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?
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
QIBA Involvement Across Modalities

- Japan QIBA
- EIBALL in Europe
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

Imaging as an Assay

• Assays are defined by their:
  • Technical performance ← QIBA activities
  • Clinical performance
  • Clinical validation
  • Clinical utility
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)
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
Objectively Assessing Tissue ‘Softness’

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

Shear wave elasticity imaging

- Push tissue remotely with long duration (100\(\mu\)s) 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 \(\sim\)1-10m/s
  - Acoustic waves travel \(\sim\)1540m/s
- Shear wave speed related to shear modulus
  - \(c_s^2 = \mu / \rho\) \((SWS)^2 = \text{modulus} / \text{density}\)


\[ F = \frac{2\alpha I_{ta}}{c} \]
Shear Modulus vs. Fibrosis Stage

SWS Threshold
4.24 kPa Fo-2:F3-4
90% sensitivity
90% specificity
0.90 AUC

This threshold is system dependent
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
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?
Should we track particle displacement or particle velocity?

Does (should) it matter?

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

- Uniform shear wave elastography phantoms provided by CIRS
  - Two stiffness – nearly lossless (‘elastic’) phantoms
  - Three stiffness – viscoelastic (lossy)
- 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)

1Hall TJ, et al. IEEE International Ultrasonics Symposium (IUS) 2013 Jul 21 (pp. 397-400).
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
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

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Wave Speed Estimation

Lossy (Viscoelastic) Material

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

Phase Speed is Frequency-Dependent

Visco-Elastic Phantom Results

~15% range in median SWS among systems

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
Viscoelastic phantoms are a reasonable representation for in vivo human liver
One manufacturer has modified their SWS estimation algorithms to provide equivalent SWS estimates with all their transducers.

SWS estimates are depth-independent.
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!
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