QIBA Profile:
Ultrasound Measurement of Shear Wave Speed for Estimation of Liver Fibrosis

Contents

Abbreviations:

CV: Coefficient of Variation

MRE: Magnetic Resonance Elastography

QA: Quality Assurance

QIBA: Quantitative Imaging Biomarkers Alliance

ROI: Region of Interest

RC: Repeatability Coefficient

RDC: Reproducibility Coefficient

SD: Standard Deviation

SWS: Shear Wave Speed

Technologist: Refers to Sonographer/Radiologist/Technician who is making SWS acquisitions

Change Log:

This table is a best-effort of the authors to summarize significant changes to the Profile.

Date	Sections Affected	Summary of Change
2015.12.30	All	New Profile transfer (Manish Dhyani, Brian Garra)
01/2016 -03/2016	All	Several iterations (Manish Dhyani, Brian Garra)
04/07/2016	All	Shared with committee for comments
4/7-10/2016	All	Word edits, consistent highlighting rules, a New Proposed Assessment Compliance Procedure added in Section 4
05/05/2016-ongoing	All	Feedback incorporation (Manish Dhyani, Brian Garra)
11/2016-12/2016	All	RSNA Discussions
03/2017	All	AIUM Discussions
8-31-17 – 10-6-17	All	Garra review and revisions along with execution checklists
10-10-17 – 11-17	Claims	Garra adding background material in claims section and adding new claims from Nancy Obuchowski
11/29/17 – 11/30/17	Table of Contents, Appendices	Corrected TOC and Added Checklists as Appendix but in separate file
12/5/17 – 12/11/17	Section 5 per draft template 7/26/17	Added new section 5 Conformance for consistency with draft template 7/26/17. Moved appropriate material from Section 4 to Section 5. Spell check,

		new hyperlinks also added to complete version for SWS committee review.
12/13/2017	All	General cleanup and alignment with template by KOD.
6-20-18	All	Began Section-by-Section Revision and Final Review by SWS Committee before submission to Coordinating Committee

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Open Issues:

The following issues are provided here to capture associated discussion, to focus the attention of reviewers on topics needing feedback, and to track them so they are ultimately resolved. In particular, comments on these issues are highly encouraged during the Public Comment stage.

Q. What is the effect of inflammation on SWS and what is its magnitude? A. Inflammation stiffens the liver but the magnitudes for the various types of inflammation are not known. References: **References (Inflammation affects SWS):** This degree to which stiffening occurs is not included in the profile but could be included if enough information becomes available to warrant change in the profile.
Q. Does Hepatic Steatosis affect assessment of liver fibrosis using elastography? A. Hepatic Steatosis so far has not conclusively demonstrated an effect, however, before closing this issue, we wish to study this further.
Q. DICOM conformance – Are new header fields needed? Yes - No new fields have been created. (Kevin asks if we want to go through the process of adding.) Consider adding fields for later versions of the profile.
Q. Number of values averaged for each pixel in the color image. We recommend the manufacturers should consider supplying this information. To be eventually included in Appendix D – Vendor specific instructions. For each software version, the vendors would need to document what is the average variance per pixel. IQR/Median ratio will be used as the primary quality assessment not the variance per pixel.
Q. How does each MFR identify and display outliers in their images. Should QIBA specify a standard handling? [Section 3.7] Manufacturer should have a means of identifying unreliable data specified in Appendix D.
Q. Detection of movement during acquisition. Auto acquire cine clip (other movement sensing pulses) of the time frame when SWS acquisition is being made - to confirm liver movement does not occur during the acquisition. OR The machine/operator discards the acquisition if it/he/she detects movement. Open issues: desire to create a motion measure. IQR/Median <0.3 only partial solution.
Q. QIBA testing to verify specifications and characterization of phantoms? Long term testing site? Currently Mayo clinic will be providing the support.

Q. Claim 2b makes the following assumptions that have not yet been fully verified: **a. SWS measurements have the property of linearity** **b. The slope of a line between the SWS measurements and truth is 1.0.** Devise a strategy for confirming the above assumptions or change claim 2b
Assessment tests for section 4 must be reviewed by SWS committee and needed text inserted.
Conformance checklists consistent with execution checklists must be added pending SWS approval and technical confirmation of execution checklists

Closed Issues:

The following have been considered closed by the biomarker committee. They are provided here to forestall discussion of issues that have already been raised and resolved, and to provide a record of the rationale behind the resolution.

Q. Give stiffness in m/sec or kPa? A. M/sec
Q. Define range of SWS values at which the claims apply. A. Closed with 0.9-5.0 m/s. Allow for manufacturer to claim greater.
Q. At what point in the respiratory cycle should acquisition occur? A. Suspended tidal respiration (references needed)
Q. Should the patient fast prior to acquisition? A. At least 4 hours prior to acquisition (references needed).
Q. Number of measurements? A. The total number of measurements that are needed to make an SWS estimate per patient **(the claim refers to this value).** ≥10 measurements. The manufacturer may specify a greater number than the minimum value of 10 (Appendix D). More recent tests suggest that 5 or fewer measurements are adequate –so the 10 value is changed to 5 B. Criteria for inclusion or exclusion for a given measurement? A qualified median measurement should have an IQR/median value of ≤0.3 (reference – SRU Guidelines).
<u>Measurement ROI Placement (when applicable)</u>

Q. ROI location in most homogenous region of SWS color map?
ROI location in most homogenous region of the color map near the center of the image.
Please refer to vendor specific instructions in Appendix D.

Q. ROI Size - If user selected – how big? (size of homogenous region versus variance)
Each manufacturer should specify an optimal ROI size and make that a default for their system.
A minimum size of 6mm (axial) X 10mm (lateral) or diameter of 10mm should be used.
Size of homogeneous region and variance considered less important than use of the IQR/median criterion and a minimum ROI size criterion.

For additional details please refer to section 3.10.2. Additional ROI placement specifications as well as acquisition specifications (Refer to sections 3.6.1 for compliance).

Variance for each ROI?
Considered unimportant when IQR/median criterion is used.

Q. BMI and assessment of liver fibrosis using SWS elastography:

A. If all other requirements of the profile are met, [Depth <6.5 cm from skin surface and >2cm away from the liver capsule], qualifying measurements can be made.
B. Subcutaneous fat attenuation and dispersion of both the ARFI pulse and the tracking B-mode signals lead to increased measurement error and increased numbers of technical failures.

Q. What is the maximum liver depth and subcutaneous tissue for making measurements?

A. Maximum acquisition depth with current technology is 6.5 cm.
B. Minimum Distance from liver capsule = 2 cm.

Phantoms

Q. QIBA testing to verify specifications and characterization of phantoms?
Testing: Currently – may be performed at Mayo clinic or at Duke University or at CIRS using a rented Verasonics system. The Verasonics results are considered to be the "gold standard" for bias estimation in this profile Open issue for future testing.
Paid for: Site/Vendor.

Q. What sort of Phantom should be used for periodic QA and compliance (Section 3.3 of Profile)

- **Viscoelastic versus elastic phantom?**
  Viscoelastic phantom to distinguish differences between different systems.
  For a single machine, elastic phantoms will be affordable and practical.
- **Complex versus simple?**
  Simple since the liver is relatively simple, unlike the breast.
- **Multiple manufacturers versus single?**

Phantom Specifications:
Attenuation: 0.6±0.2 dB/cm/MHz
Back Scatter: Approximately 10^{-4} – 10^{-3} $cm^{-1}Sr^{-1}$ at 3 MHz or sufficient to create mean speckle brightness comparable to a human liver-mimicking phantom [Reference

Ultrasonics – Pulse-echo scanners – Part 2]

Speed of Sound: 1540 ± 20 m/sec
Stiffness:
2-part phantom: Normal Liver Equivalent & Fibrotic F3 Liver equivalent. (Stiffness verified using Verasonics system and software from Duke University and Mayo Clinic. See https://github.com/RSNA-QIBA-US-SWS/QIBA-DigitalPhantoms)
A 2-part phantom is considered desirable, or two one-part phantoms are acceptable.

Volume and Shape:
Cylindrical shape preferred, rectangular shape is acceptable.
Height: 15 ± 3 cm
ID: 12.5 ± 3cm in inner diameter (ID)

Q. Long term verification of phantoms and stability testing?

Initial testing: Phantoms should be weighed upon construction and independently certified with a stiffness value.

Phantoms should be tested for stability at 6 months from initial delivery and once stability is demonstrated phantoms can be tested annually.

Stability testing: (1) The phantoms should be re-weighed and if the phantom weight changes by more than 0.5%, the phantom should be re-certified prior to using. (2) Acoustic properties (speed of sound, attenuation) may be measured by obtaining batch samples suitable for measurement by the substitution technique.
**If the phantom manufacturer has criteria for stability testing prior to acoustic property testing (instead of (1) above) – those should be used instead.*

Temporal Stability Acoustic Properties Tolerances

- SWS: <5% change in both hard and soft components over 6 months.
- Speed of Sound: <1% change over 6 months. Testing of phantom as specified by AIUM guidelines[1] and system supplier's recommendations. [2]

****If the values are changing faster than the rates above, sites should consider replacement or testing more frequently than every 6 months.***

Overall Pass-Fail Tolerances for Phantom Tests
Testing to be performed at 21±1 °C.

- Method to verify temperature of phantoms prior to testing. Temperature measurement method: TBD [open issue]

Attenuation: **± 20% (**0.5 dB/cm/MHz)

[1] Methods for Specifying Acoustic Properties of Tissue-Mimicking Phantoms and Objects, 2nd Edition, American Institute of Ultrasound in Medicine, 2014 (ISBN: 1-932962-32-8)

Back Scatter: : **± 3 dB [[**Approximately 10^{-4} – 10^{-3} $cm^{-1}Str^{-1}$ at 3 MHz or sufficient to create mean speckle brightness comparable to a human liver-mimicking phantom (± 3 dB)]
Speed of Sound: **± 2%**

- 1540 ± 30 m/sec [1510-1570 m/sec]
  Stiffness: **± 5%**
- 2-part phantom, Normal Liver Equivalent & Fibrotic F3 Liver equivalent (normal "soft" phantom: SWS 1.0±0.3 m/s; fibrotic phantom SWS 2.2±0.3 m/s - reference Barr et.al. Radiology 2015: 276 (3)

Phantoms failing these tolerance tests should be replaced.

QIBA testing to verify specifications and characterization of phantoms?
For the time being – the specifications and characterization of the phantoms will be performed and verified by the QIBA committee. This will be relative to Verasonics ultrasound system as noted above. Mayo Clinic or Duke University group will be performing characterization for the initial phantoms.

Frequency of periodic QA for systems using the phantoms?
Annually/anytime the software changes.

Q. Color Maps – Should these be QIBA specified?
Color scale and number of colors in the map.
Red = stiff and Blue = Soft
Black is stiff and White is soft.
Number of colors – Continuous scale (24-36 bit).

Q. How to best acquire from patients where intercostal approach is not feasible (narrow intercostal spacing, COPD)?

A. If the intercostal approach is unavailable a subcostal approach may be attempted, but the claims of the profile have not been validated for this approach.
B. If a subcostal approach is used, it should be documented in the patient/subject record.
C. A future version of the profile may validate a subcostal approach.
D. Consider MRE as an alternative.

Q. Claim 3b makes two assumptions that have not yet been tested in phantoms or in patients:

a. SWS measurements have the property of linearity

b. The slope of a line between the SWS measurements and truth is 1.0. (Reference: Palmeri ML, Qiang B, Chen S, Urban MW. 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. 2016 Dec 21;64(1):78-92.)

A strategy for testing these assumptions must be developed.

As noted for claim 3b, claim 4b makes two assumptions that have not yet been tested in phantoms or in patients:

a. SWS measurements have the property of linearity

b. The slope of a line between the SWS measurements and truth is 1.0.

A strategy for testing these assumptions must be developed.

1. Executive Summary

The goal of a QIBA Profile is to help achieve a useful level of performance for a given biomarker.

The **Claim** (Section 2) describes the biomarker performance.
The **Activities** (Section 3) contribute to generating the biomarker. Requirements are placed on the **Actors** that participate in those activities as necessary to achieve the Claim.
Assessment Procedures (Section 4) for evaluating specific requirements are defined as needed.

This QIBA Profile ***Ultrasound Measurement of Shear Wave Speed for Estimation of Liver Fibrosis*** addresses estimation of liver fibrosis, which is often used to determine when and how to treat patients with diffuse liver disease, and also monitor progression or response to treatment. It places requirements on ultrasound scanners (acquisition devices), Scanner Manufacturer/Vendor, Technologists/Sonographers, QA (Quality Assurance) Manager, Radiologists, Reconstruction Software and Image Analysis Tools involved in pre-delivery steps, scanner installation, site QA procedures, subject selection and handling, image data acquisition, image data reconstruction, image and other QA and image analysis. The requirements are focused on achieving sufficient accuracy and avoiding unnecessary variability of the estimation of liver fibrosis. Estimates of liver fibrosis are based on the stiffness of the liver tissue which in turn is based on a measurement of shear wave speed (SWS) in the tissue using ultrasound.

The ultimate clinical performance target is to achieve SWS measurements with a bias of the mean value of ≤ 5% and an overall coefficient of variation of 5% (SD/mean). The standard against which to measure bias has not yet been fully defined, so a bias claim is not present in this version. At the present time, bias is determined by comparison to the measured shear wave speed and stiffness using a Verasonics ultrasound system in a calibrated QIBA SWS phantom. Currently bias and precision vary depending on the magnitude of measured shear wave speed (as determined in phantom studies) so bias and variance claims are given for three ranges of measured shear wave speed values. Also, bias and precision vary depending on the conditions under which the measurements are made. Bias and precision claims are therefore also given for various measurement conditions.

This document is intended to help clinicians basing decisions on this biomarker, imaging staff generating this biomarker, vendor staff developing related products, purchasers of such products and investigators designing trials with imaging endpoints.

Note that this document only states requirements to achieve the claim, not “requirements on standard of care.” Conformance to this Profile is secondary to properly caring for the patient.

QIBA Profiles addressing other imaging biomarkers using CT, MRI, PET and Ultrasound can be found at qibawiki.rsna.org.

2. Clinical Context and Claims

Elastography is a technique for measuring tissue stiffness or elasticity. Stiffness or elasticity of all materials including tissue is defined by a parameter known as the elastic (or Young's) modulus typically given in units of pressure (Pascals or kilopascals). The elastic modulus may be measured directly by mechanical testing where pressure is applied to a sample of material and the deformation (loss of height or thickness) is measured. The slope of the plot of thickness change vs. pressure is the elastic modulus. For a given amount of pressure, the change in thickness of the overall block of material, or at any location in the material, is defined as the "strain". Samples of tissue are not usually available for mechanical testing, so elastography was developed as a means to estimate tissue elasticity non-invasively. Tissue elasticity may be calculated in two ways: 1) From an image of the strain of a region of tissue in response to external or internal compression force (known as strain elastography), and 2) by measuring the speed of propagation of a shear wave as it traverses a region of tissue (known as shear wave elastography). For the second technique, the shear wave speed (SWS) may be used as a surrogate for tissue stiffness which serves as a biomarker for level of fibrosis since it has been shown that fibrosis is the major cause of increased liver stiffness.

Clinical Context

Shear wave speed (SWS) is a biomarker to identify patients with moderate but significant liver fibrosis, defined as ≥ F2 fibrosis in the METAVIR system (or equivalent for other scoring systems) of staging liver fibrosis. This might be used to monitor progression of fibrosis or to monitor regression of fibrosis during anti-fibrosis therapy.

SWS also serves as a biomarker for the evaluation of cirrhosis, defined as F4 stage of fibrosis of the METAVIR system of staging liver fibrosis. As noted in the discussion below, the SWS biomarker may be referred to as the "measurand" elsewhere in this document.

Intended Clinical Application: SWS is measured in the liver of patients with suspected diffuse liver disease, with or without fatty infiltration of the liver and with suspected fibrosis or cirrhosis.

Multiple Claims: Ground work studies conducted by the QIBA SWS Biomarker Committee have indicated that the key measures of biomarker performance, Bias and Precision, depend on the level of fibrosis present and upon other variables such as whether or not the measurements are taken with a single machine at a single site (hospital or clinic) or not. Accordingly, several claims for bias and precision are made depending on the situation and estimated level of fibrosis. These are presented below.

In the claims presented below, the term "imaging system" refers to both the ultrasound scanner (machine) and the operator using the machine to perform SWS measurements. Changing either the operator or ultrasound scanner therefore results in a different imaging system. Conformance to this Profile <u>by all relevant staff and equipment</u> supports the following claim(s):

Claim 1 (technical performance claim):

A shear wave speed measurement has a within-subject coefficient of variation (wCV) depending on the measured SWS and depth of acquisition according to Table 2-1.

Table 2-1 Coefficient of Variation (wCV)

Measured SWS (m/s)	Depth=4.5cm*	Depth=7.0cm
0.9 < SWS <= 1.2	5%	8%
1.2 < SWS <= 2.2	4%	5%
2.2 < SWS <= 5.0	10%	12%

***For measurements taken at depths other than the two listed, the SWS Committee has determined that linear interpolation of the Coefficients of Variation is appropriate.**

Claim 2 (cross-sectional claim):
A 95% confidence interval for the true SWS (in m/sec) is Y *± (1.96 × Y × wCV/100),* where Y is the measured SWS and wCV is the within-subject coefficient of variation from Table 2-1.

Claim 3a (longitudinal claim):
A true change in SWS over two time points (Y_1 and Y_2) has occurred with 95% confidence if the measured % change, defined as $\frac{|Y_2-Y_1|}{(Y_1+Y_2)/2} \times 100$, is equal to or greater than the repeatability coefficient (RC) given in Table 2-2.

Table 2-2 Repeatability Coefficient (RC)

Measured SWS (m/s)	Depth=4.5cm*	Depth=7.0cm
0.9 < SWS <= 1.2	14%	22%
1.2 < SWS <= 2.2	11%	14%
2.2 < SWS <= 5.0	28%	33%

***For measurements taken at depths other than the two listed, the SWS Committee has determined that linear interpolation of the Coefficients of Variation is appropriate.**

Claim 3b (longitudinal claim):
A 95% confidence interval for the true change (in m/s) over two time points (Y_1 and Y_2) is $(Y_2 - Y_1) \pm 1.96 \times \sqrt{(Y_1 \times wCV/100)^2 + (Y_2 \times wCV/100)^2}$, where wCV is from Table 2-1.

Claims 3a and 3b hold when:

- **the same technologist and same ultrasound scanner are used at the two time points**

Claim 4a (longitudinal claim):
A true change in SWS over two time points (Y_1 and Y_2) has occurred with 95% confidence if the measured % change, defined as $\frac{|Y_2-Y_1|}{(Y_1+Y_2)/2} \times 100$, is equal to or greater than the reproducibility coefficient (RDC) given in Table 2-3.

Table 2-3 Reproducibility Coefficient (RDC)

Measured SWS (m/s)	Depth=4.5cm	Depth=7.0cm
0.9 < SWS <= 1.2	19%	25%
1.2 < SWS <= 2.2	14%	17%
2.2 < SWS <= 5.0	33%	39%

Claim 4b (longitudinal claim):

A 95% confidence interval for the true change (in m/sec) over two time points (Y_1 and Y_2) is $(Y_2 - Y_1) \pm 1.96 \times \sqrt{(Y_1 \times U/100)^2 + (Y_2 \times U/100)^2}$, where U is from Table 2-3b.

Table 2-3b Values of U (wCV from different technologist and/or scanner at same site)

Measured SWS (m/s)	Depth=4.5cm	Depth=7.0cm
0.9 < SWS <= 1.2	7%	9%
1.2 < SWS <= 2.2	5%	6%
2.2 < SWS <= 5.0	12%	14%

Claims 4a and 4b hold when:

- **a different technologist and/or a different ultrasound scanner is used at the same site at the two time points**

Claim 5a (longitudinal claim):

A true change in SWS over two time points (Y_1 and Y_2) has occurred with 95% confidence if the measured % change, defined as $\frac{|Y_2 - Y_1|}{(Y_1 + Y_2)/2} \times 100$, is equal to or greater than the reproducibility coefficient (RDC) given in Table 2-4.

Table 2-4 Reproducibility Coefficient (RDC)

Measured SWS (m/s)	Depth=4.5cm	Depth=7.0cm
0.9 < SWS <= 1.2	22%	28%
1.2 < SWS <= 2.2	17%	19%
2.2 < SWS <= 5.0	33%	39%

Claim 5b (longitudinal claim):

A 95% confidence interval for the true change (in m/sec) over two time points (Y_1 and Y_2) is $(Y_2 - Y_1) \pm 1.96 \times \sqrt{(Y_1 \times H/100)^2 + (Y_2 \times H/100)^2}$, where H is from Table 2-4b.

Table 2-4b Values of H (wCV from different technologist and/or scanner at different sites)

Measured SWS (m/s)	Depth=4.5cm	Depth=7.0cm
0.9 < SWS <= 1.2	8%	10%
1.2 < SWS <= 2.2	6%	7%
2.2 < SWS <= 5.0	12%	14%

Claims 5a and 5b hold when:

- **a different technologist and/or a different ultrasound scanner is used at different sites at the two time points**

The above claims were developed based on phantom studies conducted by the Ultrasound Shear Wave Speed Biomarker Committee and may not accurately reflect performance in patients. The expectation is that during the Claim Confirmation and Clinical Confirmation stages, data on the actual field performance will be collected and changes made to the claims or the details accordingly. At that point, this caveat may be removed or re-stated.

2.1 Proposed Clinical interpretation:

Currently the only consensus standard for interpretation in the United States is that formulated by the Society of Radiologists in Ultrasound in October 2014[3] According to that standard, measurements are used to classify a patient into one of the three categories below:

Example Table of Liver Fibrosis Categories and Corresponding Representative Shear Wave Speed Values. *

Ultrasound System	No Fibrosis or Minimal Fibrosis (METAVIR F0-F1)	Moderate Fibrosis (METAVIR F2 [i] and F3 [ii])	Severe Fibrosis/Cirrhosis (METAVIR F3 – F4)
System A	SWS < 1.37 m/s (< 5.7kPa) [iii]	1.37 < SWS < 2.2 m/s (> 5.7 kPa, < 15 kPa)	SWS > 2.2 m/s (> 15 kPa) [iv]
System B	SWS < 1.66 m/s (<8.29 kPa)	1.66 ≤ SWS < 1.88 m/s (≥8.29 kPa, < 10.60 kPa)	SWS ≥1.88 m/s (≥10.60 kPa)

*Considerable changes have been adopted by the clinical community since this table was developed. Some of the changes are described below:

i. Metavir F2 currently is often classified as "significant fibrosis" and is no longer grouped with F3.

ii. F3 is no longer classified as moderate cirrhosis but instead both F3 and F4 are classified as "Compensated advanced chronic liver disease" for clinical management.

iii. After acquisition of additional data with newer software, the values for this system have been revised upward. Currently the cutoff value for F2 is approximately 7kPa for both ARFI systems such as this one and Fibroscan.

iv. This value is high for the F4 cutoff and carries a significant risk of misclassification of F4 patients as F3. This value was used as it was associated with a nearly 100% specificity which was considered desirable by the consensus panel. It may be revised in the next consensus panel statement.

Further guidance regarding interpretation of shear wave speed values for chronic diffuse liver disease may be found in the updated guidelines for liver ultrasound elastography published in September 2018 by the World Federation of Ultrasound in Medicine and Biology[4]

[3] Richard G. Barr, Giovanna Ferraioli, Mark L. Palmeri, Zachary D. Goodman, Guadalupe Garcia-Tsao, Jonathan Rubin, Brian Garra, Robert P. Myers, Stephanie R. Wilson, Deborah Rubens, and Deborah Levine. Radiology 2015 276:3, 845-861

[4] Ferraioli, Giovanna & Wong, Vincent & Castera, Laurent & Berzigotti, Annalisa & Sporea, Ioan & Dietrich, Christoph & Choi, Byung Ihn & Wilson, Stephanie & Kudo, Masatoshi & Barr, Richard. (2018). Liver Ultrasound Elastography: An Update to the World Federation for Ultrasound in Medicine and Biology Guidelines and Recommendations. Ultrasound in Medicine & Biology. 10.1016/j.ultrasmedbio.2018.07.008.

For cutoff values for specific ultrasound systems, please refer to the Manufacturer Specific Protocols in Appendix D.

Tests (see **References (Inflammation affects SWS):**
have shown that active inflammation in the liver affects SWS measurements. When a patient has severe acute/chronic active hepatitis (including short-term flare-ups), SWS may OVERESTIMATE the degree of fibrosis (increased positive bias).
Similarly, SWS may OVERESTIMATE the degree of fibrosis in conditions that cause congestion of the liver, such as congestive heart failure, renal failure with volume overload, etc.

Clinical interpretation with respect to progression or response:

For measurements at multiple points in time, a patient may be reclassified clinically if the newer measurement falls into a different clinical category AND if the difference between the new measurement and prior measurement are statistically different from one another.

2.2 Discussion

Groundwork studies conducted by the QIBA SWS Biomarker Committee have indicated that the key measures of biomarker performance, Bias and Precision, depend on the level of fibrosis present and upon other variables such as whether or not the measurements are taken by a single technologist with a single machine at a single site (hospital or clinic) or not. Accordingly, several claims for bias and precision are made depending on the situation and estimated level of fibrosis.

In shear wave elastography (SWE), the biomarker is, as noted above, shear wave speed (SWS) which is the speed of a shear wave generated in a patient's liver by an acoustic radiation force impulse (ARFI) push. Another device measuring propagation of shear waves using ultrasound is the non-imaging FibroScan® device which applies force by means of a mechanical piston pressing against the skin. Measurement using the FibroScan® device is not covered by the current profile. A table for comparing FibroScan® and magnetic resonance elastography (MRE) values with ARFI SWS values obtained according to this profile will be listed at the end of this section when validated comparisons become available. The SWS biomarker is used for measurement at a single point in time intended to classify liver tissue according to fibrosis grade and also for monitoring shear wave speed (and corresponding fibrosis) changes over time.

Claim 1 describes the expected variability in terms of the coefficient of variation (%wCV) of measurements made at approximately the same time in the same patient and acquisition depth for several depths and for several ranges of SWS. These two variables (depth and SWS range) have been determined by the committee to have significant effects on technical performance but which can be controlled for by acquisition technique and data analysis. The claim is based on results from a phantom study, where 10 repeat measurements were performed at each focus, within a phantom at each site.

Claim 2 is a cross-sectional claim describing the 95% confidence interval of the true SWS measurement for several depths and for several ranges of SWS. These two variables (depth and SWS range) have been

determined by the committee to have significant effects on technical performance but which can be controlled for by acquisition technique and data analysis. The claim is based on two results from the phantom study: first, that the within-subject CV is as described in Claim 1; second, that the bias is negligible for most systems.

Claims 3a and 3b describe the significance of differences between two measurements of SWS made on the same patient at different points in time when the same operator makes the measurement on the same scanner using the technique described in this profile. These claims make the following assumptions:

a. SWS measurements have the property of linearity
b. The slope of a line between the SWS measurements and the true value is 1.0.

Claims 4a and 4b describe the significance of differences between two measurements of SWS made on the same patient at different points in time when a different operator and/or a different scanner at the same imaging site is used to make the measurements using the technique described in this profile. These claims make the following assumptions:

a. SWS measurements have the property of linearity
b. The slope of a line between the SWS measurements and the true value is 1.0.

Claims 5a and 5b describe the significance of differences between two measurements of SWS made on the same patient at different points in time when a different operator and/or a different scanner at a different imaging site is used to make the measurements using the technique described in this profile. These claims make the following assumptions:

a. SWS measurements have the property of linearity
b. The slope of a line between the SWS measurements and the true value is 1.0.

3. Profile Activities

The Profile is documented in terms of "Actors" performing "Activities". Equipment, software, staff or sites may claim conformance to this Profile as one or more of the "Actors" in the following table.

Conformant Actors shall support the listed Activities by conforming to all requirements in the referenced Section and in Table 3-1.

Table 3-1: Actors and Required Activities

Actor	Activity	Section
Ultrasound Scanner (Acquisition Device)	Pre-delivery	3.1.
	Image Data Acquisition	3.6.
Scanner Manufacturer/Vendor	Installation	3.2.
	Periodic Scanner Quality Assurance	3.3.
QA Manager	Site Quality Assurance Procedures not otherwise assigned	3.3
Technologist/Sonographer	Subject Selection	3.4.
	Subject/Patient Handling	3.5.
	Image Data Acquisition	3.6.
	Image Data Reconstruction	3.7.
Radiologist	Subject Selection	3.4.
	Subject/Patient Handling	3.5.
	Image QA	3.8.
	Image Analysis	3.10.
Reconstruction Software	Image Data Reconstruction	3.7.
Image Analysis Tool	Image Analysis	3.10.

The requirements in this Profile do not establish a Standard of Care; they only provide guidance intended to achieve the stated Claim. Failing to conform to a "shall" in this Profile is a protocol deviation. Although deviations invalidate the Profile Claim, such deviations may be reasonable and

unavoidable and the radiologist or supervising physician is expected to deviate when required by the best interest of the patient or research subject. Although the claims made in the profile are no longer guaranteed if deviations have occurred, the claims may still be met depending on the deviation.

Over time the effect of each type of deviation on profile claims will be clarified. How study sponsors and others decide to handle deviations for their own purposes is entirely up to them.

The activities described in this profile consist of pre-delivery instrument performance testing, instrument installation and testing, patient and subject selection, shear wave speed measurement and analysis of shear wave speed results for research or clinical decision making. Pre-delivery imaging instrument testing and calibration are primarily the responsibility of the vendor/manufacturer and are outlined but not described in detail as each manufacturer will have their own procedures. Patient selection is described in more detail. Checklists describe in step-by-step fashion the processes, especially those of patient selection and handling, shear wave speed data acquisition, and quality assurance processes.

The checklists are not optional since they are intended to ensure proper completion of required profile activities in proper order. The completed checklists also form the core of a site compliance program in which documentation of proper execution of the profile is available for review as needed.

The sequence of the Measurement Activities specified in this Profile is shown in Figure 1:

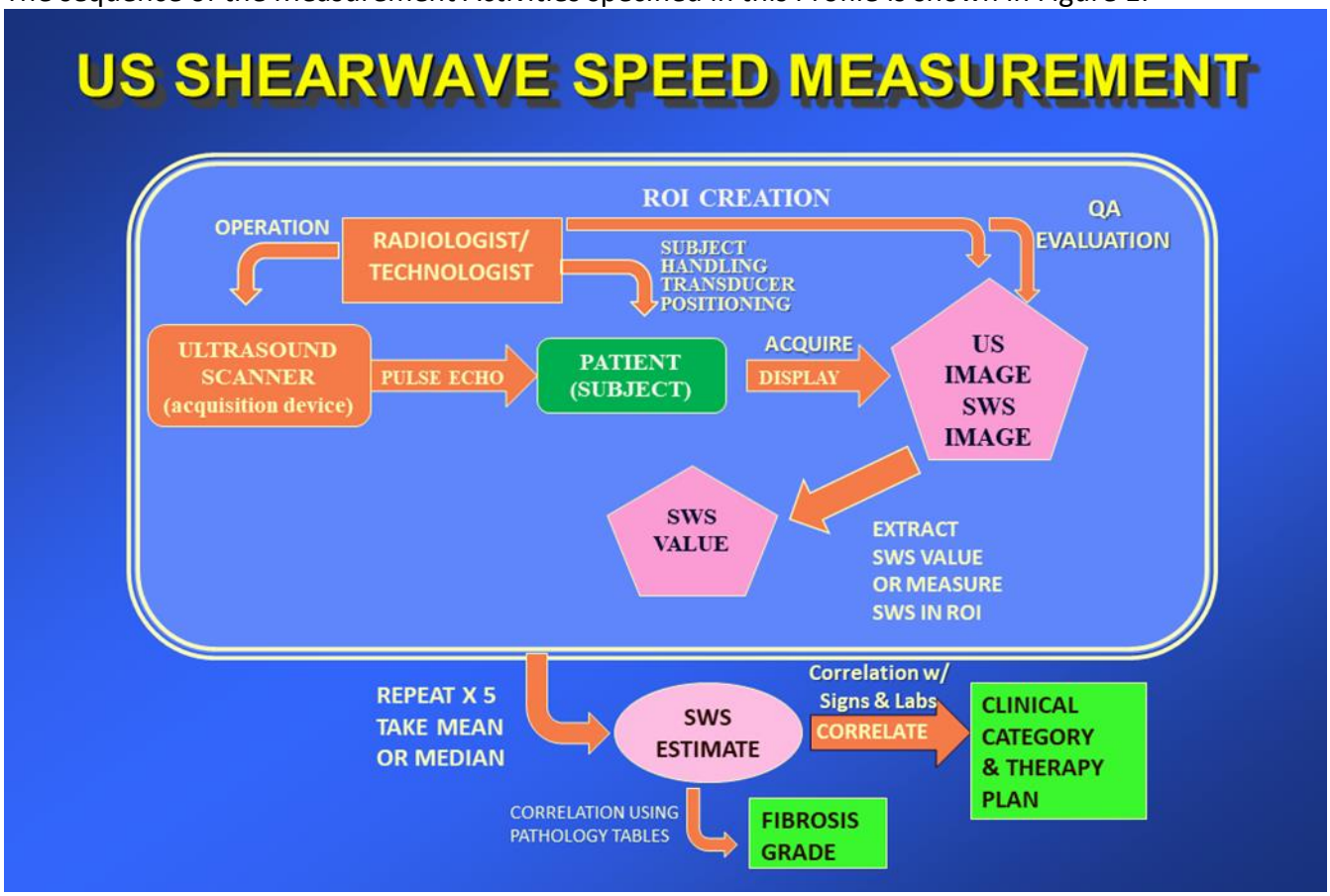

Figure 1: Ultrasound Measurement of Shear Wave Speed for Estimation of Liver Fibrosis - Activity Sequence

3.1. Pre-delivery

This activity describes calibrations, phantom imaging, performance assessments or validations prior to delivery of equipment to a site (e.g. performed at the factory) that are necessary to reliably meet the Profile Claim.

3.1.1 DISCUSSION

Ultrasonic Imaging and SWS Phantoms Used for Testing:

A commercially available standard ultrasound imaging phantom may be used to confirm imaging performance of the ultrasound systems used for SWS acquisition.

For testing of instrument (scanner) SWS performance, an elastic phantom will be used since it is both affordable and practical. A viscoelastic phantom may be used for testing in later versions of the profile to better address possible bias (bias is not part of the claims in this version).
A Simple phantom rather than a complex structured phantom will be used since the liver is a relatively homogenous organ.

The phantoms selected for instrument pre-delivery testing by manufacturer should meet the following specifications:

Ultrasonic Imaging Phantom Specifications:

a. Attenuation: 0.5 ± 0.1 dB/cm/MHz
b. Back Scatter: Approximately 10^{-4} – 10^{-3} $cm^{-1}Str^{-1}$ at 3 MHz or sufficient to create mean speckle brightness comparable to a human liver-mimicking phantom (± 3 dB)
c. Speed of Sound: 1540 ± 30 m/sec
d. Volume and Shape:
    i. Cylindrical or rectangular
    ii. Height: 15 ± 3 cm
    iii. Diameter: 12.5 ± 3cm in inner diameter (ID)

Shear Wave Speed Phantom Specifications:

a. Attenuation: 0.5 dB/cm/MHz (± 0.1 dB/cm/MHz)
b. Back Scatter: Approximately 10^{-4} – 10^{-3} $cm^{-1}Str^{-1}$ at 3 MHz or sufficient to create mean speckle brightness comparable to a human liver-mimicking phantom (± 3 dB)[5]
c. Speed of Sound: 1520-1540 m/sec
d. Stiffness: Two phantoms can be used or a single phantom with two different components: Normal Liver Equivalent & Fibrotic F3 Liver equivalent. ± 5% of the specified values. Stiffness verified using Verasonics system and software from Duke University and Mayo Clinic. See https://github.com/RSNA-QIBA-US-SWS/QIBA-DigitalPhantoms.
e. Volume and Shape – Cylindrical, 20 cm tall, 12.5 cm in diameter. (Cylindrical preferred, rectangular is acceptable if width and depth are 12.5 cm and 20cm tall)

[5] Reference - IEC 61391-2: Ultrasonics – Pulse-echo scanners – Part 2: Measurement of maximum depth of penetration and local dynamic range. 2010, Int Electrotechnical Comm: Geneva.

Ultrasonic Imaging Phantom Characterization: Phantom is weighed upon construction. It is then tested following procedures in the AIUM Guidance document.[6]

Pass Fail Tolerances for Site-Phantom Characterization and/or Retesting (these are the same specifications as the phantoms used for pre-delivery instrument testing)

Testing to be performed at 21±1 °C.

- Method to verify temperature of phantoms prior to testing. Temperature measurement method: TBD [open issue]

Attenuation: **± 20%**

- 0.5 dB/cm/MHz± 0.1 dB/cm/MHz

Back Scatter: **± 3dB**

- Approximately 10^{-4} – 10^{-3} $cm^{-1}Str^{-1}$ at 3 MHz or sufficient to create mean speckle brightness comparable to a human liver-mimicking phantom (± 3 dB)]

Speed of Sound: **± 2%**

- 1540 ± 30 m/sec [1510-1570 m/sec]

Phantoms failing these tolerance tests should be refused or replaced if already acquired.

Ultrasonic Imaging Phantom Temporal Stability testing: The phantoms should be re-weighed every six months and if the phantom weight changes by more than 0.5%, the phantom should be retested to confirm that acoustic properties are within the specifications above prior to next use.
If the phantom manufacturer has other criteria for stability testing prior to acoustic property testing, those should be used instead.

Testing of phantom acoustic properties should be as specified by the AIUM guidelines noted previously and the phantom supplier's recommendations.
**If the values are changing faster than the rates above, sites should consider replacement or testing more frequently than every 6 months.*

SWS Phantom (pre-delivery and on-site phantoms): The initial characterization of the phantoms will be performed and verified by the QIBA committee, the phantom manufacturer, Verasonics or another party using measurements obtained from Verasonics research ultrasound systems. Independent verification of phantom properties to ensure that the phantom meets the SWS Phantom specifications above is strongly recommended. If a newly procured phantom has already been independently tested within six months of the date of manufacture and those results are available then additional independent testing prior to use is not necessary. The phantom manufacturer may be contacted for assistance in finding a site that will perform independent testing.

SWS Phantom Temporal Stability Testing (pre-delivery and site-phantoms): Weigh the SWS phantom monthly and if the weight changes more than 0.5% over a six-month period the following parameters

[6] Methods for Specifying Acoustic Properties of Tissue-Mimicking Phantoms and Objects 2nd Edition. AIUM Technical Standards Committee. American Institute of Ultrasound in Medicine. 2015.

will be checked by sending the phantom to a testing facility capable of performing the tests using a Verasonics system. The phantom manufacturer may be contacted for assistance with obtaining the tests. Alternatively, a calibrated replacement phantom may be procured.
SWS Phantom Stability Tolerances:

(1) SWS: <5% change in both hard and soft components over 6 months.
(2) Speed of Sound: <1% change over 6 months.

If SWS Phantom stability is demonstrated at six months, then the timeline can be changed to annual testing.

3.1.2 ULTRASOUND SYSTEM PHANTOM TESTING

a. Grayscale imaging tests as normally conducted by the ultrasound system manufacturer or as described in the AIUM document "AIUM Quality Assurance Manual for Gray Scale Ultrasound Scanners"[7]. A link to the QA Tests and expected results Recommended by AIUM is given here:
AIUM QA guidelines:
http://www.aium.org/loginRequired/store/productDetail.aspx?cId%3d102%26page%3d2%26pId%3dRQA&cId=102&page=2&pId=RQA

b. Shear Wave Speed Estimations are obtained from the SWS phantom using the manufacturer specified procedures as defined in Appendix D of the QIBA SWS Profile.
Shear Wave Speed (SWS) Tolerance: ± 5% of the Verasonics system calibration value for the phantom as determined by the QIBA calibration site.

3.1.3 SPECIFICATION

Parameter	Actor	Requirement
Acoustic Output (SWS Mode)	Manufacturer (MFR)	Shall confirm the Ultrasound Scanner, when operating in SWS mode, is within FDA recommended maximum acoustic output levels for diagnostic ultrasound devices. MFR specification and certification.
Acoustic Transmit Focusing	MFR	MFR specification and certification for SWS measurement and Imaging.
SWS Measurement Consistency	MFR	Shall confirm that the SWS Measurement Consistency of the Ultrasound Scanner is within ± 5%. See 4.2 Assessment Procedure: SWS Measurement Performance.

[7] AIUM Quality Assurance Manual for Gray Scale Ultrasound Scanners, AIUM Technical Standards Committee, American Institute of Ultrasound in Medicine, www.aium.org, 2014 (ISBN 1-932962-31-X)

Parameter	Actor	Requirement
US Imaging Performance	Scanner Vendor	Meets MFR Specifications as published in scanner documentation
SWS Imaging Performance	MFR image processing software	Identification and display meets MFR specifications as specified in manufacturer section (Appendix D)
Software verification	MFR	Software version equals version specified in QIBA profile (Manufacturer specific section – Appendix D).
Hardware and transducer Manufacturer specified parameters	MFR	Shall ensure the equipment intended for use is listed in Appendix D as a compliant combination of System, Software Revision and Transducer.

3.2. Installation

This activity describes calibrations, phantom imaging, performance assessments or validations following installation of equipment at the site that are necessary to reliably meet the Profile Claim.

3.2.1 DISCUSSION

The QA Manager is shown as being responsible for several of these requirements being met. They may delegate actual performance of certain steps to a Scanner Vendor engineer and confirm the results.

Measurement Concordance (bias) Testing Procedure:

This section describes the testing procedure to be used to verify that the system gives approximately the same SWS in phantoms as did the calibration using the Verasonics system. These results **do not yet represent a formal claim for the profile** but could become one in a future edition. If the scanner does not meet the specifications in the table below (table 3.2.2), then the scanner may still be used, but the manufacturer should be contacted about the discrepancy to determine possible causes. For example, the acquisition procedure in appendix D may be incomplete or the site may not be following the procedure as intended by the manufacturer. The site should record and report a discrepancy found here with their results reporting until the issue is resolved (in conjunction with the manufacturer).

The assessor shall measure the shear wave speed on the phantom using the instrument settings and acquisition procedures specified by the Scanner Vendor in Appendix D according to the phantom acquisition protocol defined in section 4.2.1.1.B. Phantom SWS data acquisition.

These results will be compared to the shear wave speed obtained using the Verasonics system for the same phantom as determined by the QIBA calibration site (which may be the phantom manufacturer).

The assessor shall compute the SWS Measurement Consistency as the percentage difference between the ultrasound and MRE SWS measurements. This computation may be made according to the instructions given in section 4.2.1.2.B, Site Percentage Bias Estimation. To keep the assessor blinded to the true phantom values, the computation of Site Bias should be conducted by **someone different** than the individual acquiring the data.

3.2.2 SPECIFICATION

Parameter	Actor	Requirement
Hardware Damage	MFR Engineer	No physical damage.
	Clinical Staff	No physical damage.
Software verification	QA Manager or Designee	Software version equals the version specified in the products QIBA Conformance Statement or one listed in Appendix D.
SWS Measurement Concordance	QA Manager and/or Designee	Shall confirm that SWS Measurements Obtained with the Ultrasound SWS System are within ± 5% of the values contained in the Elastic SWS phantom specifications/independent test results. If the phantom specifications and independent test values are slightly different, the average of the two values will be used.

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3.3 Staff Qualification

This activity involves evaluating the human Actors (Radiologist, Physicist, and Technologist) prior to their participation in the Profile. It includes training, qualification or performance assessments that are necessary to reliably meet the Profile Claim.

3.3.1 DISCUSSION

These requirements, as with any QIBA Profile requirements, are focused on achieving the Profile Claim. Evaluating the medical or professional qualifications of participating actors is beyond the scope of this profile.

3.3.2 SPECIFICATION

Parameter	Actor	Specification
Operator Training	Technologist	Shall be trained and approved for SWS acquisition
Operator Qualification	Technologist	Shall meet performance requirements on phantoms & subjects: phantom testing— wCV ≤ .05 and/or case review IQR/median ≤ 0.30

Operator qualification testing. After performing approximately 20 supervised SWS acquisitions on patients and 10 on phantoms, the operator's results in terms of wCV or IQR/median are reviewed. If 90% are within the specification above then the operator is qualified to perform the SWS measurements

from a technique standpoint. Additional evaluation parameters such as patient-operator interactions, labeling etc. will be assessed in the usual manner for clinical personnel.

3.4. Site Quality Assurance

This section describes calibrations, instrument testing, operator training/testing, and performance assessments conducted periodically at the site that are necessary to reliably meet the Profile Claim.

3.4.1 DISCUSSION

Test Phantoms for Ultrasonic Imaging and SWS:
should meet the phantom requirements given in section 3.1 above.

The QA Manager is shown as being responsible for much of the phantom-based testing. The manager may delegate actual performance of certain steps to a selected Technologist and confirm the results.

3.4.2 SPECIFICATION

Parameter	Actor	Requirement
US Imaging QA	QA Manager	Shall perform standard ultrasound system QA on the Ultrasound Scanner as specified by AIUM guidelines.
SWS Measurement Consistency & System QA Testing Using SWS Phantom	QA Manager	Shall confirm that measurements of SWS on a QIBA elastic phantom using standard instrument settings and acquisition procedures annually, and after any software change are within ± 5% of the values of the Elastic SWS phantom specifications as determined by testing with a Verasonics system. If the system is already known to give results more than 5% different from the phantom values, the system should give values within ± 5% of the previously obtained results. See Measurement Concordance Test Procedure in section 3.2.1 above.
	Ultrasound Scanner	Shall be capable of performing SWS measurements at reproducible instrument settings using manufacture specific standard procedures [appendix D].
Operator training and qualification testing	Site Manager or QA Manager	The operator is trained on patient workflow and SWS acquisition then evaluated to confirm that qualification criteria are met (the requirements are in 3.3 Staff Qualification)
US Imaging and SWS Phantom Characterization and Stability Testing	Operator/QA Manager Independent Phantom QA Site	Confirmation of SWS Phantom Acoustic and Mechanical Properties at Independent Test Site Using QIBA procedures after construction and if a weight change of >0.5% has occurred.

3.5. Subject Selection

This activity describes criteria and procedures related to the selection of appropriate imaging subjects that are necessary to reliably meet the Profile Claim.

3.5.1 DISCUSSION

The profile is intended to be used in patients who require clinical assessment of liver fibrosis. The following factors affect patient selection.

Body Wall Thickness and Measurement Depth

Incorrect placement of the measurement region of Interest (ROI) can prevent effective measurement of SWS. Placement of the ROI too close to the liver capsule may result in artificially elevated SWS values as the liver is naturally somewhat stiffer near the capsule. Placement of the ROI too deep will result in noisy estimates due to attenuation of the acoustic radiation force push pulse and resulting weak, hard to measure shear waves. This can cause increased measurement error and increased numbers of technical failures. Therefore, the region being measured should be a minimum of 2cm deep to the liver capsule and a maximum of 6.5 cm deep to the skin. Because of these requirements, if the body wall thickness is greater than 4cm correct depth placement of the acquisition region of interest will not be possible.

Intercostal Space and History of COPD

A narrow intercostal space and/or COPD may make SWS data acquisition more difficult.

If an intercostal approach is not feasible, consider a subcostal approach. However, a note to document this should be made in the patient/subject note or study report. The claims in this profile have not been validated for a subcostal approach but maybe validated in a later version of the profile. Consider MRE as an alternative.

Prior Surgery

can interfere with SWS data acquisition. If subjects have had a surgical resection of the all or portions of right lobe of the liver that prevents an intercostal measurement in the right liver lobe, then the patient should be considered for exclusion. Consider MRE as an alternative. The claims in this profile have not been validated for measurements other than the right lobe of the liver, but may be validated in later versions of the profile.

Informed Consent:

Obtain informed consent as needed per institutional policy. HIPAA authorization shall be obtained for research or other purposes as outlined in institutional policies.

3.5.2 SPECIFICATION

Parameter	Actor	Requirement
Clinical Indication	Ordering Physician or Radiologist	Assess liver stiffness for liver pathology that may lead to increased organ stiffness and increased shear wave speed (for example liver fibrosis). A valid research protocol or a clinical concern supported by the literature is needed.
Approach	Radiologist or	Shall confirm an intercostal approach is feasible.

Parameter	Actor	Requirement
	Operator	
Body Wall Thickness	Radiologist or Operator	Shall confirm the patient body wall thickness is 4cm or less.
Intercostal space	Radiologist or Operator	Shall confirm a sufficiently wide intercostal space for probe placement.
Breathing	Radiologist or Operator	Shall confirm the ability of the patient to follow the breath hold instructions.
Prior Surgery	Radiologist or Operator	Shall confirm the presence of the right lobe of the liver and the absence of surgical/other scars that could cause shadowing.
Informed Consent	Technologist or Radiologist	Informed consent obtained.

3.6. Subject Handling

This activity involves handling each imaging subject at each time point. It includes subject handling details that are necessary to reliably meet the Profile Claim.

3.6.1 DISCUSSION

Subject handling for quantitative SWS measurement with ultrasound focuses on proper preparation of the patient for the acquisition of high reliability data.

An information/instruction sheet supplied to the patient prior to acquisition may be very helpful. The sheet could describe the technology, explain why it is useful, and give instructions to the patient on how to fast prior to the procedure (see 3.5.2). It may also provide information on maneuvers such as breath holding that will occur during the procedure. An example patient information sheet is given in appendix G.

In some cases (for example elastography research), an informed consent may be needed. A sample informed consent that can be used for shear wave elastography clinical studies is included in Appendix G.

3.6.2 SPECIFICATION

Parameter	Actor	Specification
Patient Instructions	Technologist	Shall instruct the patient far enough ahead of the procedure to avoid food or beverage (other than occasional small sips of water) for a minimum of 4 hours prior to the procedure. The instruction may be in the form of a patient information sheet describing how to accomplish the fasting

Parameter	Actor	Specification
		and how it is important for obtaining good SWS results as well as exceptions (e.g. oral medications, insulin).
Fasting State[1]	Technologist	Shall query the patient prior to acquisition on whether they actually fasted or not. Offer to acquire the data on a later date or later in the day if the patient is not in a fasting state.
	Radiologist	Shall query the patient prior to acquisition on whether they actually fasted. Offer to acquire the data on a later date or later in the day if the patient did not fast.
Informed Consent	Technologist or Radiologist	Presence of informed consent confirmed if needed per institutional policy. HIPAA authorization shall be obtained for research or other purposes, as outlined in institutional policies. (Sample consent form language in Appendix G)
Patient Information	Technologist or Radiologist	Shall provide general information on shear wave elastography and specific information on how the acquisition will be conducted, including number of acquisitions, transducer application between ribs, amount of pressure applied, need for breath hold etc. This can be provided as part of the patient information-instructions sheet.

3.7. SWS Image Acquisition (SWEI) and Point SWS Measurement

This section describes details of the data acquisition process that are necessary to reliably meet the Profile Claim. It includes calibrations, performance assessments or validations during acquisition that are necessary to reliably meet the Profile Claim.

3.7.1 DISCUSSION

Shear Wave Speed Acquisition – General Guidelines

Ultrasound SWS Measurement Acquisition System.

Even though efforts have been made to reduce variation in SWS estimates by different ultrasound systems, variation still exists and it may be significantly higher when acquisitions are performed in patients vs. phantoms. For this reason, every effort to acquire successive SWS measurements with the same system or with a system from the same manufacturer should be made. This guideline cannot be followed in many clinics with systems from multiple manufacturers because it results in scheduling difficulties. In cases where more than one system is used on a given patient on different exam dates, then the system should be identified and the median values the system gave using the calibration phantom should be given to aid the reader in determining if a difference in median/mean value between two systems should be taken into account during interpretation of the results.

Patient positioning:
For SWS acquisition this varies somewhat between institutions. Supine or slight (<30°) left decubitus positions are thought to be similar enough[8] so as not to induce variation in liver stiffness even though there is evidence that full left lateral decubitus positioning significantly affects measured SWS.

Suspended tidal respiration
is recommended to avoid additional pressure on the liver that might increase liver stiffness. In addition, this form of suspended respiration may result in less movement of the liver during acquisition since the diaphragm may move less than during a deep inspiration.

Instruction on how the patient should suspend respiration should be given immediately prior to data acquisition. Practice runs should be performed to allow the patient to learn how to suspend respiration. This will provide the patient or subject with useful information on what the ultrasound probe feels like and how long they will be asked to hold their breath (Appendix G).

Intercostal transducer positioning
has been shown to reduce variability in measurements. However, there are situations where intercostal acquisition is not feasible. For example, smaller patients may not have wide enough intercostal spaces to allow intercostal positioning of the transducer without partial blockage of transducer elements resulting either in obvious shadowing or loss of transmit power on the shear wave push pulse. Either will likely result in poor quality shear wave speed estimates. Another problem arises when the subject has COPD and the hyper-expanded lung pushes the liver below the costal margin. Consider subcostal only if intercostal is not feasible. The claims in this profile have not been validated for a subcostal approach. Where necessary, consider excluding the subject, and using MRE and/or liver biopsy for evaluation.

To avoid additional power loss of acoustic push for SWE acquisitions, keep the liver capsule parallel to the transducer face in both planes (transverse and elevational planes). For the same reason, the acquisition ROI placement should be in the center of the image.

Please refer to manufacturers' instructions on acquisition techniques, procedures and machine specific pitfalls for additional information. Appendix D contains this material for a number of manufacturers.

Absence of motion
during SWS acquisition is critical to obtain accurate and precise SWS measurements. Even though challenging in some patients, it is critical to ensure that no appreciable motion occurs during acquisition. Otherwise the acquisition should not be included in the analysis. Having the patient practice breath holds (suspended tidal respiration) may be helpful but avoid practicing so much that patient becomes fatigued.

Transducer Pressure
is an important variable since too much transducer pressure can increase the stiffness of underlying tissue. Only light transducer pressure should be applied during shear wave imaging and point quantification. Slightly increased pressure may be applied if it is needed to compress the abdominal wall sufficiently to enable SWS acquisition at an appropriate depth in the liver.

[8] Barr et.al. Elastography assessment of Liver Fibrosis: SRU Consensus Conference Statement. Radiology 2015; 276(3): 845-861.

Point Shear Wave Speed Measurement

The above considerations in image acquisition also apply to the measurement of shear wave speed from a single location with or without SWS imaging, often referred to as point SWS measurement. The following are some additional specifics to point SWS measurement.

Region of interest (ROI) Placement with Respect to Depth and Lateral Positioning is critical. A **depth** greater than 2cm deep to the liver capsule will avoid the slightly stiffer subcapsular liver tissue. A depth <6.5 cm will help to ensure that the shear wave amplitude is sufficient for reliable estimates of shear wave speed. Positioning away from discrete structures (e.g., vessels) is important as the algorithms used to estimate SWS assume homogeneous isotropic tissue, not heterogeneous tissue containing specific structures or lesions. An image should be acquired to document the ROI location relative to vessels so as to allow future acquisition at the same location for additional measurements, either at the same time or on follow-up examinations.

Positioning the ROI away from the **centerline** of the image may introduce variation in SWS estimates as may changing the ROI size. The effects of changing ROI size have not yet been systematically examined.

Please refer to manufacturer specific instructions and specifications for guidance on additional steps to take during point shear wave speed acquisition (see appendix D).

Positioning the measurement ROI at a **constant depth** as close as practicable from measurement to measurement and from one patient visit to another is important because SWS estimates are known to decline as a function of depth with many current SWS software implementations. Measuring at a constant depth will help to minimize variations.

Shear Wave Speed Imaging

This section deals with imaging settings that may be operator controlled which may affect diagnosis and ROI placement for point measurements

Color Map Setting.
If control of the color map used for imaging is possible, the operator (technologist or radiologist) should ensure that a map is used that is consistent from patient to patient and exam to exam. An agreed upon standard (i.e. blue is stiff or soft) has not yet been devised but the operator is encouraged to use the standard once it is agreed upon.

Color Transparency.
When color is overlaid upon the grayscale b-mode image, the amount of b-mode image that shows through the color image should be adjusted so that grayscale landmarks may be seen but changes in color are still clearly identifiable. Follow the manufacturer's recommendation as a starting point (see appendix D).

Frame Averaging.
The color display may be averaged over several frames to reduce flicker and rapidly changing colors. This should be set to manufactures specifications unless the manufacturer provides guidance for the use of other settings.

Frame Rate and Color Box Size.
If the size of the box within which color is displayed is controllable the operator should select the largest

box that provides an acceptable frame rate. Until a standard emerges the manufacturer's specification and guidance may be used (see appendix D).

Point Shear Wave Speed Measurements from Shear Wave Images

This section describes criteria and procedures related to producing quantitative measurements from the SWS images that are necessary to reliably meet the Profile Claim.

SWS Image Point Measurement ROI Location.
The location in the shear wave speed image for point measurements may depend on the type of pathology of concern. For example, for diffuse organ disease a global assessment may require positioning some ROI's in the largest homogeneous areas showing the predominate SWS in the images. Some ROI's may also be placed in the areas of high SWS for estimates of SWS in areas of greatest pathological change. Values from these ROI's should be identified as maximum SWS values to distinguish them from predominate SWS values so that the reader may provide an interpretation based on complete information.

For some focal lesions (such as breast cancers), the literature supports positioning ROI's in only areas of maximum SWS identified in the images. This is because most values in a cancer may be artificially decreased due (probably) to artifacts from shear wave reflection at lesion boundaries. Please also refer to manufacturers guidance regarding ROI positioning based on SWS image appearance. Some manufacturers have begun to supply additional images related to SWS quality and variability estimates. These images can be used to help position the ROI in the manner specified by the manufacturer.

SWS Imaging Point Measurement ROI size
may be pre-selected by the manufacturer. If adjustable use the default setting for suspected diffuse disease and consider decreasing ROI size if small areas of increased SWS speed on the SWE image are being evaluated. Check manufacturer guidance regarding reduction of ROI size and potential problems that may result.

SWS Imaging Point Measurement Data Transfer.
Follow manufacturer's instructions and/or institutional guidelines for this. Transfer may include capture of the measurement screens into PACS and/or recording of values on a worksheet. Transfer to PACS or a report via DICOM SR (structured reporting) is another option.

3.7.2 SPECIFICATION

Parameter	Actor	Requirement	DICOM Tag
SWS Measurement Acquisition Device	Ultrasound System	Acquisition shall be performed on the same ultrasound system or same brand of ultrasound system whenever possible and especially when performing successive measurements on the same patient. If this is not possible calibration values obtained for each system used on the same patient should be forwarded with the test results for use during interpretation.	

Parameter	Actor	Requirement	DICOM Tag
Patient Position	Technologist or Radiologist	Shall ensure that the patient is positioned supine or in approximately a 30° left lateral decubitus position.	
Respiration[2]	Technologist	Shall perform several practice acquisitions with patient in suspended tidal respiration so that they learn the technique and get used to the sensation of the ultrasound transducer while in suspended tidal respiration, and the duration of the required breath hold. Shall ensure that patient is in suspended tidal respiration during acquisition of shear wave data and post-acquisition image and that no other liver movement is observed during this process.	
Transducer Position	Technologist or Radiologist	Shall position the transducer at an intercostal space wide enough to accommodate the transducer and at the correct level to image/acquire from the upper right liver lobe (segments 5, 7, 8)). Shall position the transducer face long axis parallel to the intercostal space and check for correct positioning by inspection of the image for shadowing at the image edges. Shall position the transducer face in contact with the skin and parallel to the liver capsule so that the acoustic waves travel perpendicular to the capsule.	
Transducer Pressure	Technologist or Radiologist	Shall use only light pressure during SWS acquisition –just enough to maintain skin contact. May use slightly more pressure to compress body wall when needed to enable ROI to be positioned in proper position in Liver.	
Ultrasound image – location confirmation	Technologist or Radiologist	Shall confirm the absence of focal structures near image center and confirm no acoustic shadowing from the ribs.	

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Parameter	Actor	Specification
Measurement Region of Interest (ROI) Placement	Technologist or Radiologist	Shall position the ROI at least 2cm deep to the liver capsule and less than 6.5 cm from the transducer face. Shall position the ROI away from discrete structures such as liver margin, nodules, portal triads or hepatic veins.

Parameter	Actor	Specification
		Shall position the ROI near the center of the image in the lateral direction and away from the right or left image margins. Shall use the standard ROI size specified by the ultrasound vendor as the default for their system. The standard for each MFR should conform to a minimum size of 6mm X 10mm or diameter of 10mm. Should try to place the ROI at a constant depth for all acquisitions, but especially for follow-up acquisitions in the same patient or subject.
Follow-up Consistency	Technologist	Shall make follow-up acquisitions and ROI placements consistent with the baseline measurement in terms of the Transducer Position and Measurement Region of Interest (ROI) Placement.
Number of Measurements	Technologist or Radiologist	Shall make a minimum of 5 measurements should be made. The ultrasound manufacturer may specify more than 5 images in which case the manufacturer's instructions should be followed. Please refer to manufacturer specific instructions (Appendix D).
Liver Movement	Technologist or Radiologist	Shall acquire only when there is no visible liver motion.
SWS Imaging Color Map	Technologist or Radiologist	Shall ensure consistency of selection between examinations and patients. Shall adhere to institutional and/or national standards. See manufacturer specific guidelines.
SWS Imaging Color Transparency	Technologist or Radiologist	Shall set to adequately visualize color changes and grayscale anatomy. See manufacturer guidelines.
SWS Imaging Frame Averaging	Technologist or Radiologist	Shall set according to preference after initially setting according to manufacturer recommendations.
SWS Imaging Frame Rate/Color Box Size	Technologist or Radiologist	Shall set to provide as large a box as possible consistent with adequate frame rate for visualization of color. See manufacturer guidelines.
SWS Imaging Point Measurement ROI location	Technologist/ Radiologist/	See Section 3.7.1 Measurement ROI location in most homogenous region of SWS color map or other images related to SWS variability as specified by MFR (Appendix D).
SWS Imaging Point Measurement ROI size	Technologist/ Radiologist	As per MFR specifications (Appendix D). Each manufacturer should specify an optimal measurement ROI size and make that a default for their system. A minimum size of 6mm X 10mm or diameter of 10mm.

Parameter	Actor	Specification
SWS Imaging Point Measurement Data Transfer	Technologist Radiologist	Shall transfer SWS measurement objects to PACS or other storage and confirm successful storage.

3.8. Image Related QA

This activity describes criteria and evaluations of the images that are necessary to reliably meet the Profile Claim.

3.8.1 DISCUSSION

As SWS estimates may be variable with current implementations, care must be taken to avoid introducing additional variation. Assessment of the quality of each acquisition should be made and values obtained during suboptimal acquisitions should be deleted and not included in mean or median estimates. Situations where suboptimal acquisitions may be made include:

- liver movement during acquisition,
- patient talking during acquisition,
- transducer slippage during acquisition and
- inadvertent shift of ROI to a deeper or shallower depth,
- placement of the ROI near to a vessel or other discrete structure.

Acquire a pre and post SWS acquisition images immediately prior to and immediately after SWS acquisition in order to confirm lack of liver movement during the acquisition. Different ultrasound systems vary greatly in their ability to save pre-acquisition and post-acquisition images in close temporal proximity to the SWS acquisition. Experimentation to determine the best procedure for this may be necessary and often, practice to make the images quickly is needed.

Subjective assessment of motion is sufficient at this stage since the amount of motion that can be tolerated is not known. If upon further study, acquisition is extremely motion sensitive, measures to quantify motion and automatically discard suboptimal acquisitions may be required in future profile versions.

The operator should discard the acquisition if movement is detected by any method.

3.8.2 SPECIFICATION

Parameter	Actor	Requirement
Suboptimal SWS Acquisition handling	Technologist or Radiologist	Shall exclude any SWS estimate deemed to have been acquired sub-optimally, either by observations made during the acquisition or by inspection of the saved images. See section 3.6 for rules of acquisition that may result in suboptimal acquisition.
User training	Mfr	Training on user image interpretation is provided. Operator training on

Parameter	Actor	Requirement
on image display		optimal placement of measurement ROI is provided.

4. Assessment Procedures

Most of the requirements described in Section 3 can be assessed for conformance by direct observation, however some of the performance-oriented requirements are assessed using a procedure. When a specific assessment procedure is required or to provide clarity, those procedures are defined in subsections here in Section 4.

4.1. Assessment Procedure: Imaging Performance

This procedure can be used by a scanner vendor or an imaging site to assess the imaging performance of an ultrasound system. Imaging performance is assessed in terms of change compared to specifications and/or initial testing of most recent prior QA testing when imaging a phantom.

4.1.1 OBTAINING AND MAINTAINING THE IMAGING PHANTOM – SEE SECTION 3.1.2

4.1.2 ASSESSING IMAGING PERFORMANCE

The assessor shall perform grayscale imaging tests as normally conducted by the ultrasound system manufacturer or as described in the AIUM document "AIUM Quality Assurance Manual for Gray Scale Ultrasound Scanners"[9].

A link to the QA Tests and expected results recommended by AIUM is given here (login required): http://www.aium.org/loginRequired/store/productDetail.aspx?cId%3d102%26page%3d2%26pId%3dRQA&cId=102&page=2&pId=RQA

4.2. Assessment Procedures: SWS Measurement Performance

This section describes a group of procedures for assessing the performance of a site or of individual actors to determine if pre-established quantification performance specifications are met. For a site, those pre-established quantification performance specifications are the claims made in the claims section of the profile. For the individual actors, the performance specifications are those that have been shown, or are likely to be necessary for the site to meet the performance claims of the profile. The

[9] AIUM Quality Assurance Manual for Gray Scale Ultrasound Scanners, AIUM Technical Standards Committee, American Institute of Ultrasound in Medicine, www.aium.org, 2014 (ISBN 1-932962-31-X)

performance specifications for actors are based on the results of the technical and claims confirmation studies performed during the QIBA profile development process (see QIBA wiki: https://qibawiki.rsna.org/index.php/Process) and/or on typical acceptable performance achieved in clinical practice worldwide.
The overall performance of a site (and its ability to meet the profile claims) depends upon multiple actors meeting or exceeding their performance specifications, even if they already meet the procedural performance expectations of the profile (checklist compliance – see section 5). Clearly if an actor's performance does not meet specification, the profile claim may be invalidated for that site but inadequate performance on the part of one actor may be compensated for by better than expected performance of another actor. The described assessment procedures are designed to test the hypothesis that an Actor's wCV meets the Profile requirement at a specified type I error rate (usually 5%). It is not sufficient to show that the observed wCV is <10% for only a sample of cases.

Therefore, two types of assessment procedures and performance specifications are described: A) those for assessment of composite performance of a site and B) those for testing individual actors. The assessment procedures for types a and b may be the same or very similar to one another but different performance specifications will be given.

Cross-sectional claims (for a given patient at a single time point) require testing of within subject precision, often termed "repeatability" as well as bias. Longitudinal claims (for a given patient at different time points or for different imaging methods at one or more time points require testing of repeatability, bias, linearity and regression slope. As this profile makes multiple longitudinal claims and one cross-sectional claim, numerous testing procedures are described below along with the claim that each applies to.

4.2.1 SITE ASSESSMENT TOOLS AND TESTS.

4.2.1.0 Site assessment dataset. The dataset (or "parts being measured" in six sigma measurement system analysis) are livers of patients and two test phantoms.

4.2.1.1. Site assessment data acquisition

4.2.1.1.A. B-mode imaging: For Ultrasound b-mode imaging assessment a standard ultrasound test phantom shall be used to acquire test images and measurement values that will be evaluated according to the methods described in the AIUM quality assurance manual. The specification for the phantom is given in section 3.1.2 above.

4.2.1.1.B. Phantom SWS: For assessment of SWS performance and conformance in phantoms, calibrated SWS phantoms shall be used. These phantoms can be obtained from phantom manufacturers and consist of either two phantoms, one with stiffness approximating normal liver and the other with a stiffness approximating a liver with F3 fibrosis, or a single two-part phantom containing regions with each of the two stiffnesses. The specifications of the phantoms are given in section 3.1.2 above along with instructions for periodic phantom stability checks.

The site assessment phantom data will consist of SWS acquisitions obtained by each operator who has been qualified by training and testing to acquire SWS data according to the following criteria:

*Twenty (20) distinct SWS measurements will be collected from each of the two phantoms at both 4.5cm and 7 cm depths, by each operator. For these tests a measurement is defined as completed when the scanner outputs a SWS to the screen or to the data collection table within the machine. A system may acquire multiple SWS values and then report an overall SWS value (i.e. mean and median). The individual SWS values are the measurements, not this summary result. So, for each operator a total of 80 measurements, 20 for each of the two phantoms and for each of two different depths.

* If a site has ultrasound systems from more than one manufacturer, the test measurements must be performed for each manufacturer's system (only one set of test measurements per manufacturer unless the manufacturer notes that different models of their systems give different SWS results). So, for multiple different ultrasound systems being used to acquire SWS, the total number of measurements taken per operator will be 80 x n where n = the number of ultrasound systems. It is expected that acquisition of these phantom measurements will take approximately 20 minutes per machine.

* Depth is defined as the distance from the transducer surface to the center of the region of interest from which the point SWS is acquired.

*Between each measurement, the transducer will be removed from contact with the phantom and the phantom will be shifted so that each measurement is performed with the transducer oriented differently relative to the phantom in a random manner. NO effort to reposition the transducer in the same exact spot as the previous measurement should be made.

* The temperature at which the testing was performed at should be recorded. It is strongly recommended that the measurements be performed at the temperature at which the phantom was calibrated by the QIBA test site or manufacturer using approved QIBA instrumentation and methodology.

* Each ultrasound scanner will have different specific instructions that should be followed as noted above, but one important requirement is that the transducer should remain motionless during each measurement. If transducer movement is detected by any method during measurement, that value should be discarded and another measurement taken.

* The operators will be blinded with respect to the actual SWS values represented in the phantom(s). The operator will however see a large number of SWS measurements from each phantom since the phantom(s) will be used repeatedly. Therefore, the operator must NOT discard a SWS measurement solely because it appears different from the others or from the assumed "true" value for the phantom

4.2.1.1.C. In-vivo SWS data: Six volunteers having no history of liver disease and with normal AST, ALT, Alkaline Phosphatase and Total Bilirubin values will be recruited. The volunteers should cover a range of BMI values from 20 to 35. Ideally volunteers who will be available for at least several rounds of testing (months to years) can be recruited. The site assessment in-vivo data set will consist of ten (10) measurements by each operator on each of the six volunteers and at two different depths made according to the following criteria:

* Ten (10) distinct SWS measurements at each of two depths (4.5cm and 7cm) will be made from each volunteer by each operator. Depth is defined as the distance from the transducer face to the center of the region of interest used for acquisition of the SWS value (not the region defined for shear wave

imaging display).

* The measurements will be performed with the volunteer having fasted for at least six hours

* The measurements will be made according to the instructions provided by the scanner manufacturer and according to the guidelines in section 3.6 of this profile.

* The measurements should be performed for each brand of ultrasound scanner if scanners from multiple manufacturers are used to acquire SWS data. All scanners from a given manufacturer are assumed to give identical results unless otherwise specified by the manufacturer.

* Between each measurement, the transducer should be removed from contact with the volunteer, and the volunteer should get up from the scan table between each measurement. If this is not feasible due to time limitations or physical condition of the volunteer, the measurements should be divided into groups of five (5) measurements and the volunteer should get up from the scan table before lying down for the next measurement group.

* As for the phantom data collection, a SWS measurement is defined as whenever a SWS value appears on the scanner screen, NOT the mean value or median value reported by the scanner after several measurements.

* As for phantom SWS measurement, values obtained during visible patient or transducer movement should be discarded and repeated.

* SWS values that appear different from the others by a sizeable amount should never be discarded unless there was movement during the measurement, or another error occurred. Errors in measurement are defined as measurements where the manufacturer instructions were not followed. If a SWS is discarded, a repeat SWS measurement should be collected.

4.2.1.2. Site Conformance - Quality Metrics and Computation

As a number of distinct claims are made that depend on the depth that SWS is estimated and the stiffness of the tissue being examined, separate performance analysis will be performed for each combination of the two parameters, depth and material stiffness. The test data will contain data from the exact same two depths as specified in the claims but only two test phantoms will be used to assess performance at the three different stiffness ranges specified in the claims. The two phantoms are high and low stiffness and are expected to have stiffness values the will result in SWS values in the low (0.9-1.2 m/s) and at the lower bound of the high stiffness range. Performance will therefore be judged using the claims for these two stiffness ranges.

4.2.1.2.A. Within Subject Measurement Variation.

SWS claims use within subject coefficient of variation (wCV) as an important quality metric, wCV computation from the test dataset (dataset as described under 4.2.1.1.B above) is as follows (next paragraph):

For each case (corresponding to the liver of a single patient where the variable *i denotes the case number*), the first measured SWS as described in 4.2.1.1 represents the first replicate measurement (denoted Y_{i1}) and the second measured SWS represents the second replicate measurement (Y_{i2}) for that

903 case. For phantoms, there is only a single phantom for each of the two stiffness being analyzed
904 separately so i takes on the single value i =1. For patient data, there are six volunteer subjects so the
905 variable i ranges from 1 to 6. For each case and for each combination of depth and stiffness range, the
906 assessor shall first calculate the mean and variance of the measurements (five per operator per machine
907 for phantoms and three per operator per machine for human volunteers). From these values, the
908 variance divided by the square of the mean (mean^2) will be calculated for each case and the results for
909 each case will be summed and the total divided by the number of cases (one for the phantom and 6 for
910 the human data). The square root of this value is the wCV. The equations for these computations are:
911

912 $$\widehat{wCV} = \sqrt{\sum_{i=1}^{N}\left\{\frac{Variance_i}{Mean_i^2}\right\}/N}$$

913
914 Where N=6 for the patient data and N = 1 for phantom data.
915
916
917 As noted in the preceding paragraph, if data were acquired from more than one brand of machine and
918 more than one operator, the measurements from all machines and all operators should also be pooled
919 for the computation to accurately reflect these sources of variability.

920 4.2.1.2.A-1 Maximum Allowable Variance.

921 To assure site conformance to the profile claims, the upper 95% confidence bound of the wCV computed
922 above must be less than the wCV reported in the claim to ensure that the calculated wCV for a site
923 meets the claim with 95% confidence.

924

925 [Data available for maximum allowable wCV and RC:

926 Phantoms: 20 per operator, per phantom stiffness value (2 values), per depth (two different depths)

927 Patients: 10 per operator, per depth (two depths), per patient (6 patients).]

928 With 6 subjects and 10 replicates per subject per depth, and with claims stating wCV of 4% and 5% for
929 depths of 4.5 and 7.0 for moderate SWS values, the maximum allowed wCVs are 3.3 and 4.1 for depths
930 of 4.5 and 7.0, respectively.

931

932

933 4.2.1.2.B Site Percentage Bias Estimation:

934 Although bias claims are not made in the current version of the profile, this calculation is provided for
935 use in later versions of the profile where bias claims will be made. At the present time, bias claims for
936 phantoms only are expected as no verified clinical methods for estimation of true SWS in patients are
937 available. MRE may eventually be a qualified method for provision of “gold standard” SWS values for
938 computation of bias. Currently the values obtained using a standard acquisition procedure in phantoms

(using a Verasonics research system) are considered the "gold standard" for bias and linearity estimation.

As the claims are stratified by acquisition depth and SWS range, bias estimates will also be estimated by the same categories.

For each of the four measurement situations (3.5cm depth, soft phantom; 7cm depth soft phantom; 3.5cm depth stiff phantom, 7cm depth stiff phantom, the data available are 20 x N where N is the number of operators.

For each measurement, the assessor shall calculate the value of the SWS (denoted Y_i), where *i* denotes the *i*-th acquisition. The assessor shall calculate the % bias: $b_i = [(Y_i - X_i)/X_i] \times 100$, where X_i is the true value of the measurand. Over N acquisitions estimate the population bias: $\hat{b} = \sum_{i=1}^{N} b_i \, /N$. The estimate of variance of the bias is $\widehat{Var}_b = \sum_{i=1}^{N}(b_i - \hat{b})^2 \, /N(N-1)$. The assessor shall calculate the 95% CI for the bias as $\hat{b} \pm t_{\alpha=0.025,(N-1)df} \times \sqrt{\widehat{Var}_b}$, where $t_{\alpha=0.025,(N-1)df}$ is from the Student's t-distribution with α=0.025 and (N-1) degrees of freedom. The lower bound of the 95% CI must be > -5% and the upper bound of the 95% CI must be < +5%.

4.2.1.2.C Site Linearity Estimation and Slope Estimation.

The phantom data set will be used. Since the longitudinal claims specify using the same operator and ultrasound system at each point in time the measurements from each operator and US system will be analyzed separately. The test data for each operator and machine consist of 20 measurements for each of two different measurement depths and for two different stiffness values.

For each operator and ultrasound system combination calculate linearity as follows:

For each measurement, the assessor shall calculate the *SWS* (denoted Y_i), where *i* denotes the *i*-th measurement. Let X_i denote the true value for the i-th measurement. The assessor shall fit an ordinary least squares (OLS) regression of the Y_i's on X_i's. A quadratic term is first included in the model to rule out non-linear relationships: $Y = \beta_o + \beta_1 X + \beta_2 X^2$. If $|\beta_2| < 0.5$, then the assessor shall fit a linear model: $Y = \beta_o + \beta_1 X$, and estimate R^2.

The absolute value of the estimate of β_2 should be <0.50 and R-squared (R^2) should be >0.90.
For the linear model fit, let $\widehat{\beta_1}$ denote the estimated slope. The assessor shall calculate its variance as $\widehat{Var}_{\beta_1} = \{\sum_{i=1}^{N}(Y_i - \hat{Y}_i)^2 \, /(N-2)\} \, / \sum_{i=1}^{N}(X_i - \bar{X})^2$, where $\hat{Y}_i$ is the fitted value of Y_i from the regression line and $\bar{X}$ is the mean of the true values. The assessor shall calculate the 95% CI for the slope as $\widehat{\beta_1} \pm t_{\alpha=0.025,(N-2)df} \sqrt{\widehat{Var}_{\beta_1}}$.

Allowable Slope Range: For most Profiles it is assumed that the regression slope equals one. Then the 95% CI for the slope should be completely contained in the interval 0.95 to 1.05. These thresholds should be specified in Section 3 of the Profile.

977 4.2.2 ASSESSING SWS CONSISTENCY COMPARED WITH PHANTOM SPECIFICATIONS--- SEE THIS TOPIC IN
978 SECTION 3.2.1

979 4.2.3. INDIVIDUAL ACTOR TOOLS AND TESTS

980 As this profile was created based on considerable preliminary phantom data testing designed to assess
981 the contribution of various actors to overall imprecision and bias, a "top down threshold selection"
982 approach is used to assess the bias and imprecision attributable to each actor. Phantom studies have
983 shown that the site and observer are small contributors to variability in phantoms. This finding may not
984 generalize to patients however since the potential for operator errors and operator-patient interaction
985 variation is much greater. Analysis of the test data using six sigma measurement systems analysis
986 methods such as crossed gauge r and r with anova are expected to provide sufficient information on
987 relative contribution of the various actors to overall variance so that appropriate corrective measures
988 may be taken to reduce overall imprecision to levels consistent with the profile claims. (further
989 discussion in next version).

990 4.2.3.1. Technologist/Operator Qualification Testing. The test data set for phantoms and for in-vivo
991 [patients] are described in sections 4.2.1.1.B and 4.2.1.1.C. The test data are acquired by each
992 Technologist/Operator so are suitable for qualification testing. A similar data set acquired only in-vivo
993 would also suffice. See section 3.3.2 Staff Qualification for the test and test criteria for qualification.

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5. Conformance

To conform to this Profile, participating staff and equipment ("Actors") shall support each activity assigned to them in Table 3-1 in Section 3.

To support an activity, the actor shall conform to the requirements (indicated by "shall language") listed in the Specifications table of the activity. Each activity has a dedicated subsection in Section 3. For convenience, the Specification table requirements have been duplicated and organized in chronological order in the form of checklists in Appendix E.

To meet the dual needs of ensuring proper execution of the profile and assessment for conformance, two forms of the checklist are provided.

The Execution Checklist (See Appendix E.1) covers only subjects and data acquisition (Activities 3.5 – 3.7) and on processing and analysis (Activities 3.7 – 3.10). It is intended to work best for actual acquisition of quantitative image data and to be easily followed during execution of any protocol.

The Conformance Checklist (See Appendix E.2) covers all the profile requirements. Checklists are used extensively to evaluate imaging practices for conformance to practice and imaging guidelines for accreditation purposes (for example AIUM and ACR accreditation programs) and thus can be readily adapted for the QIBA profile conformance program. This sort of conformance monitoring is well understood by imaging centers since most have applied for accreditation or are already accredited.

Some requirements reference a specific assessment procedure in section 4 that shall be used to assess conformance to that requirement. Other requirements may reference vendor-specific instructions which may be documented in Appendix D.

If a QIBA Conformance Statement is already available for an actor (e.g. your analysis software), you may choose to provide a copy of that statement rather than confirming each of the requirements in that Actors checklist yourself.

Formal claims of conformance by the organization responsible for an Actor shall be in the form of a published QIBA Conformance Statement.

Vendors publishing a QIBA Conformance Statement shall provide a set of "Model-specific Parameters" (as shown in Appendix D) describing how their product was configured to achieve conformance. Vendors shall also provide access or describe the characteristics of the test set used for conformance testing.

Some activities (such as periodic QA monitoring) do not fall clearly into the acquisition chronological order and so are provided as separate checklists with tasks in approximate chronological order. More complex tasks may in the future include "sub-checklists" which will be listed as separate checklists to improve the readability of the main checklist, and are hyperlinked to the main checklist, and will be referenced in the main checklist for those using paper (vs. electronic) checklists. Sub-checklists have not yet been implemented.

Conformance to the profile will be monitored by evaluation/review of execution checklists from a random sampling of acquisitions along with review of corresponding specific assessment documentation, as outlined in the subsections below. The results of the evaluations/review are to be recorded on a conformance checklist similar to the execution checklist where each line item in the main checklist is assigned a potential point score on a three-point scale depending on how critical the line item is to the data quality needed to meet the profile claims.

For a given line item, the site achieves the maximum number of points if fully compliant, including full compliance in any related sub-checklists. A partially compliant score is assigned (less than the maximum potential score) according the assessment rules defined in the procedures covered in sections below, in assessment procedures defined in section 4, or according to the assessment of the assessor performing conformance monitoring.

The score needed to achieve conformance for a section or for the profile as a whole has yet to be determined. Data needed to determine this are being acquired. As a temporary measure, a passing score of 85% of the maximum possible points listed on the conformance checklist for each profile section will be considered a passing score.

Appendices

Appendix A: Acknowledgements and Attributions

This document is proffered by the Radiological Society of North America (RSNA) Quantitative Imaging Biomarker Alliance (QIBA), The QIBA Ultrasound Coordinating Committee and the QIBA Ultrasound Shear Wave Speed Biomarker Committee* (US SWS BC) under the leadership of Brian Garra, Tim Hall and Andy Milkowski. Paul Carson served as QIBA Ultrasound Coordinator.

Profile Editor and leading coauthor was Brian Garra. Manish Dhyani, M.D. was a major coauthor and initial editor. Special contributions in conduct of groundwork studies and their publication were made by Mark Palmeri and his colleagues at Duke University. Other leaders of groundwork studies included Anthony Samir and colleagues at Massachusetts General Hospital, Tim Hall and colleagues at the Univ. of Wisconsin, Matthew Urban and colleagues at the Mayo Clinic, Stephen McAleavey and colleagues at The University of Rochester, and Jingfeng Jiang and colleagues at Michigan Technical University. Andy Milkowski performed an initial analysis. Discussions and contributions from Nancy Obuchowski greatly improved the statistical methods used in the analysis. Proofreading and guidance on structure of the profile were provided by Kevin O'Donnell. Cooperation of the MR Elastography Biomarker Committee, through Richard Ehman's team at the Mayo Clinic, was much appreciated for their testing in phantoms for comparison with ultrasound. The 15 ultrasound system companies mentioned below were helpful in their contributions. In particular, those included in Appendix D. provided systems and/or performed studies for the groundwork. Also participating were companies producing phantoms, test equipment, contrast agents and drug studies and volunteers from government and many academic and clinical institutions.

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Many of the published papers, proceedings articles and abstracts produced in this effort are referenced in http://qibawiki.rsna.org/index.php/QIBA_in_the_Literature_Citations under the link "QIBA Literature References". Major contributors to the primary manuscript reporting much of the SWS US Biomarker Committee's work were, Mark L. Palmeri and, in alphabetical order, Richard Barr, Paul Carson, Mathieu Couade, Jun Chen, Shigao Chen, Manish Dhyani, Richard Ehman,

Brian Garra, Albert Gee , Gilles Guenette , Zaegyoo Hah , Ted Lynch, Michael Macdonald , Ravi Managuli, Veronique Miette , Kathryn R. Nightingale, Nancy Obuchowski, Ned C. Rouze, Anthony E. Samir, Vijay Shamdasani, Matthew Urban, Keith Wear, Hua Xie, Timothy J. Hall. Not in order, they are from: Duke University, Durham, NC, USA, CIRS, Norfolk, VA, USA, Mayo Clinic, Rochester, MN, USA, Philips Research, Cambridge, MA, USA, Food and Drug Administration, Silver Spring, MD, USA, Siemens Ultrasound, Issaquah, WA, USA, University of Michigan, Ann Arbor, MI, USA, The Surgical Hospital at Southwoods, Boardman, OH, USA, Philips Ultrasound, Bothell, WA, USA, General Electric, Milwaukee, WI, USA, Toshiba Medical Research Institute, Redmond, WA, USA, Massachusetts General Hospital, Boston, MA, USA, Samsung Medison, Seoul, South Korea, Zonare Medical Systems, Mountain View, CA, USA, The Cleveland Clinic, Cleveland, OH, USA, University of Wisconsin, Madison, WI, USA SuperSonic Imagine, Aix-En-Provence, France Echosens, Paris, France Hitachi Healthcare, Seattle, WA, USA

Appendix B: Background Information

Appendix C: Conventions and Definitions

Appendix D: Model-specific Instructions and Parameters

Contents

Please click on the manufacturer in the table to jump to that section

Canon

Canon Medical Systems (formerly Toshiba)

Manufacturer Name:

- Canon Medical Systems Corporation (formerly Toshiba Medical Systems Corporation)

Equipment Models:

- Aplio i-series (i600/i700/i800/i900)
- Aplio Platinum Series (300/400/500)
- Xario 200 Platinum Series

Software Versions:

- Aplio i700/800/900 V1.1 or later
- Aplio i600 V2.0 or later
- Aplio 400/500 V6.0 or later
- Aplio 300 V6.7 or later
- Xario 200 V6.0 or later

Transducer(s):

Transducer	Aplio i700/i800/i900	Aplio i600	Aplio 300/400/500	Xario 200
PVI-475BX	**X**			
PVI-475BT	**X**	**X**		
PVT-375BT	**X**	**X**	**X**	
PVT-375SC	**X**	**X**	**X**	
PVT-475BT			**X**	
PVU-375BT				**X**

Acquisition Procedures:

[See specifications in Profile Section 3.6, 3.8, & 3.10]

- Patient fasted minimum 4- 6 hours (including alcohol)
- Patient lying supine or slight left lateral decubitus position with the right arm behind the head.
- Normal gentle breathing or mid-expiration breath hold, as needed.
- Intercostal acoustic window with minimal rib shadowing and keeping the liver capsule parallel to the transducer surface; optimizing visualization of liver tissue.
- Select an area of the right lobe of the liver parenchyma free of the following structures:
    - Portal Trunk; Vessels; Visible Fibrous Bands
- Shear wave acquisition ROI:
    - ROI size: approximately 3 cm in lateral direction and 3 cm in axial direction.
    - Position acquisition ROI at least 1 cm below the liver surface.
- Shear wave measurement ROI:
    - A circular measurement ROI with a diameter of 1 cm is recommended.
    - Place measurement ROI in region of the shear wave speed /elasticity display that is homogenous and without defect.
    - The Propagation map displays can be used for additional guidance on the placement of the measurement ROI (see below). The measurement ROI should be placed in a region where smooth, parallel contour lines are observed in the Propagation display.
- Repeat at least 5 measurements from the same window in the right lobe of the liver.

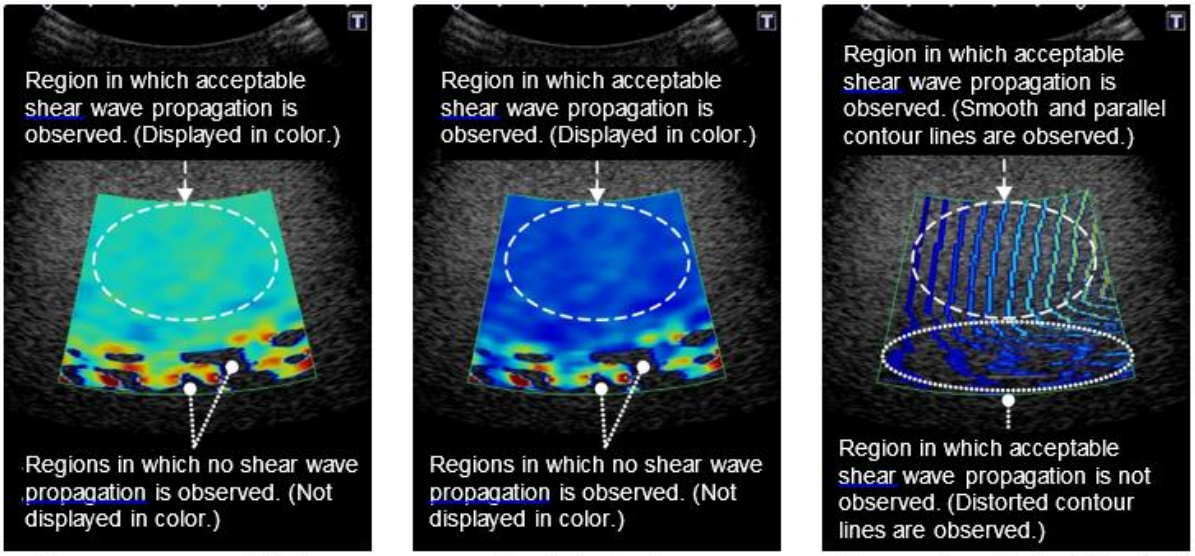
Outlier Identification specifications and instructions for use:

1286 The following shear wave display maps are available:

Map Type	Display	Description
Speed	Shear wave speed display (m/s)*1	The stiffness distribution for the scanned plane can be observed.
Elasticity	Elasticity display (kPa)*1	
Propagation	Propagation display*2	The shear wave arrival time is presented as contour lines. (The wavefront of the shear wave is displayed at regular time intervals.)
Dispersion	Frequency dispersion display*1	The change in shear wave speed between frequencies is represented (dispersion slope) in color.
Variance	Variance display*1	Minor distortions in shear wave arrival times are represented in color.

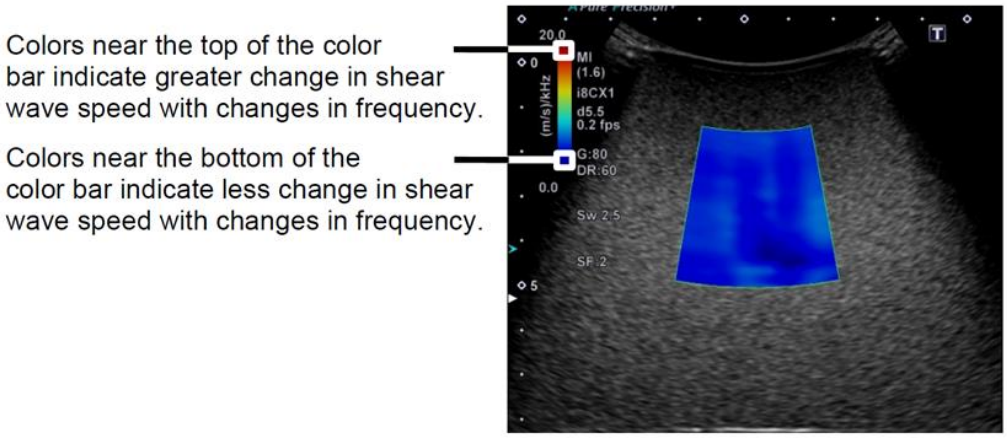
1287

1288 *1: Regions in which no shear wave propagation is observed or acceptable shear wave propagation is
1289 not observed are not displayed in color.
1290 *2: Distorted contour lines are displayed for regions where no shear wave propagation is observed or
1291 where acceptable shear wave propagation is not observed.
1292 The region in which the desired shear wave propagation is observed can be confirmed by using the
1293 propagation display together with the shear wave speed display or elasticity display.



Shear wave speed display | Elasticity display | Propagation display (Contour)

1294



Dispersion display

The mean, median, standard deviation, and IQR from multiple shear wave measurements can be displayed on a worksheet report page (up to 14 measurements). Individual measurements (i.e. outliers) can be excluded from the calculation of these statistical values as selected by the user.

General Electric

GE

Manufacturer Name: GE Healthcare

Equipment Model: LOGIQ E9, LOGIQ S8

Software Version: R5 and higher on LOGIQ E9, R3 and higher on LOGIQ S8

Transducer(s) to be used: C1-6-D, 9L-D

Acquisition Procedures:

1. Instructions
    a. ROI positioning: Place Top of Shear Wave box 1-2cm below liver capsule with middle of the Shear wave box between 3-6cm
    b. Measurement ROI size: Default measurement caliper size is recommended (Size = 1.25 cm diameter)
    c. Number of measurements: 10 measurements
2. Pitfalls: Avoid rib shadows and vessels within the SWE ROI

Outlier Identification specifications and instructions for use:

Scanning Technique for best Shear Wave Results:

- Fasting 4-6 hours
- Patient in supine position
- Elevate Right arm above head
- Scan intercostally with enough pressure to maintain stable contact

- Take measurements in Segment 7 and/or 8 of the liver
- Place Top of Shear Wave box 1-2cm below liver capsule with
- middle of the Shear wave box between 3-6cm for best results
    - Avoid rib shadows
    - Avoid vessels in the Shear Wave region of interest
- Obtain measurement on suspended breath hold, not inspiration
- Acquire at least 10 measurements using caliper tool

Locations with inaccurate measurement are not displayed in the SWE color image, and do not contribute to the quantitative measurement.

Best Practice Tips for Acquisition:

- ✓ Ensure good probe contact with patient and optimize imaging window to get best possible B-mode image quality before starting SWE acquisition
- ✓ Place ROI in shadow-free region
- ✓ Place ROI near center of image (laterally) if possible
- ✓ Place ROI in region free of vessels and 1-2cm below liver capsule

Best Practice Tips for Measurement:

- ✓ Take measurement when >50% of ROI has color-fill with default gain
- ✓ Take measurement on region with uniform color-fill and without obvious artifact like vertical stripes caused by probe movement during SWE acquisition

GE Healthcare

LOGIQ E9 Shear Wave Elastography

Liver Fibrosis Staging

Liver Fibrosis Staging	Metavir Score	kPa	m/s
Normal – Mild	F1	5.48 kPa – 8.29 kPa	1.35 m/s – 1.66 m/s
Mild – Moderate	F2	8.29 kPa – 9.40 kPa	1.66 m/s – 1.77 m/s
Moderate – Severe	F3	9.40 kPa – 11.9 kPa	1.77 m/s – 1.99 m/s
Cirrhosis	F4	> 11.9 kPa	> 1.99 m/s

A GE study has demonstrated that LOGIQ™ E9 Shear Wave Elastography is a robust technique and capable of evaluating stiffness changes in the liver associated with fibrosis. Although a limited number of subjects were evaluated at the hospital in this study, liver stiffness measurements were shown to be useful for discriminating different stages of fibrosis. It is important to note that a small number of subjects with intermediate stages of fibrosis were evaluated in this study, and that a mix of disease etiologies were present. Therefore, the values shown may not be directly applicable to other patient populations. Data was acquired using LOGIQ E9 R5.1.0 equivalent software and the C1-6-D probe. For detailed information, please see the LOGIQ E9 Shear Wave Elastography white paper.

Minimum ROI Size -

Hitachi

Hitachi

Manufacturer Name:
Hitachi, Ltd.

Equipment Model:
- ARIETTA 850
- ARIETTA 70
- HI VISION Ascendus

Software Version:
- ARIETTA 850 Ver.1 or later
- ARIETTA 70 Ver.3 or later
- HI VISION Ascendus Step 4 or later

Transducer(s) to be used:
- C252 and C251 with ARIETTA 850
- C251 with ARIETTA 70
- C715 with HI VISION Ascendus

Acquisition Procedures:

1. Instructions

a. ROI positioning

Same as QIBA profile. See below.

- Position the ROI at least 2cm deep to the liver capsule and less than 6.5 cm from the transducer face.
- Position the ROI away from discrete structures such as liver margin, nodules, portal triads or hepatic veins for acquisition of SWS estimates.
- Position the ROI near the center of the image in the lateral direction and away from the right or left image margins.

b. Measurement ROI size

Fixed ROI size with 10mm width and 15mm depth.

c. Number of measurements

10 measurements

2. Pitfalls

Under the following conditions, the generation and/or detection of shear wave will be insufficient.
- Low echogenicity
- Thick abdominal wall
- Liver capsule non parallel to the abdominal wall or not perpendicular to beams
- Place the ROI on rib shadows and/or near the liver capsule

- Large body motion by respiration

Outlier Identification specifications and instructions for use:

- Hitachi has a reliability index (VsN). Outliers are excluded using specific Vs range and/or shear wave signal quality. If VsN equals 0%, all data are outliers and error message is displayed.
- IQR/Median is displayed. Users can exclude individual measurements and the statistical values (i.e. IQR/Median) are automatically updated. (only for ARIETTA 850)

Philips

Philips

Manufacturer Name: Philips

Equipment Model: EPIQ

Software Version: Evolution 3.0

Transducer(s) to be used: C5-1 Curvilinear Transducer

Acquisition Procedures: Please refer to Philips "Quick Guide EPIQ Series ElastQ Imaging" for complete instruction

3. Instructions
    a. ROI positioning
        i. Ensure good transducer contact
        ii. Before starting shear wave elastography, always scan the region of interest in 2D mode to assess tissue consistency
        - Do not position the shear wave imaging region of interest (ROI) box over fetal tissue, tissue with gas pockets (lung, stomach, bowels), a bone tissue boundary, gallstones, metal, or the borders of the image.
        - Avoid rib shadow in the image, when possible.
        - Position the ElastQ Imaging ROI box in the center of the image.
        - Do not place the ElastQ Imaging ROI box on or near a rib shadow or liver capsule.
        - Place the top of the ROI box 1.0 to 1.5 cm below the liver capsule, to avoid reverberation artifacts
        - Do not place the circle caliper on a rib shadow, blood vessels
        - Position the circle caliper in the area of the ROI box that displays the majority of the uniform color
    - ROI size
        iii. ElastQ Imaging ROI: maximum size ~5cm (height) x 7 cm (width)
        iv. Making stiffness measurement and calculations
            1. Default circle caliper size: dimeter 1cm
            2. User has the option to calculate the average stiffness in the entire ElastQ Imaging ROI

3. User has the option to make single point measurements in the ROI
4. Stiffness measurement is also available for areas defined by the user in the form of ellipse and continuous trace

b. Number of measurements

- Take a minimum of 8 to 10 liver stiffness measurements

4. Pitfalls

Outlier Identification specifications and instructions for use:

To ensure high quality stiffness measurement, a concurrent real-time confidence map that combines multiple image quality metrics is also available along with the stiffness image. Outliers in stiffness measurement are automatically detected and excluded from subsequent quantification and statistical analysis. In addition, users are provided with the ratio of stiffness interquartile range (IQR) to median as a measure of variability for further measurement quality control.

Samsung

Samsung

Manufacturer Name:

Samsung Medison Co., Ltd.

Equipment Model:

- RS80A
- RS85

Software Version:

- RS80A v2.0 or later
- RS85 v1.0 or later

Transducer(s) to be used:

- RS80A
  - CA1-7A
  - LA2-9A
- RS85
  - CA1-7A
  - LA2-9A

Acquisition Procedures:

- Patient position
  - Supine / oblique left decubitus position is recommended
  - The right arm would better be elevated to make the intercostal spaces wider
  - Scan while patients' holding a normal breath (If not possible, ask the patient to breath as shallowly as possible)
  - Prolonged breath holding should be avoided
  - Patients should not move during the measurements

- Liver segment
  - Right hepatic lobe (between 5 and 8 segment from the right intercostal space) is recommended.
  - Avoid the left hepatic lobe because the measurement is affected by cardiac movements.
  - Segment 4 of the liver is sensitive to the motion artifact. There are more chances of the failure of measurement.

ROI positioning

- Position the ROI Box neat the homogeneous region
- Position the ROI Box at the suspected lesion without obscuring vessels.
- The ROI must be positioned at least 1.5 cm below the liver capsule.
- To obtain a stable measurements, position the ROI on the same locations and repeat the measurements
- The depth of ROI is recommended 6cm or less (if the depth is more than 6cm, the result may not be reliable). The bottommost depth should be less than 7cm.
- ROI is recommended to be positioned near the center line.

ROI size

Point shear wave: 1.0cm X 1.0cm
S shear wave: 2.5cm X 3.0cm

Number of measurements:

10 times or more

Scanning instruction

- After checking the probe and the application, start a scan.
- When you get the desired image, tap the **S-Shearwave Imaging** on the touch screen.
- Use the track ball to move to a desired ROI measurement position.
- Press the **Freeze** button on the control panel, and then the **Elasticity Measure** button on the touch screen.
- Use the trackball to move to a desired ROI measurement position within the Elasticity Image ROI.
- Pressing the **Set** button will display elasticity statistics within the Measure ROI, and save the value.
- A maximum of four Sites can be specified, and a maximum of ten Measure ROIs can be specified per Site

2. Pitfalls

(1) Weak shear waves

Avoid the ROI in the region where B mode image is too dark. This can induce insufficient tissue displacement by the push pulse to measure shear wave speed. Severe attenuation in tissue/muscle layer, shadowing by the ribs, defocusing of push pulses, loose probe contact can be the reasons.

(2) Reverberation

Obese patients typically have a thick fat/muscle layer and produce reverberations deep in the liver. The reverberations distort scanning pulses to produce erroneous shear wave speed readings. To

reduce reverberation artifact, depth of ROI should be at least twice the thickness of the muscle/fat layer, and the probe angle should be chosen to minimize reverberation between strong parallel reflectors. Measurements deemed contaminated by reverberation will display RMI (Reliability Measurement Index) value of 0.0.

(4) Reflections
Abrupt changes at the tissue/ tumor boundary produces reflections that may alter the observed propagation of shear waves. Typically this alteration may produce higher stiffness at the periphery of stiff tumors.

Outlier Identification specifications and instructions for use:

- Reliable Measurement Index (RMI) shows how reliable the measurement is and it is more reliable if the value gets closer to the maximum value of 1. (If RMI is 0.4 or higher, it is considered as very reliable.)
- It is recommended that this process is repeated more than 10 times.
- Auto profiling automatically removes outliers with RMI less than 0.4 or too far away from the calculated median value. The process automatically repeats itself until the number of remaining measurements is bigger than 5 and IQR/MED is less than 0.3.
- Following table is the chart provided by Samsung for liver fibrosis staging.

Liver Grading	Normal – Mild	Mild	Moderate – Severe	Severe
METAVIR Scoring	F0 - F1	F1 - F2	F3 - F4	F4
Kpa	2 - 5.4kpa	5.4 - 7.4kpa	7.4 - 11.6kpa	11.6 – 21.4kpa
m/s	0.81 - 1.34 m/s	1.34 - 1.57 m/s	1.57 - 1.97 m/s	1.97 – 2.7 m/s

Siemens

Siemens

Manufacturer Name:

Siemens Medical Solutions, USA, Inc.

Equipment Model:

ACUSON Sequoia
ACUSON S2000, S3000

Software Version:

ACUSON Sequoia: VA10A or later
ACUSON S2000, S3000: VC20A or later

Transducer(s) to be used:

ACUSON Sequoia: 5C1, DAX, 4V1, 10L4

ACUSON S2000, S3000: 6C1HD, 4C1, 4V1

Acquisition Procedures:

Follow cross-vendor recommendations in Profile

Best Practice Techniques

- Patient has fasted for a minimum of 4-6 hours
- Position patient supine or slight (30°) left lateral decubitus position with right arm raised above head
- Scan with the transducer parallel to ribs and in an intercostal space in the right lobe of the liver (segments 5 or 8)
- Optimize B-mode image so liver parenchyma is bright and large vessels, bile ducts and rib shadows are avoided

Activate Virtual Touch from the Abdomen exam preset

- ACUSON Sequoia
  - Press **VT** button on control panel
  - Select **pSWE** for point Shear Wave Elastography or **SWE** for 2D Shear Wave Elastography
- ACUSON S2000 and S3000 systems
  - Press **E** button on control panel
  - Select **VTQ** (Virtual Touch Quantification) on the touch screen

Position the Region of Interest (ROI)

- Position the ROI between 3–6 cm deep and at least 1–2 cm below liver capsule
- To position the ROI, roll the trackball
- In SWE, if desired, press **Set** key and roll trackball to resize the ROI

Perform Acquisition

- Perform acquisition during suspended respiration, neither deep inspiration nor expiration; patient may resume normal breathing after audible “beep” is heard
- To begin acquisition, press **Update** on the control panel; an audible tone indicates when the acquisition ends

Store Measurement Result

- ACUSON Sequoia pSWE
  - The **Liver Site 1** label is automatically selected; change the measurement label if desired on the touch screen
  - Press **Image** to store an image, or Press right or left **Set** key to store the measurement without storing an image
- ACUSON Sequoia SWE
  - Press **Caliper** to enter measurement workflow
  - Select desired measurement label on the touch screen
  - Roll the trackball to position measurement caliper

- If needed, rotate **ROI Diameter** control to resize measurement caliper
- Press **Image** to store an image, or Press right or left **Set** key to store the measurement without storing an image
    - ACUSON S2000 and S3000 systems
- Select desired measurement label on the touch screen
- Press **Image** to store an image, or Press right or left **Set** key to store the measurement without storing an image

Study Conclusion

- Acquire and store 10 total valid measurements at the same imaging location
- Select Report on left side of touch screen
- Ensure IQR/Median is less than 0.3

Outlier Identification specifications and instructions for use:

The ACUSON Sequoia pSWE and ACUSON S2000/S3000 VTQ measurements display X.XX m/s when the threshold for measurement quality was not reached. Users should discard those measurements and repeat the acquisition until the system displays a numerical value.

The ACUSON Sequoia SWE image provides a Quality map to confirm that shear wave generation was adequate and identify regions of the shear wave image where shear wave velocity or elasticity estimations may be incorrect due to poor shear wave signal quality. To view the quality map, rotate the **Shear Wave** control from **Velocity** to **Quality**. The measurement caliper should be placed in regions of the highest visible quality and near the center of the acquisition ROI.

Ensure overall IQR/Median ratio for acquired measurements is less than 0.3 as provided in the patient report.

Supersonic Imagine

Supersonic Imagine

Manufacturer Name:
SuperSonic Imagine

Equipment Model:
Aixplorer®

Software Version:
Most recent version released: V11.1.1

Transducer(s) to be used:
SC6-1 from version V3.0 to V11.1
XC6-1 from version V9.3.1 to V11.1

1. Number of values averaged for each pixel in the color image:
   The number of values averaged for each pixel depends on imaging parameters.
   Operator-adjustable parameters are:
   - Map persistence: the operator can change the number of frames averaged from 1 to 3
   - Map smoothing: this spatial filtering uses sizeable 2D areas to calculate and display one pixel value on the color image. The size of this 2D area ranges from 3x3 to 19x19, the default size being 11x11 values.

2. Average Variance per pixel:

Acquisition Procedures:

5. Instructions – Pre-requisites
   Optimal acoustic window should be found, assessed on grayscale imaging, prior to engaging SWE™ Mode by appropriate patient's positioning and proper probe holding.
   a. Patient's positioning:
      i. Patient is placed in supine position to favor acquisitions and measurements on the right liver lobe
      ii. Right arm in maximum abduction
      iii. Change to left lateral decubitus only when necessary
   b. Probe holding
      i. Acquisitions and measurements should be preferably performed on the right liver lobe via intercostal access
      ii. Probe should be placed parallel to the intercostal space to avoid shadowing from the ribs
      iii. Probe should be held orthogonal to the liver capsule to maximize ultrasound transmission, shear wave generation and shear wave propagation recording
      iv. When scanning intercostally, extra pressure should be applied on the probe to:
         1. Enlarge intercostal space
         2. Decrease subcutaneous fat thickness
         3. Ensure optimal contact between the probe and patient's thoracic wall

   Image stabilization must be achieved before freezing the image
   - Motion from the operator and the probe must be avoided
   - Appropriate patient's normal breath hold for 3-4 seconds must be achieved

6. Instructions – SWE Acquisition
   a. ROI positioning
      i. The colored SWE Box should be positioned:
         1. At a minimum depth of 2 cm from the liver capsule,
         2. Ideally enabling measurements between 3 to 7 cm in depth,
         3. Over morphologically homogeneous, vessel-free, liver parenchyma
      ii. The Q-Box™ ROI should be placed:
         1. In the central area of the SWE Box; borders of the SWE Box should be avoided.

2. Over an area of relative homogeneous elasticity, avoiding recognizable artifacts
3. From V10.0, use the stability index to reject any location for which the SI would be < 90%

b. ROI size [See specifications in Profile Section 3.10.2]
The SWE default settings have been optimized for the assessment of liver fibrosis. Default settings should be used first, and adjusted only when necessary.
   i. The default size of the SWE Box is 2 cm in height and 3 cm in width.
   ii. The default size of the Q-Box ROI may be enlarged to encompass the largest quantification area possible, while ensuring no vessels, no parenchyma heterogeneity and no artifact are included.

c. Number of measurements
   i. Because of the large amount of SWS measurements included in 1 Q-Box ROI, a total number of 3 valid measurements* performed on 3 independent valid acquisitions are recommended.
   ii. The average value of 3 valid measurements* can be considered as the estimation of SWS for a given patient.

* Invalid measurements obtained with XC6-1 probe from V10.0 must be defined as measurements obtained with a Stability Index < 90%. Invalid measurements obtained with SC6-1, regardless of software version, or XC6-1 probe before V10.0 software release must be defined as measurements obtained from unstable SWE map evaluated as non-reliable acquisitions.

7. Pitfalls
   a. Usual limitations of conventional ultrasound apply to SWE™ mode
      i. Narrow intercostal spaces,
      ii. Thick layer of fat,
      iii. Highly attenuating medium, low echogenicity
   b. Several clinical factors influence liver stiffness measurements, and should be considered when assessing liver SWS:
      i. Respiration, deep breath
      ii. Central venous pressure
      iii. Intrahepatic cholestasis
      iv. Hepatic necro-inflammatory activity
      v. Peliosis hepatitis
      vi. Hepatic vein thrombosis
      vii. Congestive hepatopathy

Outlier Identification specifications and instructions for use:

Acquisitions that are performed in sub-optimal acoustic conditions should be discarded and may present high risk for generating unreliable SWS measurements and outliers. Such sub-optimal conditions are:

- Lack of acoustic coupling and reduced acoustic transmission,
- Unstabilized grayscale and/or SWS image, particularly due to lack of breath control,
- Large highly attenuating or hypoechoic areas, especially from ribs shadowing.

Acquisitions that are unstable as illustrated by SWS maps being highly unstable over time, or with varying color patterns, should be considered as unreliable acquisitions and should be discarded. Such unreliable acquisitions may present high risk for generating unreliable SWS measurements and outliers.

Unreliable measurements and outliers should be expected in areas close to major hepatic vessels, focal liver nodules, and any visible structure on grayscale ultrasound that looks different from liver parenchyma.

Ultrasound System	No Fibrosis or Minimal Fibrosis (METAVIR F0-F1)	Moderate Fibrosis (METAVIR F2 and F3)	Severe Fibrosis/Cirrhosis (METAVIR F3 – F4)
System A			

Other

Other

Appendix E: Primary Checklists for Profile Execution and Conformance

See the Microsoft Excel file in this folder for the checklists. A link is given below:
Appendix E - clean version for public.xlsx

Appendix F: Secondary Checklists for Profile Execution and Conformance

Appendix G: Patient information sheet and Data collection.

Standardized case report form for Elastography studies

Subject ID: _____

A. Patient Demographics

1. Gender M F
2. Age (years) _____
3. Patient Fasting Yes No
   Hours _____
4. Height (inches) _____
5. Weight (pounds) _____

B. Clinical Data

1. Confounders:
   a. Right Heart Failure Yes No
   b. Steatosis (on US) Yes No
   c. Elevated markers for inflammation Yes No

2. Reason for Exam

☐ Elevated LFT's?

☐ **F/U Known Hx of Liver Disease**	☐ **Diagnostic for Fibrosis**
☐ HCV	☐ **?NASH**
☐ HBV	☐ **?AIH**
☐ HIV + HCV	☐ **?Drug Toxicity** _____
☐ AIH _____	
☐ Alcoholic Liver Disease	
☐ Healthy volunteer	
☐ Other _____	

C. **Serum Biomarkers** (If evaluated)

i. Platelets (x10^9/L) _____
ii. AST (IU/L) _____
iii. ALT (IU/L) _____
iv. Alkaline phosphatase _____
v. Total Bilirubin (μ mol/L) _____

Automated Calculations from above values:

1. AST/ALT ratio
2. APRI
3. Fib-4

Optional

FibroSURE _____

D. SWS Examination

Depth of liver capsule from skin _____

Measurement No.	Depth of measurement from capsule (cm)	SWS (m/sec)	Comments
1			
2			
3			
4			
5			
6			
7			
8			
9			
10			

IQR/Median Value: _____

References (Steatosis has no effect):

1. Yoneda M, Mawatari H, Fujita K, Endo H, Nozaki Y, Yonemitsu K, et al. Noninvasive assessment of liver fibrosis by measurement of stiffness in patients with nonalcoholic fatty liver disease (NAFLD). Dig Liver Dis [Internet]. 2008 May; 40(5):371–8. Available from:http://eutils.ncbi.nlm.nih.gov/entrez/eutils/elink.fcgi?dbfrom=pubmed&id=18083083&retmode=ref&cmd=prlinks

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3. Lupsor M, Badea R, Stefanescu H, Sparchez Z, Branda H, Serban A, et al. Performance of a new elastographic method (ARFI technology) compared to unidimensional transient elastography in the noninvasive assessment of chronic hepatitis C. Preliminary results. J Gastrointestin Liver Dis. 2009 Sep;18(3):303–10.

4. Fierbinteanu-Braticevici C, Andronescu D, Usvat R, Cretoiu D, Baicus C, Marinoschi G. Acoustic radiation force imaging sonoelastography for noninvasive staging of liver fibrosis. World J Gastroenterol [Internet]. 2009 ed. 2009 Nov 28;15(44):5525–32. Availablefrom:http://eutils.ncbi.nlm.nih.gov/entrez/eutils/elink.fcgi?dbfrom=pubmed&id

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