RSNA/QIBA Ultrasound Shear Wave Speed Biomarkers Committee

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ORGANIZATION & QIBA PROFILE

1. **Organizational structure updates**, e.g., brief description of new Biomarker Committees, Task Forces (i.e., Profile writing groups) or new biomarkers being considered, etc.

QIBA Steering Committee recently implemented the following organizational changes:

A. **Coordinating Committees (CC)** will replace Modality Committees. The CCs will be responsible for the oversight and planning of all activities within the modality to ensure alignment with the overall QIBA goals and processes. If Co-chair leadership was deemed more appropriate, this model could be accommodated as well.
   - **CC Chair / Vice Chair** to be solicited from the QIBA membership
   - **CC members** can be self-nominated.
   - **CCs** will meet by teleconference at least quarterly.
   - **Voting:** As established by the Steering Committee (SC), voting privileges will require participation in two consecutive teleconferences.

B. **Biomarker Committees (BC)** will replace Technical Committees, but will function the same way.
   - **BC Co-chairs** to be solicited from the QIBA membership
   - **BC members** can be self-nominated
   - **BC** will host bi-weekly, etc teleconferences
   - **Voting:** As established by the Steering Committee (SC), voting privileges will require participation in two consecutive teleconferences.

C. **Task Force Groups (TFG)** will replace all other subcommittees, writing groups and working groups.

2. **Profile Development - status update**

A profile is the QIBA document that describes the method to be used to make QIBA compliant measurements of a quantitative biomarker such as SWS. The first complete draft of the ultrasound shear wave speed profile was completed in May 2015 by the profile writing task force. A copy was sent to the US SWS biomaker committee members for comment. The claims section of the profile contains placeholders for bias and variance claims pending the results of the phase II phantom test analysis.

The QIBA process committee has since drafted a revised version of the profile template and work has commenced on a new version of the profile. This version will have a more complete claims section and will conform to the style and language of the new template. A first draft of a section outlining the manner in which compliance with the profile is determined will be added to the new profile version. In addition, appendices contain SWS acquisition protocols and drafts of manufacturer specific guidance for acquisition with each type of ultrasound scanner capable of measuring SWS.

3. **Conformance procedure update**

The first version of this document will be drafted as part of the new version of the profile currently being written.

4. **Groundwork project status/results follow**
   - **A. US SWS Technical Projects**
   - **B. US SWS Clinical Project**

Quantitative Imaging Biomarkers Alliance

RSNA

A. US SWS TECHNICAL PROJECTS

PHASE II VISCOELASTIC PHANTOM STUDY

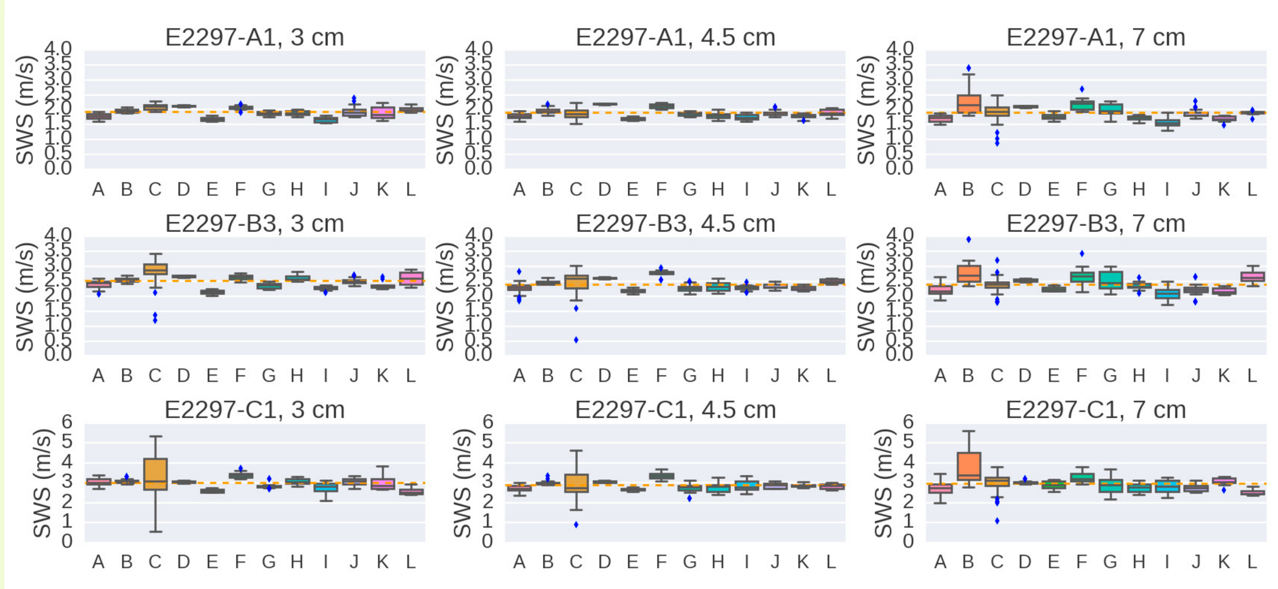
Objective

Perform a comparison of shear wave speed (SWS) measurements between commercially-available systems using calibrated phantoms that have viscoelastic behavior similar to that observed in normal and fibrotic liver.

Methods

- CIRS, Inc. (Norfolk, VA) fabricated 3 phantoms (E2297-A1, -B3, -C1) using a proprietary oil-water emulsion in a Zerdine® hydrogel.
- The phantoms were characterized by phase velocity at 200 Hz and linear dispersion slope (dc/df) from 100–400 Hz to provide a metric of their dispersion.
- These metrics were compared to *in vivo* human SWS measurements with different degrees of fibrosis acquired at Duke and the Mayo Clinic/Philips Research, and the phantoms represent: healthy liver (A1), mildly fibrotic (B3) and significantly fibrotic (C1) tissue.
- The phantoms were shipped to and measured at academic, clinical, government and vendor sites using different systems with curvilinear arrays at multiple focal depths (3.0, 4.5 and 7.0cm).

Vendor System Model
General Electric (phantom mode) LOGIQ E9
Hitachi Aloka HI VISION Ascends
Philips Epiq
Philips IU22
Samsung Medison RS80A
Siemens S2000
Siemens S3000
SuperSonic Imagine Aixplorer
Toshiba Aplio 500
Zonare ZS3



Results

SWS measurements for each system (randomized order) in each phantom for each focal depth. Each box plot represents the 25th–75th percentile range of all measurements made with that system (potentially at multiple sites), with the black horizontal line in each box representing the 50th percentile. The whiskers extend to include 1.5× the IQR of the measurement data, with outliers represented as individual points beyond that range. The dashed orange line in each plot represents the grand median across all of the systems for that specific phantom and focal depth. Notice that the range of SWS for each row of plots is held constant, but varies as a function of each phantom.

Conclusions

1. All of the current-generation ultrasound SWS measurement systems were able to report SWS that differentiated each of the viscoelastic materials tested in this study.
2. The deepest focal depth yielded the greatest inter-system variability for each phantom (maximum of 17.7%) as evaluated by IQR.
3. Inter-system variability was consistent across all 3 phantoms and was not a function of stiffness.
4. Median SWS estimates for the greatest outlier system in each phantom/focal depth combination ranged from 12.7–17.6%.

DIGITAL PHANTOM STUDY

Objective

Create Finite Element Method (FEM) simulation data matching the viscoelastic Phase II phantoms for a variety of focal configurations to test shear wave estimation algorithms.

Deliverable

Source code for elastic and viscoelastic simulations are available at ***https://github.com/orgs/RSNA-QIBA-US-SWS/***

The digital phantom datasets are available at ***https://qidw.rsna.org***

ROUND IV CLINICAL STUDY

Ultrasound Shear Wave Speed Elastography

Variations of fibrosis assessment as a function of depth, force and distance from central axis of the transducer with a comparison of different systems.

Abstract submitted for 2016 annual AIUM convention

Purpose of the Study

To evaluate the accuracy of ultrasound elastography in the assessment of fibrosis using different systems, and to assess variation at different depths, forces and distance from central axis of the transducer.

Material and Methods

In this IRB approved single-institution prospective study, 20 patients underwent ultrasound elastography assessment on 3 systems (FibroScan, Siemens, Supersonic). All subjects had undergone non-focal liver biopsy within the past 6 months as part of their clinical care. ARFI and SWE measurements were obtained at five different positions in the liver (3, 5, 7cm from the skin and 2cm, 4cm off axis). ARFI and SWE measurements were also obtained under 3 different pressures applied to the probe (4 Newton, 7 Newton and 10 Newton) at 5cm depth. Fibroscan was also performed on the same day. A single blinded pathologist, scored for fibrosis (F0-F4) using the METAVIR criteria. Spearman correlations of shear wave speed with fibrosis stage were calculated and the area under the receiver operating characteristic curves (AUROC) to differentiate ≥F2 fibrosis from lesser grades (F0, F1) was charted.

Results

A total of 20 subjects (M:F=12:8) with a mean age of 54 years and varying fibrosis stages (F0=4, F1=9, F2=3, F3=2, F4=2) participated in the study. **Scanner A** values showed high correlation with the fibrosis stage (r=0.579, p=0.009) and an AUROC of 0.879 (95% CI: 0.726-1.032). For **Scanner B** system, there was a statistically significant difference (p=0.003) between values obtained at three different depths, with the highest correlation (r=0.667, p=0.001) and AUROC (0.923, 95% CI: 0.804-1.042) at a depth of 7cm. Similarly, for **Scanner C** system, the correlation (r=0.620, p=0.004) and AUROC (0.819, 95% CI: 0.629-1.009) was highest at a depth of 7cm, but the difference across depths was not statistically significant. Variation in preload force at a 5cm measurement depth made no statistically significant difference (Table). Measurements along the central axis had the highest AUROC for both **Scanner B** (0.846, 95% CI: 0.669-1.023) and **Scanner C** (0.764, 95% CI: 0.547-0.981) systems, but this was not significantly different from measurements 2 and 4cm off-axis.

Conclusions

1. In this small study, **Scanner C** and **Scanner B** systems performed best for differentiation between advanced fibrosis (F≥2) and lesser or no fibrosis (F0, F1) at a depth of 7cm along the central axis. Further evidence is required prior to recommending a deeper measurement location than is presently standard practice.
2. Preload force variations between 4 and 10 Newtons do not appear to affect measurements made via an intercostal approach.

Acknowledgements & Disclaimers

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B. US SWS CLINICAL

		Correlation	AUROC (95% CI)	Cut-off for ≥F2	Sensitivity	Specificity	
Scanner A		0.602(p=0.005)	0.879 (0.726-1.032)	1.4125	85.7%	76.9%	
Depth Variation							
Scanner B	3cm	0.189 (p=0.425)	0.703 (0.455-0.951)	2.5725	71.4%	69.2%	p=0.003
	5cm	0.541 (p=0.014)	0.846 (0.669-1.023)	1.5050	71.4%	92.3%	
	7cm	0.667 (p=0.001)	0.923 (0.804-1.042)	1.455	85.7%	92.3%	
Scanner C	3cm	-0.032 (p=0.894)	0.61 (0.335-0.885)	2.175	71.4%	69.2%	p=0.482
	5cm	0.311 (p=0.182)	0.764 (0.547-0.981)	1.675	85.7%	69.2%	
	7cm	0.620 (p=0.004)	0.819 (0.629-1.009)	2.275	85.7%	76.9%	
Force Variation (depth of 5cm)							
Scanner B	Variable	0.541 (p=0.014)	0.846 (0.669-1.023)	1.5050	71.4%	92.3%	p=0.131
	4N	0.189 (p=0.425)	0.703 (0.474-0.933)	1.51	85.7%	53.8%	
	7N	0.24 (p=0.309)	0.714 (0.478-0.951)	1.39	71.4%	69.2%	
	10N	0.456 (p=0.043)	0.775 (0.533-1.016)	1.475	71.4%	84.6%	
Scanner C	Variable	0.311(p=0.182)	0.764 (0.547-0.981)	1.675	85.7%	69.2%	p=0.922
	4N	0.261 (p=0.266)	0.709 (0.45-0.967)	1.95	71.4%	69.2%	
	7N	0.38 (p=0.099)	0.758 (0.533-0.983)	1.625	85.7%	69.2%	
	10N	0.358 (p=0.121)	0.736 (0.502-0.971)	1.85	71.4%	69.2%	
Lateral to Center A xis (depth of 5cm)							
Scanner B	0	0.541 (p=0.014)	0.846 (0.669-1.023)	1.5050	71.4%	92.3%	p=0.131
	2cm	0.549 (p=0.012)	0.802 (0.556-1.048)	1.42	71.4%	92.3%	
	4cm	0.379 (p=0.1)	0.659 (0.381-0.938)	1.67	71.4%	69.2%	
Scanner C	0cm	0.311 (p=0.182)	0.764(0.547-0.981)	1.675	85.7%	69.2%	p=0.922
	2cm	0.374 (p=0.104)	0.725 (0.48-0.971)	2.475	57.1%	84.6%	
	4cm	0.336 (p=0.148)	0.758 (0.525-0.992)	1.875	100%	46.2%	

PARTICIPATING SITES

- Duke University, Durham, NC
- Echosens, Paris, France
- General Electric, Milwaukee, WI
- Hitach Aloka, Wallingford, CT
- Hôpitaux Universitaires Paris-Sud, Paris, France
- Institut Langevin, Paris, France
- CIRS, Norfolk, VA
- Massachusetts General Hospital, Boston, MA
- Mayo Clinic, Rochester, MN
- Michigan Technological University, Houghton, MI
- Philips Ultrasound, Bothell, WA
- Rheolution, Inc, Montreal, Canada
- Royal Marsden Hospital, London, United Kingdom
- Samsung Medison, Seoul, South Korea
- Siemens Ultrasound, Issaquah, WA
- Southwoods Imaging Center, Youngstown, OH
- Supersonic Imagine (SSI), Aix-en-Provence, France
- Toshiba Medical Research Institute, USA
- University of California at San Diego, CA
- University of Michigan, Ann Arbor, MI
- University of Rochester, Rochester, NY
- University of Wisconsin, Madison, WI
- Food and Drug Administration, USA
- Veterans Affairs Medical Center, Washington DC
- Zonare, Mountain View, CA