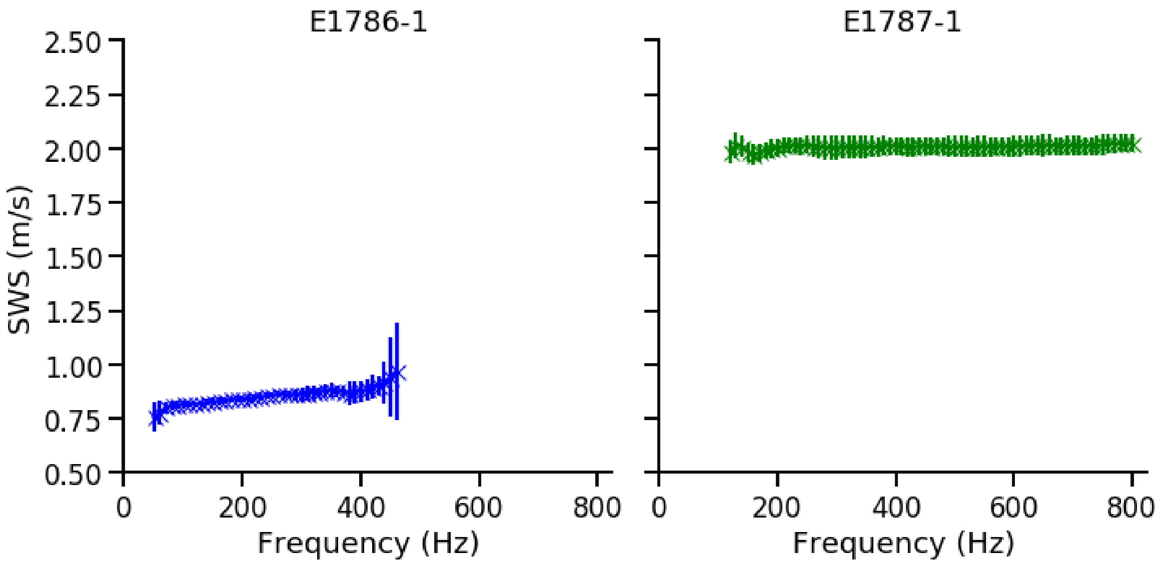
JUM_15609_phase1_sws_system_alldepths.png



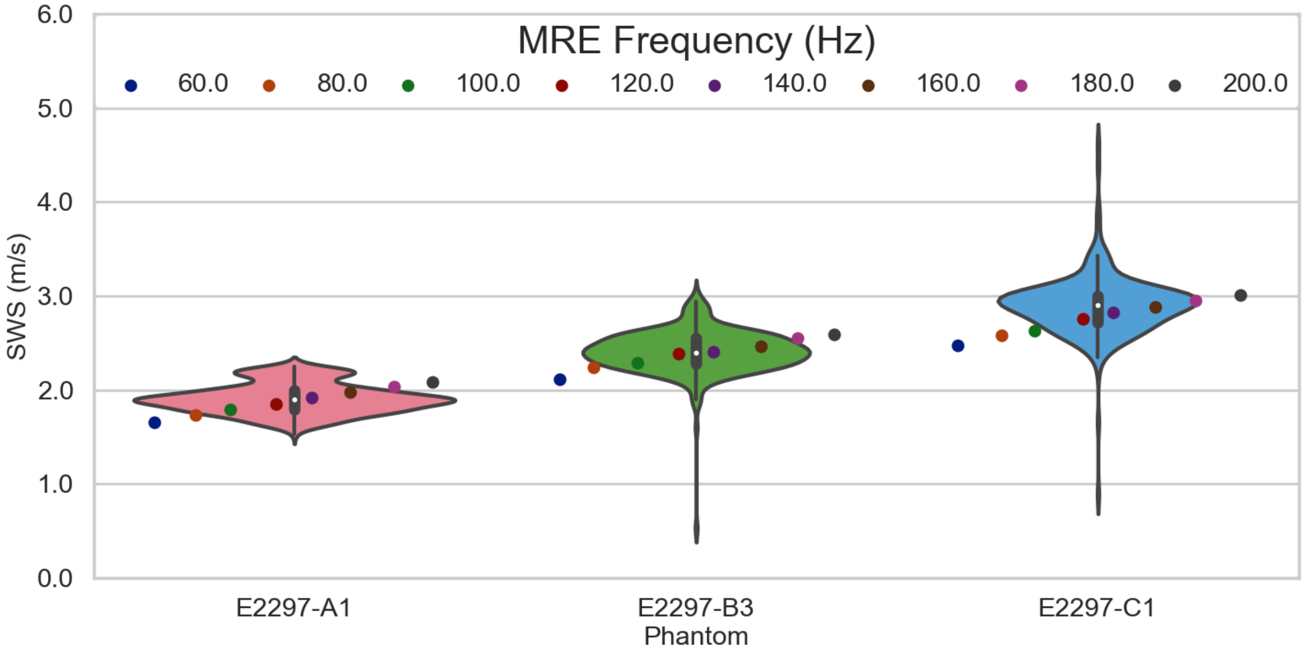
JUM_15609_phase1_tukey_mean_diff.png



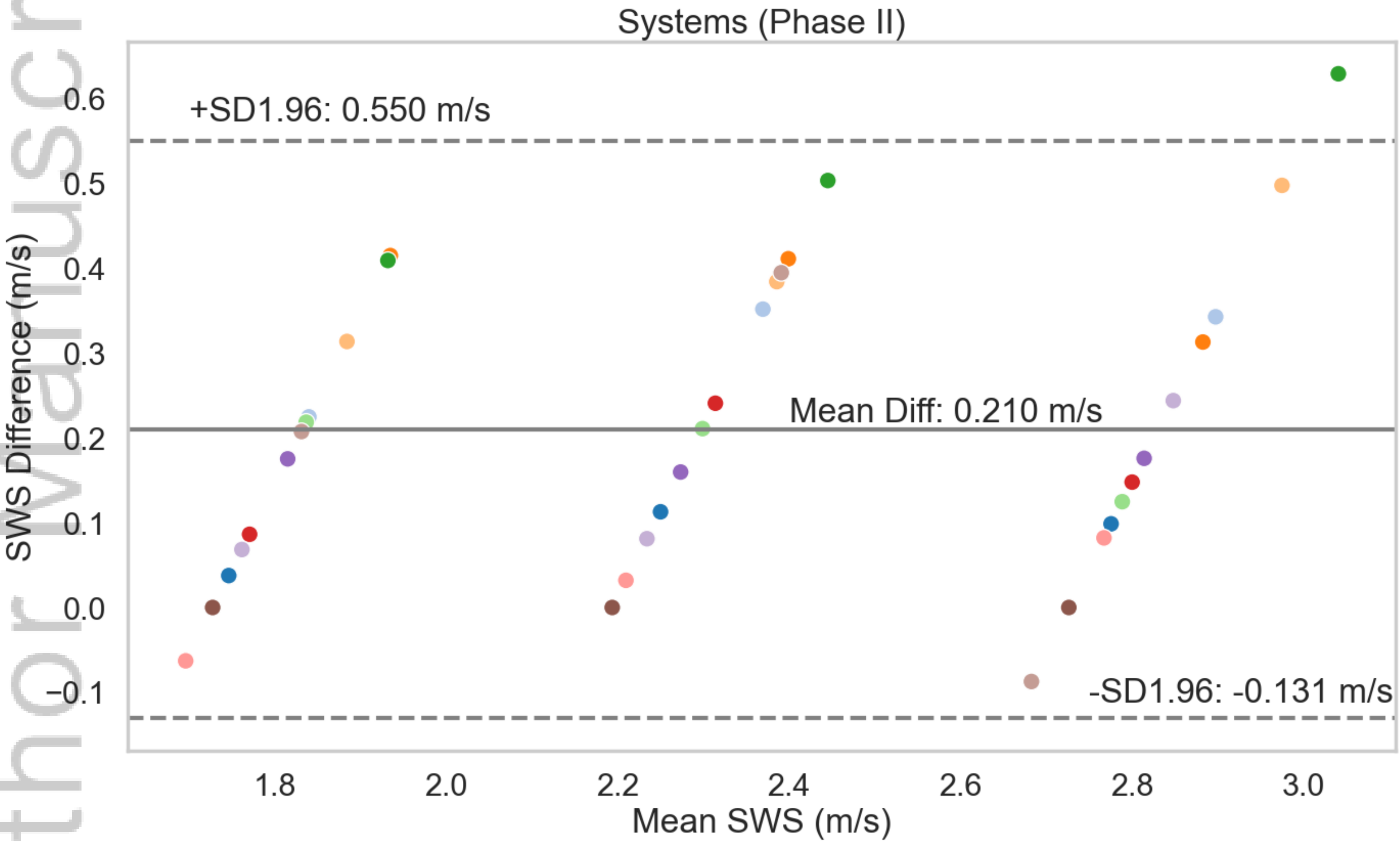
JUM_15609_phase1groupvelocity.png



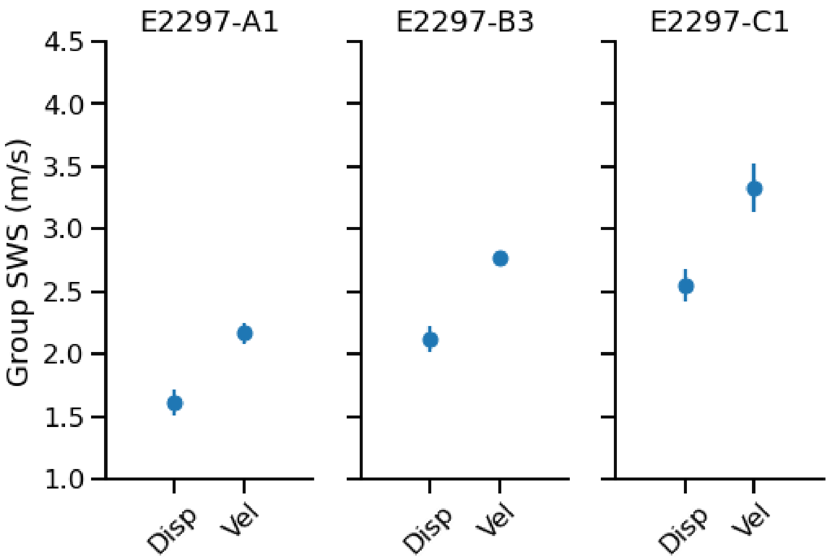
JUM_15609_phase1phasevelocity.png



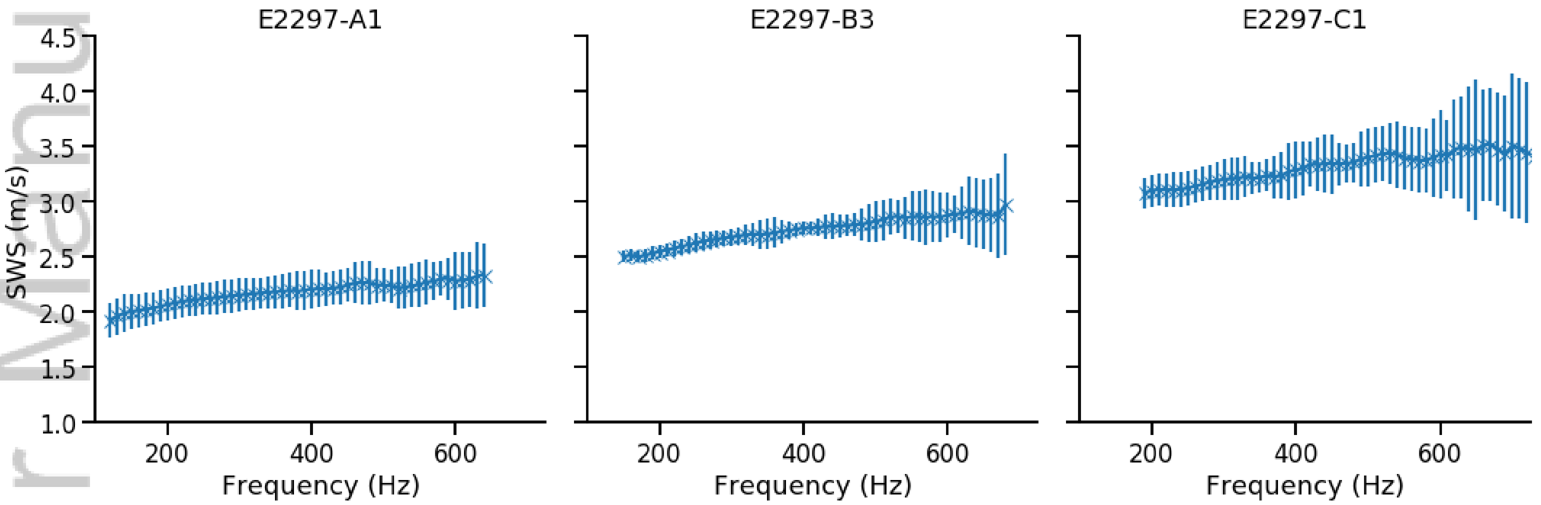
JUM_15609_phase2_mod_compare.png



JUM_15609_phase2_tukey_mean_diff.png



JUM_15609_phase2groupvelocity.png



JUM_15609_phase2phasevelocity.png

ICMJE Form for Disclosure of Potential Conflicts of Interest

Instructions

The purpose of this form is to provide readers of your manuscript with information about your other interests that could influence how they receive and understand your work. The form is designed to be completed electronically and stored electronically. It contains programming that allows appropriate data display. Each author should submit a separate form and is responsible for the accuracy and completeness of the submitted information. The form is in six parts.

1. Identifying information.

2. The work under consideration for publication.

This section asks for information about the work that you have submitted for publication. The time frame for this reporting is that of the work itself, from the initial conception and planning to the present. The requested information is about resources that you received, either directly or indirectly (via your institution), to enable you to complete the work. Checking "No" means that you did the work without receiving any financial support from any third party -- that is, the work was supported by funds from the same institution that pays your salary and that institution did not receive third-party funds with which to pay you. If you or your institution received funds from a third party to support the work, such as a government granting agency, charitable foundation or commercial sponsor, check "Yes".

3. Relevant financial activities outside the submitted work.

This section asks about your financial relationships with entities in the bio-medical arena that could be perceived to influence, or that give the appearance of potentially influencing, what you wrote in the submitted work. You should disclose interactions with ANY entity that could be considered broadly relevant to the work. For example, if your article is about testing an epidermal growth factor receptor (EGFR) antagonist in lung cancer, you should report all associations with entities pursuing diagnostic or therapeutic strategies in cancer in general, not just in the area of EGFR or lung cancer.

Report all sources of revenue paid (or promised to be paid) directly to you or your institution on your behalf over the 36 months prior to submission of the work. This should include all monies from sources with relevance to the submitted work, not just monies from the entity that sponsored the research. Please note that your interactions with the work's sponsor that are outside the submitted work should also be listed here. If there is any question, it is usually better to disclose a relationship than not to do so.

For grants you have received for work outside the submitted work, you should disclose support ONLY from entities that could be perceived to be affected financially by the published work, such as drug companies, or foundations supported by entities that could be perceived to have a financial stake in the outcome. Public funding sources, such as government agencies, charitable foundations or academic institutions, need not be disclosed. For example, if a government agency sponsored a study in which you have been involved and drugs were provided by a pharmaceutical company, you need only list the pharmaceutical company.

4. Intellectual Property.

This section asks about patents and copyrights, whether pending, issued, licensed and/or receiving royalties.

5. Relationships not covered above.

Use this section to report other relationships or activities that readers could perceive to have influenced, or that give the appearance of potentially influencing, what you wrote in the submitted work.

Definitions.

Entity: government agency, foundation, commercial sponsor, academic institution, etc.
Grant: A grant from an entity, generally [but not always] paid to your organization
Personal Fees: Monies paid to you for services rendered, generally honoraria, royalties, or fees for consulting , lectures, speakers bureaus, expert testimony, employment, or other affiliations
Non-Financial Support: Examples include drugs/equipment supplied by the entity, travel paid by the entity, writing assistance, administrative support, etc**.**
Other: Anything not covered under the previous three boxes
Pending: The patent has been filed but not issued
Issued: The patent has been issued by the agency
Licensed: The patent has been licensed to an entity, whether earning royalties or not
Royalties: Funds are coming in to you or your institution due to your patent

INTERNATIONAL COMMITTEE of MEDICAL JOURNAL EDITORS

ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 1. Identifying Information

1. Given Name (First Name): Richard
2. Surname (Last Name): Ehman
3. Date: 21-October-2020

4. Are you the corresponding author? ☐ Yes ☑ No

Corresponding Author's Name

5. Manuscript Title
RSNA/QIBA Shear Wave Speed as a Biomarker for Liver Fibrosis 1 Staging: Elastic and Viscoelastic Phantom Studies

6. Manuscript Identifying Number (if you know it)

Section 2. The Work Under Consideration for Publication

Did you or your institution **at any time** receive payment or services from a third party (government, commercial, private foundation, etc.) for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc.)?

Are there any relevant conflicts of interest? ☐ Yes ☑ No

Section 3. Relevant financial activities outside the submitted work.

Place a check in the appropriate boxes in the table to indicate whether you have financial relationships (regardless of amount of compensation) with entities as described in the instructions. Use one line for each entity; add as many lines as you need by clicking the "Add +" box. You should report relationships that were **present during the 36 months prior to publication**.

Are there any relevant conflicts of interest? ☐ Yes ☑ No

Section 4. Intellectual Property -- Patents & Copyrights

Do you have any patents, whether planned, pending or issued, broadly relevant to the work? ☑ Yes ☐ No

If yes, please fill out the appropriate information below. If you have more than one entity press the "ADD" button to add a row. Excess rows can be removed by pressing the "X" button.

Patent?	Pending?	Issued?	Licensed?	Royalties?	Licensee?	Comments
MR Elastography IP	☐	☑	☑	☑		

ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 5. Relationships not covered above

Are there other relationships or activities that readers could perceive to have influenced, or that give the appearance of potentially influencing, what you wrote in the submitted work?

- [x] Yes, the following relationships/conditions/circumstances are present (explain below):
- [ ] No other relationships/conditions/circumstances that present a potential conflict of interest

RLE and the Mayo Clinic have intellectual property rights and a financial interest in magnetic resonance elastography technology.

At the time of manuscript acceptance, journals will ask authors to confirm and, if necessary, update their disclosure statements. On occasion, journals may ask authors to disclose further information about reported relationships.

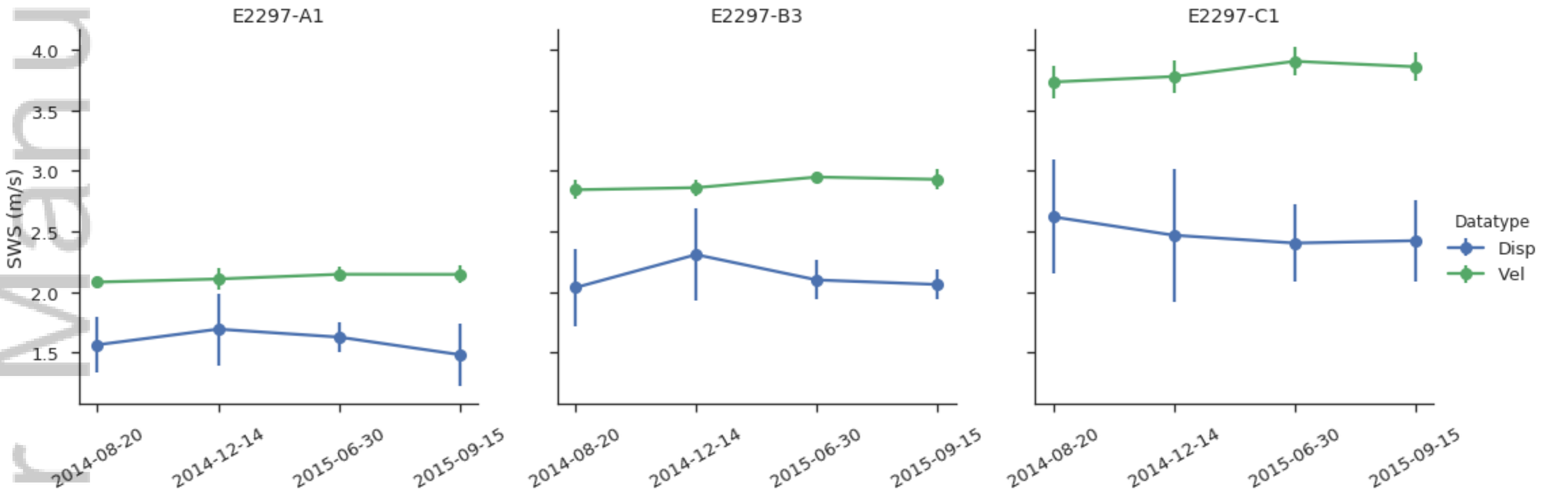
Section 6. Disclosure Statement

Based on the above disclosures, this form will automatically generate a disclosure statement, which will appear in the box below.

RLE and the Mayo Clinic have intellectual property rights and a financial interest in magnetic resonance elastography technology.

Evaluation and Feedback

Please visit http://www.icmje.org/cgi-bin/feedback to provide feedback on your experience with completing this form.



JUM_15609_temporal_stability.png