QIBA Newsletter

Quantitative Imaging Biomarkers Alliance — RSNA

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QIBA MISSION: Improve the value and practicality of quantitative imaging biomarkers by reducing variability across devices, patients and time.

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Edward F. Jackson, PhD, QIBA Chair

IN MY OPINION

An Oncologist's View of Quantitative Imaging

By James L. Mulshine, MD

As a medical oncologist interested in lung cancer, defining an optimized imaging process is actually essential in allowing responsible integration of quantitative tools either for clinical research or for routine care, especially as it provides an exciting new window in the management of early lung cancer.

Lung cancer remains the most lethal of the cancers, but we now have federal reimbursement for low-dose CT screening of eligible individuals to identify early and potentially curable cancers. As a result, high-risk individuals are now participating in lung cancer screening programs. Practice guidelines have emerged that base screening management on the size of the pulmonary nodules, and screening participants found to have only non-calcified nodules smaller than 6 mm in diameter are asked to return a year later for repeat analysis. Individuals found to have nodules larger than 6 mm in diameter are recommended to undergo a more intensive diagnostic evaluation. This size threshold for guiding the screening work-up approach has resulted in efficient lung cancer screening. However, as this screening practice is being disseminated nationally, how confident are we that this type of size discrimination can be reliably scaled beyond the research setting?

To mitigate this concern, a new QIBA [CT Lung Nodule Volumetry Profile](#) defines a process for CT nodule quantification to minimize variance in these measurements based on available sources of information regarding factors contributing to measurement noise. As demonstrated in Table 1, which is extracted from the Small Lung Nodule Profile, with smaller nodule size the noise in the measurement increases. We now also know that a smaller lung cancer is more likely to be a curable lung cancer, so measurement precision is critical.

At the recent RSNA Annual Meeting, the Small Pulmonary Nodule Profile group presented an approach to quantitative imaging quality control that could be quickly and economically scaled. One member of this profile group, Rick Avila, developed a software tool to assess the imaging platform acquisition settings for nodule size characterization. This involved having screening sites image an array of three simple inexpensive reference objects positioned across the table of the scanner used for lung cancer screening. In a pilot study, this approach was explored in a crowd-sourcing exercise with a number of screening sites. Analysis of the reference images provided a means of determining if the CT imaging site could achieve the level of accuracy required to be in conformance with the parameters specified in the Small Lung Nodule Profile. Further, this analysis can generally indicate the source of quantitative variance, allowing the site to improve the imaging performance and potentially achieve conformance with the Small Nodule Profile. The crowd-sourcing experiment involved over 50 international sites and found that the majority could experience significant improvement in the quality of their quantitative analyses by using these simple tools to change acquisition parameters, such as slice thickness.

From a thoracic oncology perspective, this quality control improvement has important implications. Success in applying this quality control approach in a Phase II trial may mean that a smaller trial size could be used as more consistent fully evaluable imaging results will be obtained. In addition, the treatment interval may be shortened because the confidence in measuring small changes in volume may also be improved. As thoracic oncology is currently experiencing not only the emergence of CT screening but also

an explosion of new molecularly targeted drugs, the opportunity to integrate robust quantitative imaging techniques to assess the intrathoracic impact of these approaches could not have come at a better time.

Table 1. Coefficient of Variation as a Function of Nodule Size

Nodule Diameter (mm)	Nodule Volume (mm^3)	Coefficient of Variation (CV)
≥ 6 and < 8 mm	≥ 113 and < 268	0.29
≥ 8 and < 10 mm	≥ 268 and < 524	0.19
≥ 10 and < 12 mm	≥ 524 and < 905	0.14
> 12 mm	> 905	0.11

James L. Mulshine, MD, is a professor of Internal Medicine at Rush University Medical Center, Chicago. His research interests include the use of quantitative CT to manage early lung cancer. He is a co-chair of the Small Pulmonary Nodule Profile Task Force and a member of the QIBA Steering Committee.

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Each issue of **QIBA Newsletter** *features a link to a dynamic search in PubMed, the National Library of Medicine's interface to its MEDLINE database*. Link to articles on: "An Oncologist's View of Quantitative Imaging."

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ANALYSIS TOOLS & TECHNIQUES

Collaborative Efforts of the MRE and US SWS Biomarker Committees

By Mark L. Palmeri, MD, PhD

Ultrasonic Shear Wave Speed (US-SWS) imaging and Magnetic Resonance Elastography (MRE) methods have been developed over the past two decades to produce quantitative estimates of tissue viscoelasticity (stiffness). Both US-SWS and MRE have found important initial clinical applications in detecting and staging liver fibrosis noninvasively, providing patients with a more comfortable and less expensive alternative to invasive needle biopsies. Both elasticity imaging modalities reliably demonstrate increasing liver stiffness with increasing stages of fibrosis.

While both modalities provide clinicians with similar quantitative information about tissue stiffness, they are based on very different approaches:

- MRE uses an external device to generate shear waves at a specific frequency (typically 60 Hz) in the liver. The MRI system is used to image the pattern of propagating shear waves and a processing algorithm automatically runs to generate cross-sectional images showing the (complex) shear modulus of tissue. [1-2]
- US-SWS methods rely on a focused acoustic radiation force excitation to generate shear waves internally in the liver that are relatively more broadband (< 1 kHz). Shear wave speed, not shear modulus, is typically estimated by a time-of-flight approach, where shear wave arrival times are measured at a multiplicity of spatial locations offset from the excitation. [3-5]

A common assumption that many elasticity imaging systems make is that the tissue is purely elastic, which implies that the shear wave speed (SWS) and shear modulus (µ) share a constant relationship to one another that is independent of the shear wave frequency content:

$$SWS = \sqrt{\frac{\mu}{\rho}}$$

where ρ = 1.0 g/cm^3 is the assumed constant density of water. It should be noted that the relationship between SWS and shear modulus is nonlinear, meaning a simple scaling factor cannot be used to relate the two quantities, making comparisons of measurements using the two modalities challenging in the clinical literature.

In 2012, QIBA formed a Biomarker Committee for US-SWS which focused on establishing how well existing commercial imaging systems, now being produced by over six different manufacturers, compare to one another. Working closely with CIRS, Inc., the US-SWS Biomarker Committee developed both elastic and viscoelastic liver-mimicking phantoms that were systematically measured with different US-SWS systems and were also measured with MRE at a multitude of discrete frequencies. [6-7] The first generation of the US-SWS QIBA Profile has been strongly rooted in achieving inter-manufacturer agreement in reported values in both elastic and viscoelastic phantoms.

When the MRE QIBA Biomarker Committee was formed in 2014, formal liaisons were immediately established between the US-SWS Biomarker Committee and the MRE Biomarker Committees. Unlike US-SWS, the FDA-cleared MRE add-ons provided by different MRI manufacturers share the same shear wave generation hardware, default imaging parameters, and processing algorithms, providing a basis for cross-platform comparability.

The first-generation QIBA Profiles for US-SWS and MRE will emphasize different confounders that can lead to differences in reported metrics when measuring liver stiffness and will also recommend reporting different metrics (SWS or shear modulus) based on existing traction in the literature. Strong collaboration between the US-SWS and MRE Biomarker Committees has led to the inclusion of MRE measurements in the US-SWS phantom validation protocol as an aspect of QIBA conformance processes. Ongoing and future efforts will focus on developing a common methodology for characterizing the viscoelastic properties of tissues, along with reporting a common metric characterizing liver stiffness that is agnostic to modality or manufacturer.

Mark L. Palmeri, MD, PhD, is an Associate Professor of the Practice in the Departments of Biomedical Engineering and Anesthesiology at Duke University, Durham, N.C. His research interests include acoustic radiation force shear wave elasticity imaging, ultrasonic imaging, finite element analysis of soft tissue response to acoustic radiation force excitation, medical

image and signal processing and medical instrumentation design. Dr. Palmeri is a member of the RSNA QIBA Ultrasound SWS Biomarker Committee, a co-chair of the Ultrasound SWS System Dependencies Subcommittee, liaison to the MRE Biomarker Committee and serves on the QIDW Oversight Committee.

References:

3. Muthupillai R, et al. Magnetic resonance elastography by direct visualization of propagating acoustic strain waves. *Science*. 1995;269:1854–1857.
4. Venkatesh SK, Yin M, Ehman RL. Magnetic resonance elastography of liver: technique, analysis, and clinical applications. *J. Magn. Reson. Imaging.* 2013;37:544–555.
5. Palmeri ML, et al. Quantifying hepatic modulus in vivo using acoustic radiation force. *J. Hepatology.* 2008;34:546-558.
6. Deffieux T, et al. Shear save spectroscopy for In vivo quantification of human soft tissues visco-elasticity. *IEEE TMI.* 2009;28:313-322.
7. Song P, et al. Comb-push ultrasound shear elastography (CUSE): A novel method for two-dimensional shear elasticity imaging of soft tissues. *IEEE TMI* 2012;31:1821-1832.
8. Hall TJ, et al. RSNA/QIBA: shear wave speed as a biomarker for liver fibrosis staging. Proceedings of the 2013 IEEE IUS 2013:397-400.
9. Palmeri ML, et al. RSNA QIBA ultrasound shear wave speed Phase II phantom study in viscoelastic media. Proceedings of the 2015 IEEE IUS 2015:1-4.

FOCUS ON

Cancer Moonshot Initiative

QIBA Profiles Included in Cancer Moonshot Initiative

RSNA/QIBA is very pleased to announce that two of the QIBA Profiles relevant to cancer patients have been referenced and supported by the Federal Cancer Moonshot Initiative (https://medium.com/cancer-moonshot).

The section on Standards for Quantitative Imaging Biomarkers to Advance Research and Outcomes as part of the Cancer Moonshot can be found [here](#).

Read the Digital First announcement on QIBA's involvement in Cancer Moonshot in *RSNA News* [here](#).

Our sincerest appreciation to all of the QIBA participants who helped us arrive at this important milestone.

Edward Jackson, PhD, QIBA Chair

QIBA Annual Meeting 2017

QIBA Annual Meeting Planned for May 2017

The next QIBA Annual Meeting will be held May 17-18, 2017, in Alexandria, VA. Regrettably, due to space limitations, we cannot accommodate everyone who might be interested in attending. Attendance is by–invitation–only, with priority given to the QIBA Steering Committee, Coordinating Committee Co-Chairs, Biomarker Committee Co-Chairs, Task Force Co-Chairs, Project PIs and Scientific Liaisons, along with local government representatives and invited speakers. All other requests will be considered on a space-available basis, to be determined in early April. If interested in this option, please contact QIBA@rsna.org.

QIBA leadership will act as representatives for their respective groups; please provide any feedback to your Biomarker Committee Co-Chairs prior to the meeting. We thank you for your continued commitment to QIBA.

For more information, QIBA meeting summaries, the *QIBA Newsletter* and other documents are available in two locations:

- QIBA page on RSNA website: RSNA.org/QIBA
- QIBA wiki: http://qibawiki.rsna.org/

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QIBA and QI/Imaging Biomarkers in the Literature

This list of references showcases articles that mention QIBA, quantitative imaging, or quantitative imaging biomarkers. In most cases, these are articles published by QIBA members or relate to a research project undertaken by QIBA members that may have received special recognition. New submissions are welcome and may be directed to QIBA@rsna.org.

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