Achievements, Challenges, and Present Status of QIBA's Ultrasound Shear Wave Speed Biomarker Committee

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Overview

- Who/What is the Quantitative Imaging Biomarker Alliance (QIBA)?
- Why shear wave speed estimation?
- What is the goal of QIBA in this effort?
  - What is the role of physicists in this effort?
- What has been done to date?
  - What were the findings?
  - What are the implications?

Quantitative Imaging Biomarkers Alliance

- QIBA was initiated in 2007
- RSNA Perspective: *One approach* to reducing variability in medical imaging is to extract objective, quantitative results from imaging studies.
- QIBA Mission
  - Improve the value and practicality of *quantitative imaging biomarkers* by reducing variability across devices, sites, patients, and time.
  - "***Industrialize*** imaging biomarkers"

Current Status of QIBA

- Over 1,100 individuals have joined the QIBA effort
  - Representation by all major stakeholders in medical imaging
  - Over 300 individuals from at least 166 imaging device companies
  - 22 from the FDA
  - 41 from USA government (excluding FDA; 63 government agencies)
  - 33 professional societies are represented
  - Representatives from major Pharma companies
  - Representatives from contract research organizations (clinical trialist)
  - Many physicists/engineers (>400 academics), physicians (>300 radiologists), statisticians…
- Vast majority of stakeholder efforts are voluntary

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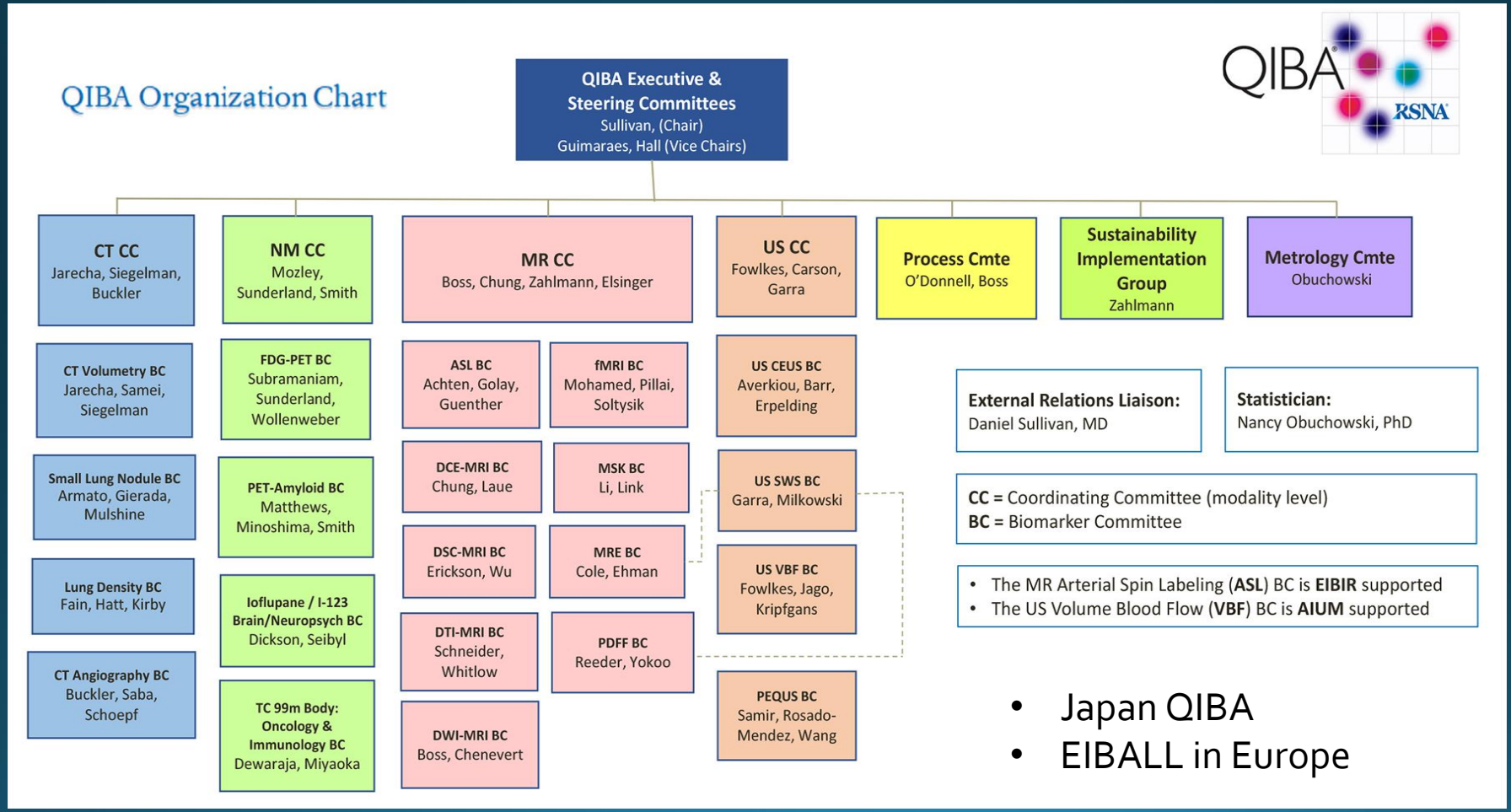
QIBA Involvement Across Modalities



- Japan QIBA
- EIBALL in Europe

Quantitative Imaging Biomarkers

Biomarkers are characteristics that are *objectively measured* and evaluated as an indicator of normal biologic processes, pathogenic processes, or pharmacologic responses to a therapeutic intervention.[1]

Quantitative imaging biomarkers (QIBs) are objective characteristics derived from *in vivo* images *measured on interval or ratio scales* as indicators of normal biological processes, pathogenic processes, or a response to a therapeutic intervention.[2]

[1]NIH Biomarkers Definitions Working Group, Clin Pharmacol Therap 69(3):89-95, 2001

[2]Kessler et al., Stat Methods Med Res, epub Jun 2014 (www.rsna.org/qiba)

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Imaging as an Assay

- Assays are defined by their:
  - Technical performance ← QIBA activities
  - Clinical performance
  - Clinical validation
  - Clinical utility

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QIB Challenges

Diagnostic Imaging Equipment ≠ Measurement Device

- Measurement Device:
  - Specific measurand(s) with known bias and variance (confidence intervals)
  - Specific requirements for reproducible quantitative results
  - Example: thermometer – many kinds for different applications
- Diagnostic Imaging Equipment:
  - Historically: best image quality in shortest time (*qualitative*)
  - No specific requirements for reproducible *quantitative* results (with few exceptions)

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Goal of QIBA

In a word: *Reproducibility*

- Estimate and increase the reproducibility of Quantitative Imaging Biomarkers (QIBs) across imaging centers, imaging equipment, participants, and time

➢ Convert "imaging systems" into "measurement systems" and maximize their performance

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Objectively Assessing Tissue 'Softness'

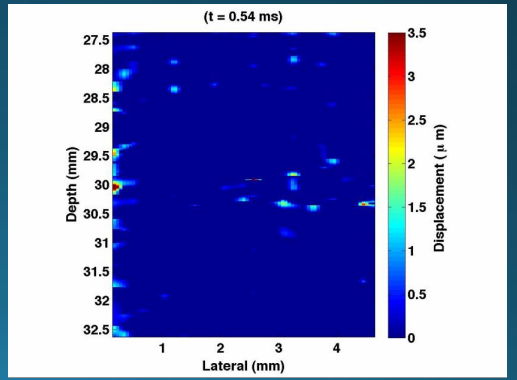
Elasticity imaging techniques in wide-spread use in radiology and hepatology (liver fibrosis)[1]

$$F = \frac{2\alpha I}{c_L}$$

Shear wave elasticity imaging

- Push tissue remotely with long duration (100μs) ultrasound pulse
  - Typical ultrasound pulse is sub-microsecond
  - Force from a long pulse excites a shear wave
- Track tissue displacement (wave motion) perpendicular to push
  - Shear waves travel ~1-10m/s
  - Acoustic waves travel ~1540m/s
- Shear wave speed related to shear modulus
  - $c_s^2 = \mu / \rho$ $\quad$ $(SWS)^2$ = modulus / density

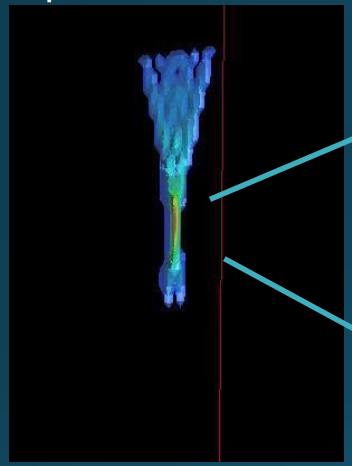
Dan Russell http://www.acs.psu.edu/drussell/demos.html



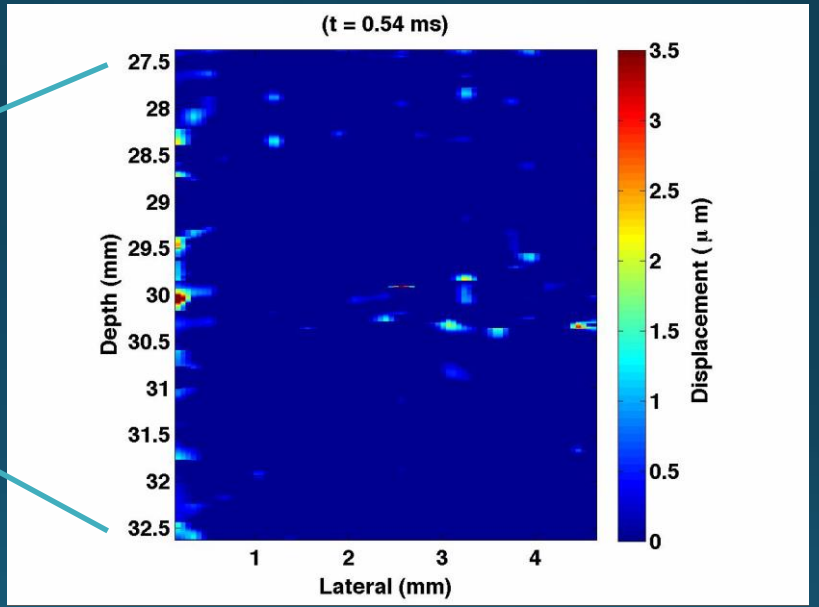
[1] Ferraioli G, et al.. UMB 2015 May 1;41(5):1161-79.

Simulated Shear Wave in Homogeneous Medium

Simulated acoustic pressure field



$$F = \frac{2\alpha I_{ta}}{c}$$



Palmeri et al "A finite element method model of soft tissue response to impulsive acoustic radiation force", *IEEE UFFC*, 52(10): 1699-1712, 2005.

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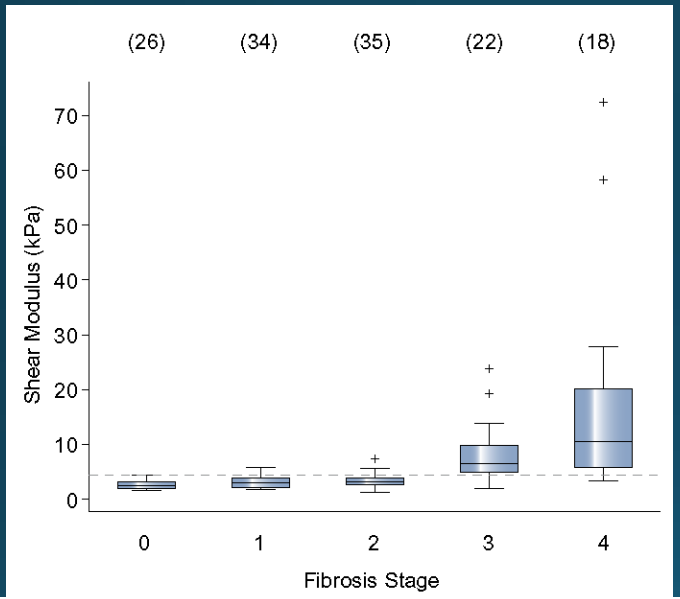
Shear Modulus vs. Fibrosis Stage



Noninvasive evaluation of hepatic fibrosis using acoustic radiation force-based shear stiffness i Journal of Hepatology **2011** vol. 55 | 666–672
with nonalcoholic fatty liver disease

Mark L. Palmeri[1,*], Michael H. Wang[1], Ned C. Rouze[1], Manal F. Abdelmalek[2], Cynthia D. Guy[3], Barry Moser[4], Anna Mae Diehl[2], Kathryn R. Nightingale[1]

[1]*Department of Biomedical Engineering, Duke University, Durham, NC, USA;* [2]*Division of Gastroenterology and Hepatology, Duke University Medical Center, Durham, NC, USA;* [3]*Department of Pathology, Duke University Medical Center, Durham, NC, USA;* [4]*Department of Biostatistics and Bioinformatics, Duke University Medical Center, Durham, NC, USA*

SWS Threshold
4.24 kPa Fo-2:F3-4

90% sensitivity
90% specificity
0.90 AUC

This threshold is system dependent

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Goal of QIBA

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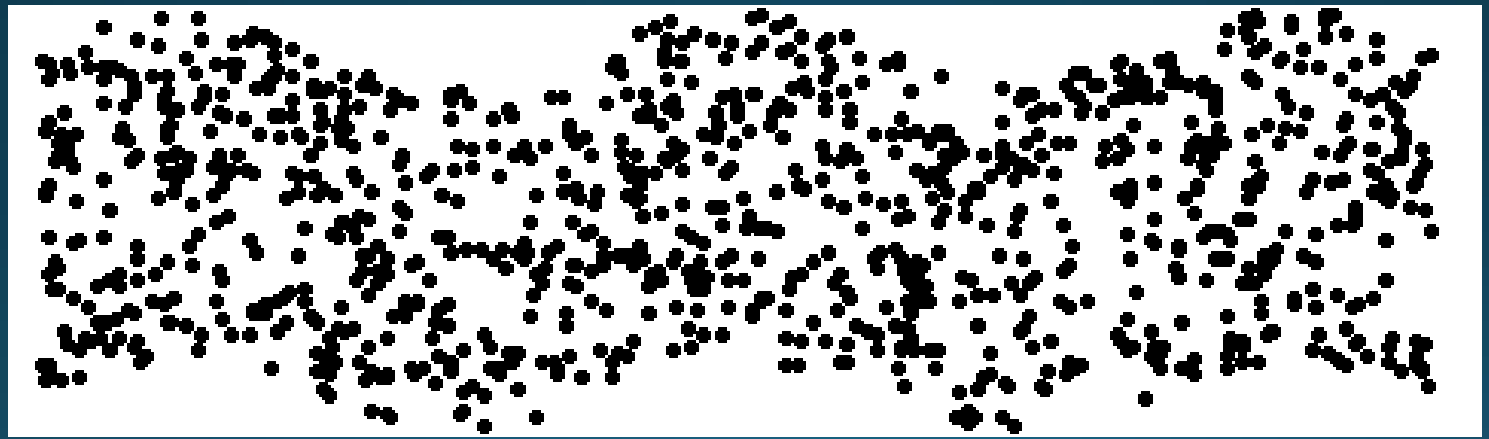
What is the Role of a Physicist?

- Think of this as a metrology problem
  - What is the fundamental *thing* we're trying to measure?
  - What are the components of variance in the estimate?
  - How do we minimize estimate bias?
- Fundamentally, we're studying wave mechanics
- How do we model the phenomenon?
  - Does the model fit the data?
  - Can we use it to interpret results?
    - Can we estimate the real (elastic; storage modulus) and imaginary (viscous; loss modulus) components of the complex shear modulus?

Motion Tracking for SWS Estimation

Should we track particle displacement or particle velocity?

Does (should) it matter?



Dan Russell http://www.acs.psu.edu/drussell/demos.html

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QIBA SWS Studies

- Uniform shear wave elastography phantoms provided by CIRS
  - Two stiffness – nearly lossless ('elastic') phantoms[1]
  - Three stiffness – viscoelastic (lossy) [2]
- 12 sites around the world involved in data acquisition
  - Multiple commercial systems at some sites
- Commercial ultrasound systems from
  - Canon (Aplio 500)
  - Echosens (Fibroscan)
  - GE Logiq E9
  - Hitachi (HiVision Ascendus)
  - Philips (Epiq 5)
  - Samsung (RS80)
  - Siemens (ACUSON S2000)
  - Supersonic Imagine (Aixplorer)
  - Plus several experimental systems in academic labs + MRE (shear modulus inversion) [3, 4]

[1]Hall TJ, et al. IEEE International Ultrasonics Symposium (IUS) 2013 Jul 21 (pp. 397-400).
[2]Palmeri M, et a. IEEE International Ultrasonics Symposium (IUS) 2015 Oct 21 (pp. 1-4).
[3]Muthupillai R, et al. Science. 1995 Sep 29;269(5232):1854-7.
[4]Sarvazyan A, et al. Current Medical Imaging. 2011 Nov 1;7(4):255-82.

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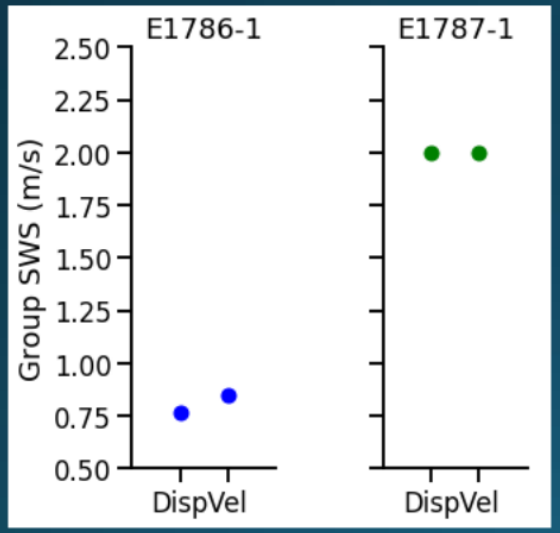
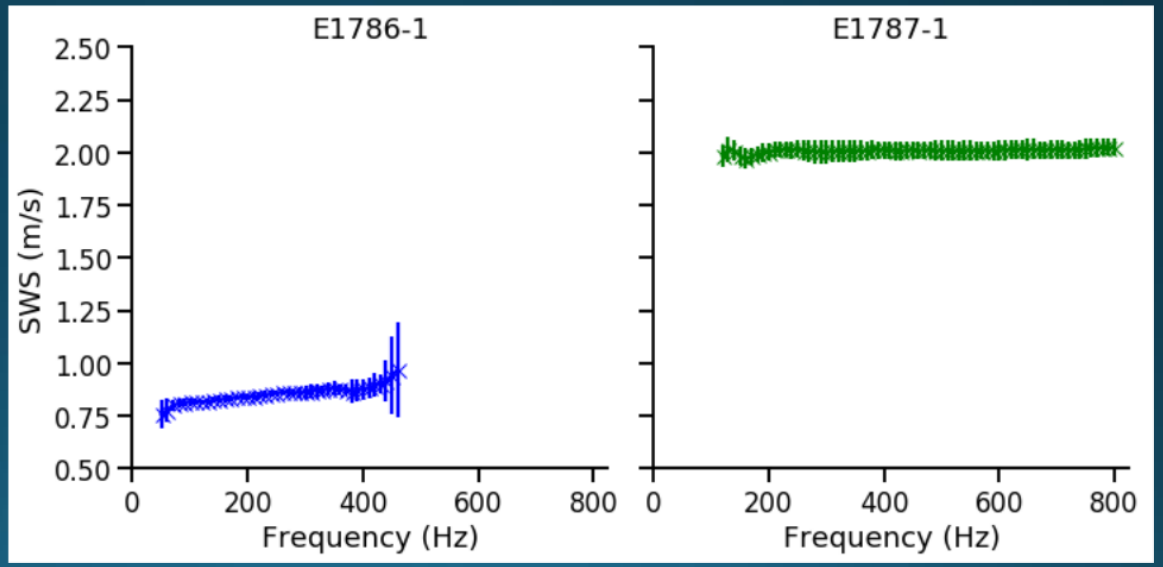
Wave Speed Estimation

(Nearly) Lossless Material

Group Shear Wave Speed



Phase Shear Wave Speed



Little difference in SWS with Displacement-based v Velocity-based SWS Estimates

Phase Speed Nearly Independent of Frequency

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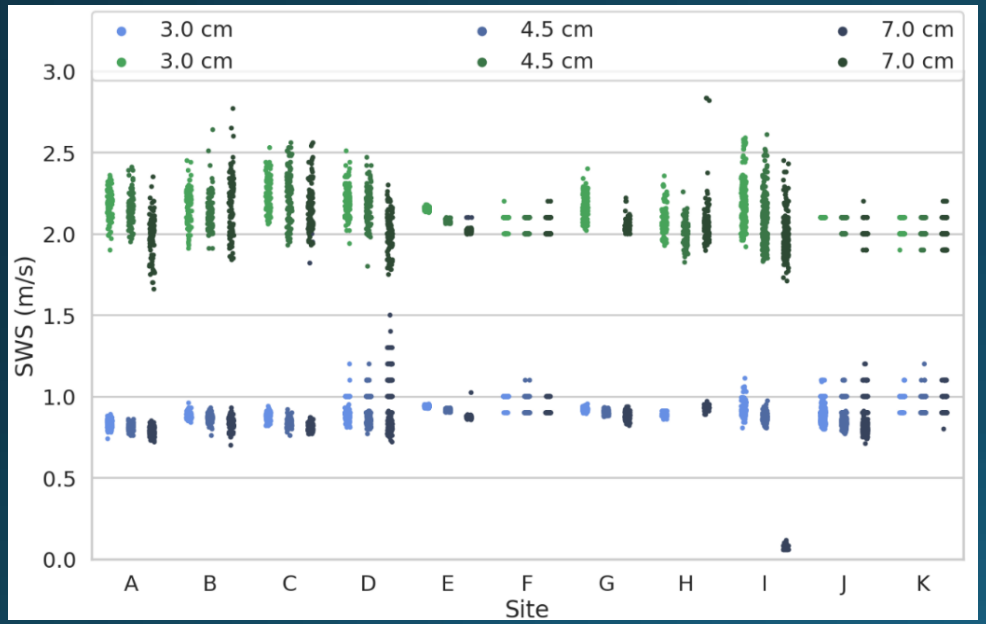
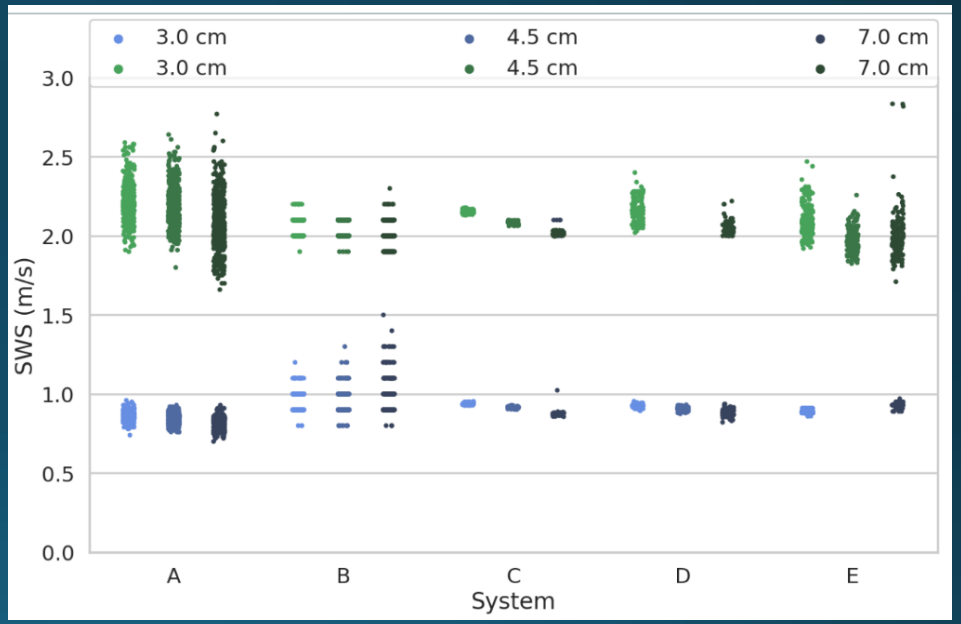
Elastic (Lossless) Phantom Results

Grouped by Site



Grouped by System



Note the depth-dependent estimates for some systems

~5% range in median SWS among systems

Hall TJ, et al. IEEE International Ultrasonics Symposium (IUS) 2013 Jul 21 (pp. 397-400).

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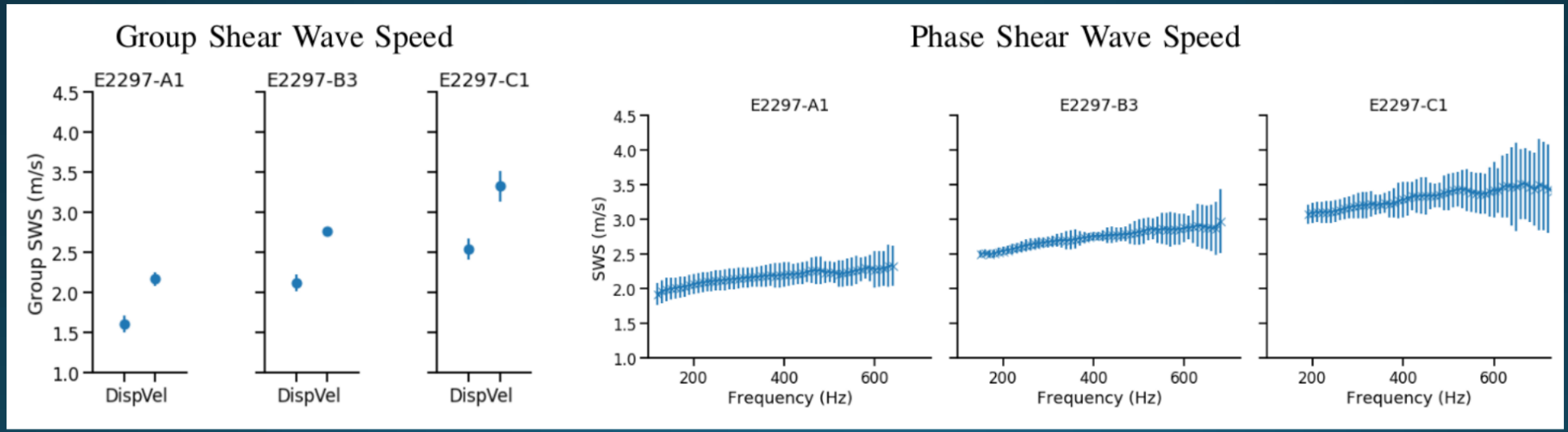
Wave Speed Estimation

Lossy (Viscoelastic) Material



Large difference in SWS with Displacement-based v Velocity-based SWS Estimates

Phase Speed is Frequency-Dependent

Nightingale KR,et al. IEEE UFFC 2015 Jan 12;62(1):165-75.
Palmeri M. et al. UMB 2019 Jan 1;45:S24.

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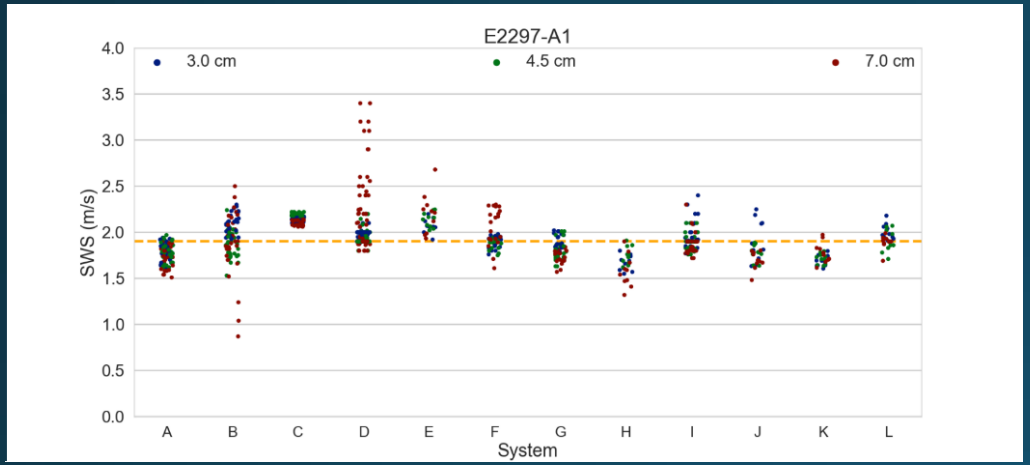
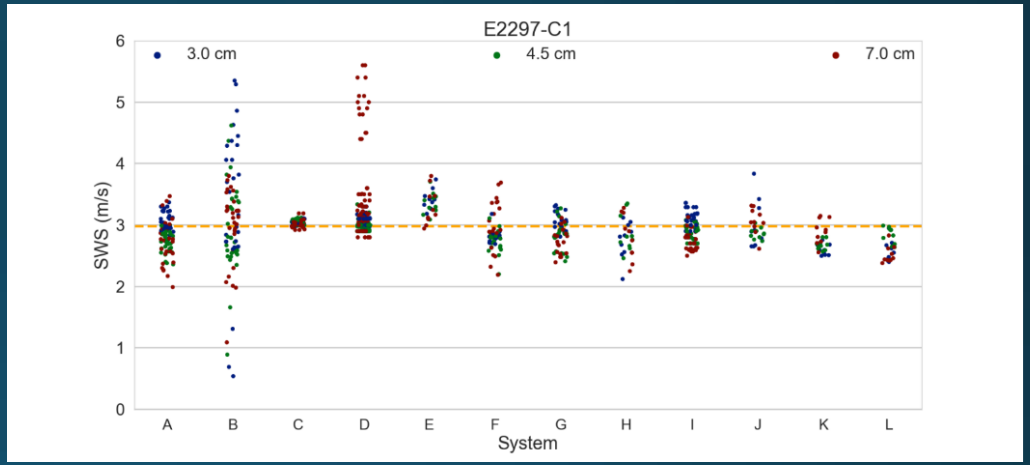
Visco-Elastic Phantom Results



Softer Phantom



Stiffer Phantom

~15% range in median SWS among systems

Palmeri M, et a. IEEE International Ultrasonics Symposium (IUS) 2015 Oct 21 (pp. 1-4).

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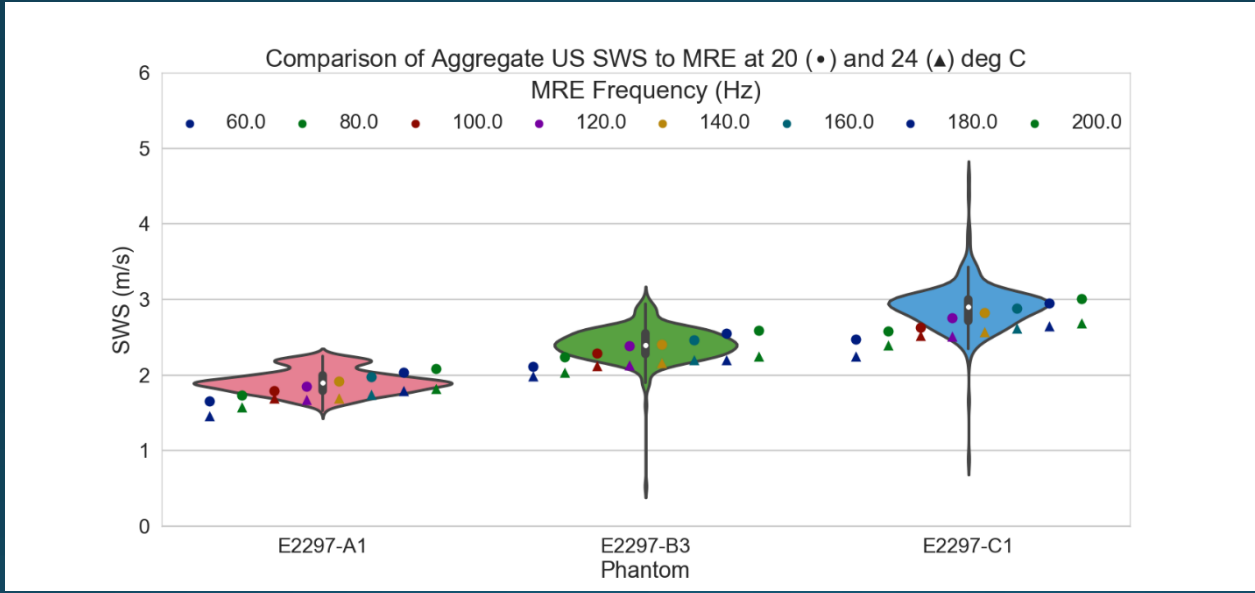
MRE vs US SWS



Violin plot combining all ultrasound SWS data for each phantom

MRE typically performed at 60 -- 80 Hz in human liver
MRE and Ultrasound agree when MRE is performed at ~140 Hz

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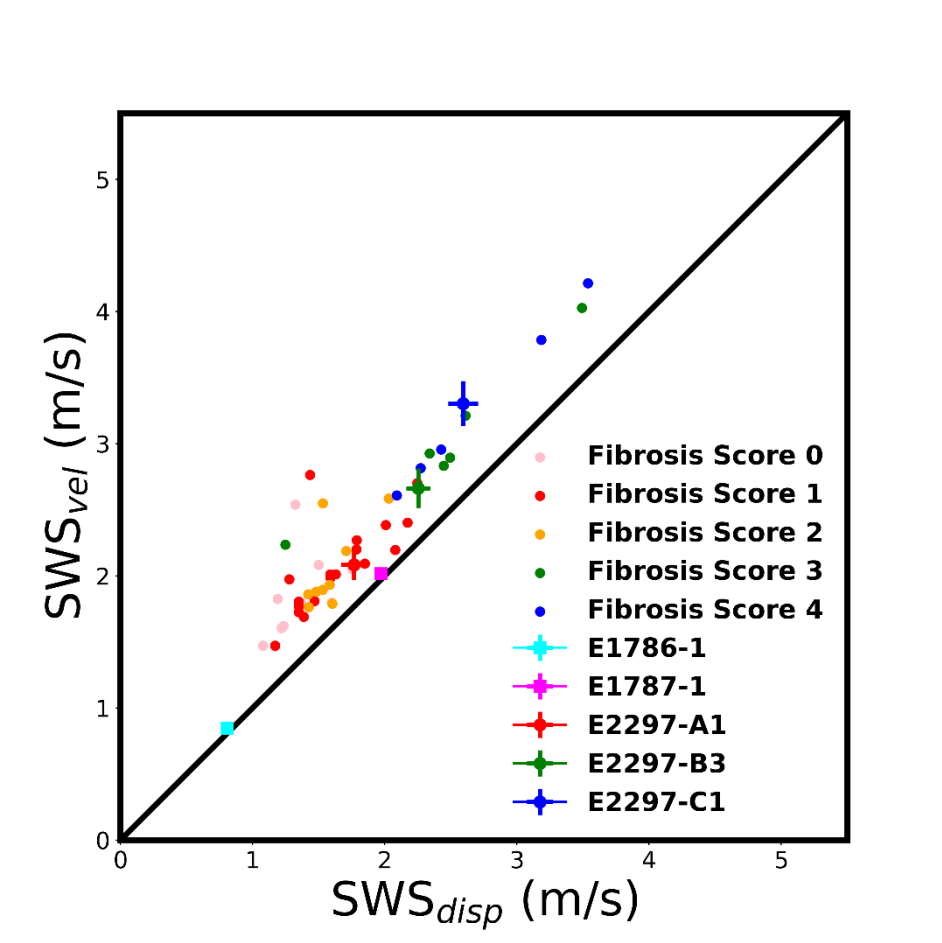
Phantom SWS Estimates v Human Liver



Viscoelastic phantoms are a reasonable representation for in vivo human liver

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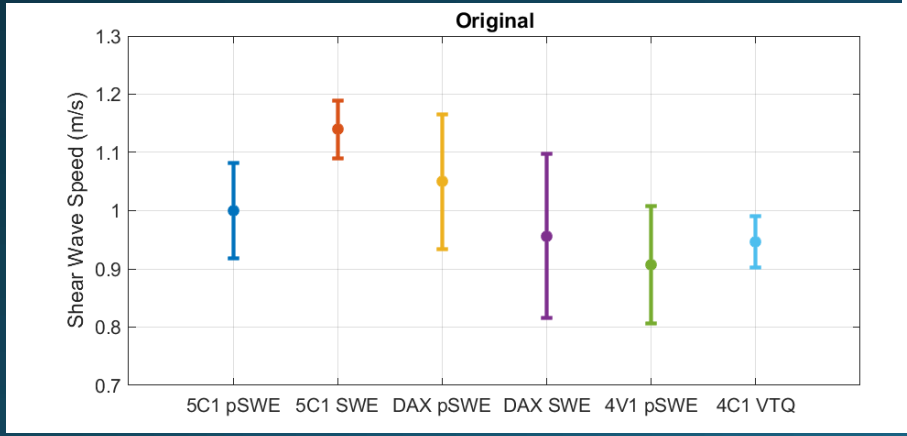
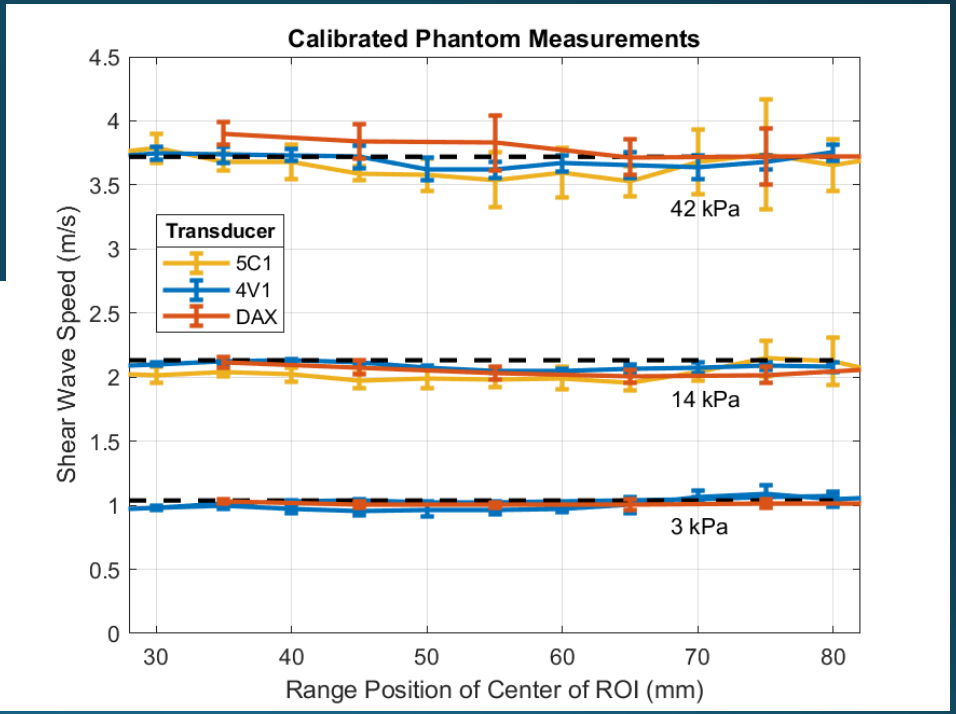
Next Steps for Manufacturers

One manufacturer has modified their SWS estimation algorithms to provide equivalent SWS estimates with all their transducers





SWS estimates are depth-independent

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Summary

- The Quantitative Imaging Biomarker Alliance (QIBA) is an international organization involving all stakeholders in medical imaging
- Shear wave speed (SWS) estimated with commercial ultrasound systems is an alternative to serial biopsy for assessing liver fibrosis
- QIBA efforts are intended to increase the reproducibility of SWS estimates across imaging centers, imaging equipment, participants, and time
- The physicists' role in this is to approach the problem like any other metrology problem
- We have demonstrated that the perceived clinical variability in SWS estimates is likely not due to the imaging systems (technical performance)
  - SWS estimates in 'elastic' materials within about 5% among commercial systems
  - SWS estimates in viscoelastic materials within about 15% among commercial systems
  - We can do better than that!

Acknowledgments

- RSNA and RSNA QIBA Staff
- RSNA QIBA Process Committee & Metrology Working Group
- Ted Lynch (CIRS) - Shear wave imaging phantoms
- QIBA SWS Biomarker Committee & Task Force Co-Chairs & Members
- NIBIB Contracts HHSN268201000050C, HHSN268201300071C, HHSN268201500021C

www.rsna.org/qiba qibawiki.rsna.org

NIH National Institute of Biomedical Imaging and Bioengineering

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