QIBA Newsletter

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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

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Chair's Message——The Road to Implementing Quantitative Imaging

By EDWARD F. JACKSON, PhD

The RSNA Strategic Plan strives to advance the radiological sciences and foster the development of new technologies. This can be achieved in part by promoting the quantification of imaging results. The added value of quantification in both research and clinical environments is likely to increase as healthcare initiatives place increased pressure on radiologists to provide decision support for evidence-based care. In the era of Precision Medicine, the demand for quantitative results from imaging studies will increase as treatment decisions are driven by such results. In order to establish the link between quantitative imaging (QI) results and patient outcomes, we need to understand the bias and variance of QI results. Today, there remain substantial barriers to reproducible QI measures in clinical trials and patient care, including the inherently large number of variables that impact the bias and variance of QI measures, the diversity of proprietary industry platforms, and the lack of acceptance of QI measures by radiologists.

A critical barrier to the implementation of QI in radiology is the lack of standardization among vendor platforms. Collaboration in the pre-competitive space is challenging, yet it is crucial to addressing standardization and the integration of QI measurements into clinical workflows, which will be necessary for wider adoption. Obstacles to overcome with practicing radiologists include a distrust of the reliability of QI results, lack of consolidation of QI results in the radiology workflow, and concerns of diminished value of radiologists' expertise through automation and commoditization. The **Quantitative Imaging Biomarkers Alliance** (QIBA) was officially launched by RSNA in 2007 as a means to unite researchers, healthcare professionals, and industry stakeholders in the advancement of QI. The mission of QIBA is to improve the value and practicality of QI biomarkers by reducing variability across devices, patients, and time. This report summarizes many of our activities, results, and future plans. We hope you will join one of the eleven QIBA Biomarker Committees and help in the effort to best prepare the practice of radiology for the new era of precision medicine and evidence-based care, which will increasingly rely on quantification of results.

~ Edward F. Jackson, PhD, is the Chair of QIBA and Professor and Chair of the Department of Medical Physics at the University of Wisconsin-Madison School of Medicine and Public Health.

What is QIBA?

A widely-accepted definition of a biomarker is "a characteristic that is objectively measured and evaluated as an indicator of normal biological processes, pathogenic processes, or a response to a therapeutic intervention".[1] The term quantitative imaging has recently been defined as "the extraction of quantifiable features from medical images for the assessment of normal findings or the severity, degree of change, or status of a disease, injury, or chronic condition relative to normal findings".[2] Combining these two concepts, a quantitative imaging biomarker (QIB) can be defined as "an objectively measured characteristic derived from an *in vivo* image as an indicator of normal biological processes, pathogenic processes, or response to a therapeutic intervention".[2]

The responsible development of quantitative imaging is a strategic priority for the RSNA, and the organization is uniquely poised to convene the relevant stakeholders to address the complex, inter-related issues involved in extracting quantitative results from medical images. To be clinically useful and valuable, it is essential that quantitative results from imaging scans be reproducible. Major impediments to reproducibility are the current differentiation in imaging vendor products and image analysis tools as well as the independent activities of clinicians. Recognizing these fundamental issues, RSNA organized QIBA in 2007 to unite researchers, healthcare professionals and industry stakeholders to advance the use of quantitative imaging.

One goal of QIBA is to work with imaging system vendors to help transform the manufacturing of imaging systems from devices that provide qualitative results to devices that provide quantitative measurements that are consistent across vendors, in much the same way blood pressure cuffs or thermometers provide the same numerical reading no matter which vendor manufactures the device. Since the process of acquiring and processing a clinical imaging scan is complex, this goal requires coordinated activities among many stakeholders.

Validating a quantitative imaging biomarker requires identifying and characterizing all of the sources of bias and variance that affect the end measurement. A useful starting point is to group the factors affecting measurement into three broad classes defined by the imaging equipment, the software methods applied to measure the imaging feature, and the observer. These factors are interrelated and each must be analyzed to assess their effect on systematic and random error.

QIBA Biomarker Committees develop QIBA Profiles, *i.e.*, documents of standardized specifications for

image acquisition and image analysis. Profile Claims focus on a specific clinical application and are written using a statistically rigorous framework and language. Profile Details specify what must be achieved and/or what technical capabilities must be demonstrated in using the imaging device to realize the Claim. QIBA Profiles take into consideration technical (product-specific) standards, user activities, and the relationship to a clinically meaningful metric, such as therapeutic response or other patient outcome measure. QIBA is also developing a conformance program to allow vendors and users to determine whether equipment manufacturers and other "actors" are QIBA-Profile-conformant, using QIBA-branded or recommended physical and synthetic phantoms (test objects), publicly available data sets and associated metadata, publicly available software applications, and other tools.

To develop a Profile, data relating to bias and variance of the biomarker measurement (referred to as groundwork data) are extracted from the literature, and gaps in the published data necessary to understand the sources of bias and variability are noted. These gaps lead to QIBA groundwork projects to obtain such missing data. All data created by QIBA are available to the public, either for secondary analyses by other investigators or to allow others to check and validate the conclusions drawn by QIBA participants. To facilitate such data availability, RSNA created the Quantitative Imaging Data Warehouse for use by QIBA Biomarker Committees and others. Details about all these QIBA activities follow in this report.

1. Aronson J. "Biomarkers and Surrogate Endpoints". *British Journal of Clinical Pharmacology* 59 (5): 491–494, 2005.
2. Sullivan DC, Obuchowski NA, Kessler LG, *et al.* "Metrology Standards for Quantitative Imaging Biomarkers", *Radiology* 277(3): 813-825, 2015. Available at: https://www.rsna.org/research/quantitative-imaging-biomarkers-alliance/metrology-papers.

Who We Are

From the time of its formation in 2007 until mid-2015, the QIBA Chair was Daniel C. Sullivan, MD. Dr. Sullivan led QIBA during a period of dramatic expansion and we are very fortunate as he continues to be heavily involved in QIBA efforts as the vice chair of the QIBA Process Committee and as the Liaison for External Relations. In June 2015, Edward F. Jackson, PhD, previously the QIBA Vice Chair, was appointed as the QIBA Chair, and Eric S. Perlman, MD was appointed as the QIBA Vice Chair. The current QIBA organizational structure can be found at www.rsna.org/qiba.

The forum created by QIBA for an organized and effective cooperative effort among key participants has advanced through the generous efforts of many volunteer members from academia, the medical device, pharmaceutical and other business sectors, and government. QIBA participants span a wide range of expertise including (but not limited to) clinical practice, clinical research, physics, engineering, statistics, marketing, senior management, regulatory affairs, pharmaceutical industry, and computer science. The structure of QIBA explicitly includes the imaging device industry, which allows for precompetitive cooperation across all the vendors to achieve standardization of quantitative imaging biomarkers. **Appendix 1** provides a list of the more than 150 entities (imaging hardware and software companies, academic institutions, federal agencies, professional organizations and other entities) across North America, Europe and Asia that have representatives participating in or monitoring QIBA activities. Although based primarily in the U.S., international participation in QIBA is substantial. In addition, QIBA-related meetings are held in both the U.S. and Europe.

From its inception, QIBA established communication with members of the FDA, NIH and NIST at several levels, and these essential interactions continue. FDA and NIST staff scientists participate in

QIBA Biomarker Committees and other working groups such as the QIBA Metrology Working Group, have *ex officio* representation on the QIBA Steering Committee, and receive QIBA documents for comment. FDA participation assures that the agency's perspective and recommendations are incorporated into QIBA Profiles, when appropriate.

QIBA exemplifies a collaborative Model for Partnership and Leadership. The QIBA structure has been developing and evolving over the past eight years and is now widely recognized and respected by industry, academia and government agencies and is having a positive impact on imaging in clinical trials and clinical care.

During the past year, international interest in QIBA processes have dramatically increased. A formal collaboration of QIBA with the European Society of Radiology (ESR) has been achieved through the establishment of a European Imaging Biomarker Alliance (EIBALL) subcommittee of the ESR, with the Chair of QIBA serving as a member of EIBALL and the chair of EIBALL serving on the QIBA Steering Committee. Expanded interactions with Asian professional radiology organizations were also established during the past year, and a special QIBA symposium will be held at the 75th Annual Meeting of the Japan Radiological Society in April 2016.

The QIBA Kiosk provides an excellent information resource for RSNA Annual Meeting attendees.

Biomarker Committee Reports by Quantitative Imaging Modality

CT Volumetry

QIBA CT Volumetry Biomarker Committee - Est: June 2008

Co-Chairs

- Samuel G. Armato, III, PhD - (University of Chicago)
- Gregory V. Goldmacher, MD, PhD, MBA - (Merck)

- Jenifer Siegelman, MD, MPH - (Harvard Medical School/Brigham and Women's Hospital)

Purpose:

To investigate the technical feasibility and clinical value of quantifying changes over time in volume. Lung cancer was selected as the first example. Success will be defined as sufficiently rigorous improvements in CT-based outcome measures to (1) allow individual patients in clinical settings to switch treatments sooner if they are no longer responding to their current regimens, and (2) reduce the costs of evaluating investigational new drugs to treat lung cancer. This mechanism is cost-effective for stakeholders while simultaneously advancing the public health by accelerating the adoption of treatments which prove effective. If the specific aims are achieved in the lung cancer setting, then the paradigm will be extrapolated to other clinical scenarios where volumetry is medically meaningful.

Activities and Deliverables

- QIBA Profile: CT Tumor Volume Change v2.2 (Publicly Reviewed Version)

    - CT Volumetry Biomarker Committee. CT Tumor Volume Change Profile, Quantitative Imaging Biomarkers Alliance. Version 2.2. Publicly Reviewed Version. QIBA, August 8, 2012. Available at *RSNA.org/QIBA*

- **Claim: Measure Change in Tumor Volume**
- A measured volume change of more than 30% for a tumor provides at least a 95% probability that there is a true volume change; P(true volume change > 0% | measured volume change >30%) > 95%.
    - Note, the claim is undergoing revision for the next version of the Profile. Part of this process is the reformulation of the claim to comply with the standards set by the QIBA Metrology Working Group.
- This claim holds when the given tumor is measurable (i.e., tumor margins are sufficiently conspicuous and geometrically simple enough to be recognized on all images in both scans), and the longest in-plane diameter of the tumor is 10 mm or greater. Volume change refers to proportional change, where the percent change is the difference in the two volume measurements divided by the average of the two measurements. By using the average instead of one of the measurements as the denominator, asymmetries in percentage change values are avoided.
- For details on the derivation and implications of the claim, refer to Appendix B in the Profile.
- While the claim has been informed by an extensive review of the literature, it is currently a consensus claim that has not yet been fully substantiated by studies that strictly conform to the profile specifications. There have not yet been a sufficient number of studies performed using the Profile acquisition criteria. The expectation is that during a field test, data on the actual field performance will be collected and changes made to the claim or the details accordingly.
- The Profile is currently under public review. For compliance, the committee is currently preparing a checklist of actions for each "actor" to establish compliance. The conformance procedures have been divided into those related to patient handling activities, those related to scan acquisition and reconstruction, and those related to image analysis. Each set of procedures is being defined by dedicated subgroups of the committee. Procedures for claiming conformance to the Image Data Acquisition and Image Data Reconstruction activities have been provided (See Section 4 in the Profile). Procedures for claiming conformance to the Image Analysis activity are proposed in draft

form and will be revised in the future.

- The QIBA Profile describing measurements of change in tumor volume for advanced disease (the "CTV" Profile) has been updated to align with the Metrology Work Group definitions. Significant discussion has accumulated around points in the QIBA Profile, and much of it has now been incorporated into the text, with a plan and timeline for incorporating the remainder. The claims are being updated to reflect the committee consensus on appropriate thresholds of performance based on the state of the current methods and technology, as demonstrated in prior groundwork projects.
- The requirements for compliance have been revised, incorporating considerations previously not included in the QIBA Profile (for example, regarding the proper use of contrast).
- A protocol for a field test of the QIBA Profile was designed and is now undergoing revision following feedback from various stakeholders. The first step will check whether sites can take the QIBA Profile and execute its requirements. The second step will be to collect data on the precision of clinical lesion measurements, so the precision can be combined with prior information on bias to provide a more complete description of measurement variability.
- A CT liver phantom has been designed and fabricated. Scans have been performed on the phantom, and analysis of the resulting scan data is in progress.

Funded projects

Round 1 of funding (2011-2012):

Project title: **Inter-scanner/Inter-clinic Comparison of Reader Nodule Sizing in CT Imaging of a Phantom**

PI/Institution: Michael McNitt-Gray, PhD (UCLA)

PI/Institution: David Clunie, MBBS (CoreLab Partners)

Status: Completed

Publications:

- Petrick N, Kim HJG, Clunie D, Borradaile K, Ford R, Zeng R, Gavrielides MA, et al. Comparison of 1D, 2D, and 3D Nodule Sizing Methods by Radiologists for Spherical and Complex Nodules on Thoracic CT Phantom Images. *Academic Radiology*, 2014; 21(1), 30–40.
  http://dx.doi.org/10.1016/j.acra.2013.09.020

Meeting Presentations:

- Petrick N, Kim HJG, Clunie D, Borradaile K, Ford R, Zeng R, Gavrielides M, et al. Evaluation of 1D, 2D and 3D Nodule Size Estimation by Radiologists for Spherical and Non-spherical Nodules Through CT Thoracic Phantom Imaging. *Medical Imaging, 2011;* 79630D 1–7. Lake Buena Vista, FL: SPIE. doi:10.1117/12.878265

Project title: **Assessing Measurement Variability of Lung Lesions in Patient Data Sets**

PI/Institution: Michael McNitt-Gray, PhD (UCLA)

Status: Completed

Meeting Presentations:

- McNitt-Gray M, Kim HJG, Zhao B, Schwartz L, Clunie D, Borradaile K, Byrne K, et al. Estimating the Minimum Detectable Change of Lung Lesions Using Patient Datasets Acquired Under a "No Change" Condition. RSNA Annual Meeting, 2011, Chicago.

Project title: Validation of Volumetric CT as a Biomarker for Predicting Patient Survival

PI/Institution: Binsheng Zhao, DSc (Columbia University)

Status: Completed

Publications:

- Zhao B, Lee S, Lee HJ, Tan Y, Qi J, Persigehl T, Mozley PD and Schwartz LH. Variability in assessing treatment response: metastatic colorectal cancer as a paradigm. *Clin Cancer Res*. Published Online First on April 29, 2014; doi: 10.1158/1078-0432.

Meeting Presentations:

- Zhao B, Lee S, Lee H, Qi J, Persigehl T, Tan Y, Mozley D, Buckler A, Sullivan D, Schwartz LH, Inter-reader and Intra-reader Variability in Assessing Change of Total Tumor Volume. Computer Assisted Radiology and Surgery (CARs*), Joint Congress,* 2013, June 26-29, Heidelberg, Germany.

Posters:

- Zhao B, Lee S, Lee HJ, Qi J, Persigehl T, Tan T, Schwartz LH. Relationship of Variability in Tumor Measurement and Response. *American Society of Clinical Oncology (ASCO) Annual Meeting,* June 1-5, 2012, Chicago.
- Zhao B, Lee S, Qi J, Mozley PD, Mauro D, Schwartz LH. Minor Response Rate Predicts Patient Survival. *ASCO Annual Meeting,* June 2-6, 2013, Chicago.

Project title: Development of Assessment and Predictive Metrics for Quantitative Imaging in Chest CT

PI/Institution: Ehsan Samei, PhD (Duke University)

Status: Completed

Publications:

- Chen B, Richard S, Barnhart H, Colsher J, Amurao M, Samei E. Quantitative CT: technique dependency of volume assessment for pulmonary nodules. *Physics in Medicine and Biology* 57: 1335–1348, 2012.
- Chen B, Barnhart H, Richard S, Robins M, Colsher J, Samei E. Volumetric quantification of lung nodules in CT with iterative reconstruction (ASiR and MBIR) *Medical Physics* 40(11): 111902 - 111202-10, 2013.

- Chen B, Christianson O, Wilson J, Samei E. Assessment of volumetric noise and resolution performance for linear and nonlinear CT reconstruction methods. *Medical Physics* 41, 071909, 2014.
- Chen B, Samei E. Developing a prediction model for volume quantification performance in computed tomography. *Medical Physics* (in press, 2014).

Project title: **Quantifying Variability in Measurement of Pulmonary Nodule (solid, part-solid and ground glass) Volume, Longest Diameter and CT Attenuation Resulting from Differences in Reconstruction Thickness, Reconstruction Plane, and Reconstruction Algorithm.**

PI/Institution: Kavita Garg, MD (University of Colorado)

Status: Completed

Publications <mark>(in preparation):</mark>

- Scherzinger A, Garg K, Kim HJG, et al. Accuracy and Reproducibility of Semi-automated 3D Quantitative Measurements of Part-solid Nodules in a Thoracic CT Phantom. Planning submission to *Academic Radiology.*

- Garg K, Scherzinger A, Kim HJG, et al. Quantitative Measurement of Part-Solid Nodule Size on CT in a Chest Phantom: Effect of Dose on Accuracy. Planning submission to *Investigative Radiology-* special issue

Meeting Presentations:

- Scherzinger A, Garg K, Kim G, et al. Quantitative Measurement of Part-Solid Nodule Size on CT in a Chest Phantom: Effect of Dose on Accuracy, *RSNA 2013*.

Round 2 of funding (2012-2013):

Project title: Extension of Assessing Measurement Variability of Lung Lesions in Patient Data Sets: Variability Under Clinical Workflow Conditions

PI/Institution: Michael McNitt-Gray, PhD (UCLA)

PI/Institution: David Clunie, MBBS (CoreLab Partners)

Status: Completed

Project title: Comparative Study of Algorithms for the Measurement of the Volume of Lung Lesions: Assessing the Effects of Software Algorithms on Measurement Variability

PI/Institution: Hyun (Grace) Kim, PhD (UCLA)

 Status: Completed

Project title: Impact of Dose Saving Protocols on Quantitative CT Biomarkers of COPD and Asthma

PI/Institution: Sean Fain, PhD (University of Wisconsin, Madison)

Status: Completed

Round 3 of funding (2013-2014):

Project title: Second 3A Statistical and Image Processing Analysis

PI/Institution: Andrew Buckler, MS (Elucid Bioimaging, Inc.)

Status: Completed

Publications: The publication on the algorithm challenge project is complete and available at
http://www.ncbi.nlm.nih.gov/pubmed/26376841

Buckler AJ, et al. **Inter-Method Performance Study of Tumor Volumetry Assessment on Computed Tomography Test-Retest Data**. *Acad Radiol.* 2015 Nov; 22(11):1393-408. doi:10.1016/j.acra.2015.08.007. Epub 2015 Sep 14.

Project title: Phantoms for CT Volumetry of Hepatic and Nodal Metastasis

Binsheng Zhao, DSc (Columbia University)

Status: Completed

Round 4 of funding (2014-2015):

Project title: Methodology and Reference Image Set for Volumetric Characterization and Compliance

PI/Institution: Ehsan Samei, PhD (Duke University)

Status: Completed

Project title: Phantoms for CT Volumetry of Hepatic and Nodal Metastasis-Yr2

PI/Institution: Binsheng Zhao, DSc (Columbia University)

Status: Completed

Round 5 of funding (2015-2016):

<u>**Project title:**</u> Reference Image Set for Quantitation Conformance of Algorithmic Lesion Characterization

PI/Institution: Ehsan Samei, PhD (Duke University)

Status: In progress

QIBA CT Volumetry Task Force, Group 3A (algorithm challenges) - Est: November, 2011

Chair

- Maria Athelogou, PhD - (Definiens, Munich, Germany)

Purpose: The primary aim of the QIBA Volumetric Study 3A is to estimate inter- and intra-algorithm variability of volume estimation from CT scans. Participants include academic and commercial algorithm developers.

The study is not intended to determine which image analysis algorithm is best, but rather to assess individual algorithm performance against a defined test set of cases, providing knowledge to inform the QIBA Profile specifications.

Activities and Deliverables

- The algorithm challenge group (project 3A) has prepared a manuscript for publication, and secured permission to publish. A publication from the phantom data project is in the revision process after submission. The group dedicated to this project is now organizing to provide support for the upcoming "field test" of the CT volumetry biomarker profile.

QIBA Lung Nodule Assessment in CT Screening Task Force - Est: September, 2012

Co-Chairs:

- Samuel G. Armato, III, PhD - (University of Chicago)
- David S. Gierada, MD - (Washington University in St. Louis)
- James L. Mulshine, MD - (Rush University Medical Center)

Purpose: To define evidence-based consensus standards and processes for CT imaging in the setting of lung cancer screening, to allow for quantification of biologically meaningful longitudinal volume changes with

acceptable range of variance across vendor platforms. The concept is similar to the CT volumetry Profile for advanced cancer, but in this case, the QIBA Profile is being optimized for the small nodules detected on CT screening for lung cancer.

Activities and Deliverables

In progress:

QIBA Profile: CT Volumetry: Lung Nodule Volume Assessment and Monitoring in Lung Cancer Screening.

The Task Force has been working to ensure that the small nodule claims are consistent with the established claims of the advanced disease QIBA CT Volumetry Profile. Published results and unpublished data from members of the group have been used to inform development of claim details. The group is close to being able to finalize its "small nodule" QIBA Profile document.

The experimental data of group members and also literature data needed to establish the claim is under review. The draft specifications and accompanying discussions have gone through multiple revisions and are nearly final. We are currently engaging with manufacturer's representatives to obtain guidance regarding technical parameters for individual scanner models for quantitative applications.

QIBA Lung Density Biomarker Committee - Est: June 2009

Co-Chairs:

- Sean Fain, PhD (University of Wisconsin, Madison)
- Matthew Fuld, PhD (Siemens AG Healthcare)
- David Lynch, MD (National Jewish Health)

Purpose: Reduce and characterize bias and variance across CT manufacturers, software versions, and sites in support of quantitative CT lung densitometry and morphology.

Initial Objectives:

- Characterize the bias and precision of phenotyping and progression measurements in emphysema and asthma.
- Classify phenotype and assess longitudinal changes as medically meaningful surrogates for health status.
- Compare the sensitivity of CT measurements to spirometry and other accepted measures.
- Determine if progressive lung disease can be detected significantly sooner with quantitative imaging techniques than with currently accepted methods.

Activities and Deliverables

A draft Profile and claim development are in progress, based on critical evaluation of literature, for a lung

density protocol. The acquisition and reconstruction specification of CT images has been completed and is being evaluated by a working group of vendor scientists who are developing compliance procedures using the COPDGene Phantom. The image analysis section of the Profile also needs to be completed.

- The group has developed recommendations for pulmonary quantitative CT (qCT) protocols to be used on Siemens, GE, and Toshiba scanners, using automatic exposure control and iterative reconstruction. These protocols should guide efforts to lower CT dose for ongoing and future clinical research studies with qCT of the lungs focused on measures of parenchymal density. These protocols may be used in conjunction with low dose screening for lung cancer, and will be immediately implemented in the COPDGene study.
- Specific Lung Density Profile Status: A Task Force of CT vendor scientists has been formed to develop a compliance checklist and to suggest changes to the acquisition and reconstruction parameter specifications in efforts to mitigate measurement bias. The Task Force has organized a project that involves scanning the same COPDGene Phantom using three radiation doses on two models of each vendor's CT scanners. The CT Vendor Task Force has completed a first round of scanning and is planning to complete a second more rigorous round of scanning by March 2016.
- The Biomarker Committee has completed a meta-analysis of the CT lung density repeatability literature, thus finalizing their measurement repeatability claim for assessing emphysema progression. The meta-analysis may be the basis for a submission of a manuscript for publication in the peer-reviewed literature.
- Radiation Dose - Automatic Exposure Control Project: The final report of this project includes the first comprehensive set of recommendations for reduced dose quantitative CT protocols for Siemens, GE and Toshiba scanners, tested by phantom analysis. This important advance will facilitate the incorporation of quantitative CT metrics with reduced dose CT screening for lung cancer in cigarette smokers. These protocols will find immediate use in the COPDGene longitudinal study of cigarette smokers.

Funded projects

Round 2 of funding (2012-2013):

Project title: Impact of Dose Saving Protocols on Quantitative CT Biomarkers of COPD and Asthma

PI/Institution: Sean Fain, PhD (University of Wisconsin, Madison)

Status: Completed

Airway measurements are not accurate with reconstruction parameters currently used in ongoing clinical research studies. Improved spatial resolution enables accurate measurements by using reduced DFOV and a higher resolution reconstruction Kernel. The combination of ASIR with higher spatial resolution reconstruction shows promise to reduce X-ray dose and improve qCT of lung airways.

Publications:

Rodriguez A; Ranallo FN; Judy PF; et. al., CT Reconstruction Techniques for Improved Accuracy of Lung CT Airway Measurement; submitted for publication.

Meeting Presentations:

Rodriguez A; Ranallo FN; Judy PF; et. al., Improved Airway Measurement Accuracy for Low Dose Quantitative CT (qCT) Using Statistical (ASIR), at Reduced DFOV, and High Resolution Kernels in a Phantom and Swine Model; American Association of Physicists in Medicine (AAPM) Annual Meeting, 2014, Austin, Texas.

Posters:

Rodriguez A; Ranallo FN; Judy PF; et. al., Airway Measurement Accuracy For Low Dose Quantitative CT (qCT) Using Statistical (ASIR), And Model Based Reconstruction Techniques (Veo), American Thoracic Society (ATS) International Conference, 2014,San Diego Convention Center [Poster Board # 618] [Publication Number: A2395].

Collaborations:

The Committee has collaborated with the Society of Thoracic Radiology (STR) to present one-day conferences on QCT of the lung. These conferences were held before the STR Annual Meetings in 2012 and 2014. The Committee also had a half-day session during the 6th International Workshop for Pulmonary Functional Imaging, July 18-20, 2013, Madison, Wis. The Committee is working with the COPDGene project to develop reduced dose CT techniques that can be implemented for quantitative measurements, and are potentially suitable for use in individuals undergoing lung cancer screening.

The Committee plans to evaluate lower radiation dose protocols and will determine the impact of AEC and IR for qCT of lung density and airway measurements across scanner platforms. Members hope to establish equivalent performance for AEC and IR across the major vendor platforms represented in the installed base of 64 slice systems (e.g., GE, Siemens, Philips, Toshiba).

Round 4 of funding (2014-2015):

Project title: Low CT Dose Lung Protocols for Repeatable Quantitative Measures in Multi-center Studies

PI/Institution: Sean Fain, PhD (University of Wisconsin, Madison)

Status: Completed

This project developed a method for harmonizing AEC parameter settings across Siemens, GE, and Toshiba scanners using standard CTDI vol phantoms. Testing of the method was performed in two anthropomorphic Alderson chest phantoms containing lung equivalent foam densities in the lungs. Iterative reconstruction was also evaluated to establish best practices and guide efforts to lower CT dose for ongoing and future clinical research studies with qCT of the lungs focused on measures of parenchymal density.

Project title: Investigation of Methods of Volume Correction for Lung Density

PI/Institution: Sean Fain, PhD (University of Wisconsin, Madison)

Status: In progress

Magnetic Resonance Imaging (MR)

QIBA Perfusion, Diffusion and Flow-MRI (PDF-MRI) Biomarker Committee - Est: June 2008

Co-Chairs:

- Michael Boss, PhD - (NIST, Boulder, CO)
- John Kirsch, PhD - (Siemens Medical Solutions USA, Inc.)
- Mark Rosen, MD, PhD - (University of Pennsylvania)

Purpose: To make Dynamic Contrast Enhanced Magnetic Resonance Imaging (DCE-MRI), Dynamic Susceptibility Contrast (DSC) MRI, Diffusion Weighted Imaging (DWI), and Diffusion Tensor Imaging (DTI) acquisition across different vendors more comparable by protocol specification, standardized phantom calibration, and development of literature-supported claim statements regarding the reproducibility of quantitative imaging biomarkers (QIBs).

Activities and Deliverables

PDF-MRI Biomarker Committee Task Forces (TFs) have been formalized for the development of a v2.0 DCE-MRI Profile (which will address 3.0T and parallel imaging applications), DWI activities, DSC profile efforts, and for anisotropic diffusion MRI (DTI). In addition, the PDF Biomarker Committee has developed a suite of digital reference objects (DROs) for DCE-MRI, along with tools for quantitatively comparing the bias and precision of DCE software analysis packages.

The DCE-MRI TF is presently focused on defining systematic literature review procedures, and their application for select organ/tumor sites, to support the DCE-MRI v2.0 Profile claims. The DWI TF is recasting its Profile language into the revised QIBA Profile template. The DWI TF successfully developed a physical phantom and related analysis software and has started development of a DWI DRO. The DSC and DTI task forces are identifying appropriate QIBs for claim development; DSC is simultaneously beginning a NIBIB-funded groundwork project to create an appropriate DSC phantom.

QIBA Profile. DCE-MRI v1.0 (Publicly Reviewed Version)

- **Claim:**
  - Quantitative microvascular properties, specifically transfer constant (K^{trans}) and blood-

normalized initial-area-under-the-gadolinium-concentration curve (IAUGC$_{BN}$), can be measured from DCE-MRI data obtained at 1.5 T using low-molecular-weight extracellular gadolinium-based contrast agents with a 20% within-subject coefficient of variation for solid tumors at least 2 cm in diameter.*

- o Profile specified for use with patients with malignancy, for the following indicated biology: primary or metastatic, and to serve the following purpose: therapeutic response.
- o A 20% within-subject coefficient of variation is based on a conservative estimate from the peer-reviewed literature. In general, this suggests that a change of approximately 40% is required in a single subject to be considered significant.

The DCE Profile v 1.0 has been publicly reviewed and is available for public use. A conformance document which will supplant section IV of DCE Profile v 1.0 has been drafted and is expected to be integrated within the Profile by the end of 2015.

A DCE-MRI phantom study was completed, investigating the effects of parallel imaging (*e.g.*, SENSE) and B$_1$ inhomogeneity at 1.0, 1.5, and 3.0 Tesla, across 2 vendors with the DCE-MRI phantom. MR data were uploaded to the QIDW for public access. The conclusion of this study is that the use of SENSE does not adversely affect T$_1$ relaxometry results (measurement of 1/T$_1$), but the benefit of B$_1$ correction remains unknown. Good reproducibility of results was seen across field strengths.

An open-source software package to facilitate comparison of parametric images generated by different DCE-MRI analysis packages when utilizing the DRO created as part of a previous funded project. This software is capable of importing 2D and 3D DICOM images, or binary data formats, as well as imaging formats such as TIFF and PNG. It generates difference and ratio maps (exportable as PNG), scatter diagrams and box-plots, and ANOVA statistics to more easily compare analysis packages. The summary results are exported to a pdf file. This software is available for Mac, Windows, and Linux operating systems, and further development continues past the original project timeline. The software is available on the QIDW and can be used for demonstrating compliance of software.

The v1.0 DCE-MRI QIBA Profile lead editor, Dr. Alex Guimaraes, generated a compliance document for DCE-MRI. This document underwent extensive review by the wider PDF-MRI Biomarker Committee, and has informed the compliance section for the DWI Profile as well.

An automated software analysis package was developed to be used with the QIBA DCE-MRI Phantom for site qualification / conformance as well as ongoing quality control for DCE-MRI studies. The software was tested using phantom data acquired for site qualification for the ACRIN 6701 clinical trial. The analysis software and user manual have been uploaded to the QIDW, along with example data from various scanners and the associated reports produced by the software.

A DCE-DRO extension project resulted in a broader range of baseline T1 values to better simulate lesions in breast or bone marrow, the addition of 3.0T DRO data (adjusted baseline tissue and vascular T1 values), and the incorporation of an option for a vascular input function simulating reduced cardiac output. This project provides a more comprehensive set of DCE-MRI and T1 relaxometry DROs for compliance evaluation of analysis packages.

QIBA Profile DCE-MRI, v2.0 – Draft in progress.

QIBA Profile, DWI v1.34- This profile is in active development, with focused efforts on the organ-specific

longitudinal claims. The DWI TF anticipates release for public comment in the near future.

Draft Claim: Cross-sectional scanner performance assessed with an ice-water phantom

Isocenter is the point in the magnet where imaging gradients have no effect on the magnetic field strength. For water at 0 °C, at magnet isocenter:

For an ADC measurement in 10^{-3} mm^2/s, a 95% confidence interval for the true Quantitative Imaging Biomarker (QIB) value is 1.1 ± .04.

There is a 95% probability that the measured value for ADC *± 4 %* encompasses the true value of ADC.

Draft Claim: Longitudinal *in vivo* change of ADC

Due to differences in ADC reproducibility due to heterogeneity within an organ and/or across individuals, we specify a longitudinal claim on an organ-by-organ basis:

There is a 95% probability that the measured change in ADC ± *x* % encompasses the true change in ADC. Here *x* is ___ % for brain, ___ % for breast, and … for …

The DWI TF is finalizing the initial version of the isotropic diffusion-weighted imaging (DWI) QIBA Profile, which incorporates results from two Round 3-funded (2013-2014) groundwork projects (DWI-MRI ADC Phantom, PI Michael Boss, and Software Development for Analysis of QIBA DWI-MRI ADC Phantom Data, PI Thomas Chenevert). A production phantom for DWI was finalized, fabricated, and disseminated across 13 QIBA test sites to assess reproducibility of phantom data collected over time. Acquired phantom data has been aggregated on the RSNA QIBA/RIC QIDW, downloaded by NIST scientists, and reduced to repeatability/reproducibility/bias statistics using the Round 3-funded DWI analysis software to further support DWI Profile claims. Results were presented at the 2015 RSNA Annual Meeting. DWI phantom scan procedure instructions are being further refined specifically for each MRI vendor platform. This process will enable systematic and consistent comparison of results, better establishing the reproducibility of the ADC biomarker.

Funded projects

Round 1 of funding (2011-2012):

Project title: DCE-MRI Phantom Fabrication, Data Acquisition and Analysis, and Data Distribution

PI/ Institution: Edward Jackson, PhD (MDACC)

Status: Completed

Meeting Presentations:

- Bosca RJ, Ashton E, Zahlmann G, Jackson EF. RSNA Quantitative Imaging Biomarkers Alliance (QIBA)

DCE-MRI Phantom: Goal, Design, and Initial Results. Proceedings of the RSNA 98th Scientific Assembly and Annual Meeting (Oral Presentation), 11/2012

Posters: RSNA QIBA PDF-MRI Technical Committee posters (2011 and 2012)

Other:

- Example datasets uploaded for testing of QIDW. Four copies of phantom fabricated, filled and cross-validated at 1.5T and 3.0T. Three copies were released for site qualification use (ACRIN 6701, PI: Rosen, Phase II Project)

Project title: Software Development for Analysis of QIBA DCE-MRI Phantom Data

PI/ Institution: Edward Ashton, PhD (VirtualScopics)

Status: Completed

Project title: Digital Reference Object for DCE-MRI Analysis Software Verification

PI/ Institution: Daniel Barboriak, MD (Duke University)

Status: Completed

Publications:

- Barboriak DP, Price R. Digital Reference Objects for Dynamic Contrast-enhanced MRI. *QIBA Newsletter,* January 2013: Volume 5, Number 1.

- Huang W, Li X, Chen Y, Chang MC, et. al., Variations of Dynamic Contrast-Enhanced Magnetic Resonance Imaging in Evaluation of Breast Cancer Therapy Response: A Multicenter Data Analysis Challenge. *Translational Oncology*, in press

Meeting Presentations:

- Cron GO, Sourbron S, Barboriak DP, et. al., Bias and Precision of Three Different DCE-MRI Analysis Software Packages: A Comparison Using Simulated Data, Computer presentation at ISMRM 2014, Milan

Posters: RSNA QIBA posters

Other:

- DROs are online on the QIDW and also at https://sites.duke.edu/dblab/qibacontent/; Also, reports on software have been developed and distributed to DRO evaluation participants.

Round 2 of funding (2012-2013):

Project title: Test-Retest Evaluation of Repeatability of DCE-MRI and DWI in Human Subjects

PI/ Institution: Mark Rosen, MD, PhD (University of Pennsylvania)

Status: Completed

Round 3 of funding (2013-2014):

Project title: DW-MRI ADC Phantom

PI/ Institution: Michael Boss, PhD (NIST - Boulder, CO)

Status: Completed

Meeting Presentations:

- Thermally-Stabilized Isotropic Diffusion Phantom for Multisite Assessment of Apparent Diffusion Coefficient Reproducibility; AAPM Annual Meeting, July 2014
- Temperature-controlled Isotropic Diffusion Phantom with Wide Range of Apparent Diffusion Coefficients for Multicenter Assessment of Scanner Repeatability and Reproducibility; ISMRM Annual Meeting, May 2014
- Tissue Water Mobility by MRI: Diffusion Coefficient Reproducibility with a Temperature-Controlled Phantom at University of Oregon Diffusion NMR; DOSY and MRI Workshop, April 2014
- **Multicenter Study of Reproducibility of Wide Range of ADC at 0 °C, RSNA Annual Meeting, November 2015**

Posters: QIBA Perfusion, Diffusion, & Flow MRI Technical Committee: Current Status (RSNA 2013)

Project title: Software Development for Analysis of QIBA DW-MRI Phantom Data

PI/ Institution: Thomas Chenevert, PhD (University of Michigan)

Status: Completed

Project title: DCE-MRI Phantom Study to Evaluate the Impact of Parallel Imaging and B1 Inhomogeneities at Different MR Field Strengths of 1.0T, 1.5T, and 3.0T

PI/ Institution: Thorsten Persigehl, MD (University Hospital Cologne, Germany)

Status: Completed

Project title: Development of a Tool to Evaluate Software Using Artificial DCE-MRI Data and Statistical Analysis

PI/ Institution: Hendrik Laue, PhD (Fraunhofer MEVIS, Germany)

Status: Completed

Collaborations:

  A. Collaboration with QuIC-ConCePT to implement DW-MR Profile in liver mets clinical trial
  B. Collaboration with ACRIN to implement DCE-MRI Profile in prostate cancer clinical trial

Round 4 of funding (2014-2015):

Project title: Digital Reference Object for DCE-MRI analysis software verification 2

PI/Institution: Daniel Barboriak, MD (Duke University)

Status: Completed

Project title: RSNA DCE-MRI Phantom Automated Analysis Software Package Development

PI/Institution: Edward Jackson, PhD (University of Wisconsin, Madison)

Status: Completed

Project title: Digital Reference Object for DCE-MRI analysis software verification 2 (statistical support)

PI/Institution: Nancy Obuchowski, PhD (Cleveland Clinic Foundation)

Status: Completed

Round 5 of funding (2015-2016):

Project title: DWI-DRO Development for ADC Analysis

PI/Institution: Dariya Malyarenko, PhD (University of Michigan)

Status: In progress

Project title: Dynamic Susceptibility Contrast MRI Phantom

PI/Institution: Ona Wu, PhD (Harvard Medical School/MGH)

Status: In progress

QIBA DCE-MRI Task Force

Co-Chairs:

- Hendrik Laue, PhD - (Fraunhofer MEVIS, Germany)
- Caroline Chung, MD - (Princess Margaret Hospital in Toronto, Canada)

Purpose: To expand the DCE Profile from 1.5T to 3.0T and include parallel imaging.

Activities and Deliverables

There is a draft Profile v2.0 in progress. A previous profile, v1.0, was released for public comment. A DCE phantom was developed as a Round 1 project, with associated analysis software provided from a Round 4 project.

QIBA DTI Task Force - Est: May, 2014

Co-Chairs:

- James Provenzale, MD - (Duke University)
- Walter Schneider, PhD - (University of Pittsburgh)

Purpose: To establish a set of standards to allow for comparison of DTI metrics across vendor platforms

QIBA DWI Task Force – Est: February, 2012

Co-Chairs:

- Michael Boss, PhD - (NIST, Boulder)
- Thomas Chenevert, PhD - (University of Michigan)

Purpose: To establish a set of standards to allow for comparison of DWI across vendor platforms

Activities and Deliverables

There is a draft Profile in progress. An isotropic diffusion phantom and cross-vendor software to analyze data collected with it were developed as Round 3 projects.

QIBA DSC Task Force – Est: May, 2015

Co-Chairs:

- Bradley Erickson, MD, PhD - (Mayo Clinic)
- Ona Wu, PhD - (Harvard/BWH)

Purpose: To establish a set of standards to allow for comparison of DSC across vendor platforms

Activities and Deliverables

There is a draft Profile in progress, and a Round 5 groundwork project to develop a DSC phantom.

Proton Density Fat Fraction (PDFF) Biomarker Committee – Est: November, 2015

Co-Chairs:

- Claude Sirlin, MD – (University of California, San Diego)
- Scott B. Reeder, MD, PhD – (University of Wisconsin, Madison)

Purpose: To develop a Profile to standardize the PDFF image acquisition process.

Activities and Deliverables

PDFF Profile development is beginning.

QIBA Functional Magnetic Resonance Imaging (fMRI) Biomarker Committee - Est: December, 2009

Co-Chairs:

1. Edgar DeYoe, PhD - (Medical College of Wisconsin)
2. Jeffrey Petrella, MD - (Duke University Medical Center)
3. James Reuss, PhD - (Prism Clinical imaging, Inc.)

Purpose: To create and support implementation of a QIBA Profile for functional MRI as a pre-surgical assessment tool.

Activities and Deliverables

Draft Profile: Mapping of Brain Regions Using Blood Oxygenation Level Dependent (BOLD) functional MRI as a Pre-surgical Assessment Tool. Latest version updated: June 2015

Draft Claims:

Claims characterizing *re*producibility of BOLD response

A. Biomarker measurand: Local T2* MRI contrast change (reflecting a hemodynamic response to change in brain activity) – commonly referred to as the BOLD fMRI signal (the biomarker is a measurable physical property)
   a. Context of use: Preoperative fMRI mapping of eloquent cortex for treatment planning/guidance
      i. Cross-sectional measurement: Localization of BOLD signal as index of eloquent cortex (motor, language, and/or visual cortical areas)
         1. Index: the center of mass of activation of a focus of interest
            - Bias Profile:
            - Precision Profile
               - On a test-retest basis, the center of mass of activation of a focus of interest can be determined with a 5mm repeatability coefficient
         2. Index: the spatial extent half-maximum border of activation clusters (to be defined for normalized and non-normalized parametric maps)
            - Bias Profile:
            - Precision Profile:
               - On a test-retest basis the spatial location of the half-maximum border of an activation cluster can be determined with a 10mm repeatability coefficient

      ii. For each index, should also indicate Reproducibility (Intra-class Correlation Coefficient [ICC]; Concordance Correlation Coefficient [CCC], Reproducibility Coefficient [RDC]):

         - Specify conditions, e.g.,
            - Measuring system variability (hardware and software)
            - Site variability
            - Operator variability (Intra- or Inter-reader)
            - Time interval (across days/weeks etc.)

         - Longitudinal change measurement (if specified)
            - List Indices: (as above, including sub-parts)

Profile V1.0 is in the draft stage. The committee has narrowed the focus to pre-surgical mapping of the motor cortex and is refining the claims to this clinical context. Likewise, members are in the process of completing Section 3 – Profile Details – specific to the mapping of motor cortex. To inform compliance procedures, members are conducting groundwork studies focused on software analysis specifications.

Bias Task Force: Meets on alternate weeks, bimonthly, to focus on the issue of bias in our measurand. This activity will inform our Profile claims definition and guide development of methodological sequences for image analysis that best achieve the claims.

The **fMRI Biomarker Committee** continues work on v1.0 of its Profile for pre-surgical mapping of eloquent brain tissue. Refinements to the clinical claims and context were made, particularly the acquisition

guidelines, as well as accompanying appendices with detailed performance specifications.

DRO testing was completed at 8 sites, all analyzing the same bilateral hand motion DRO but with each site employing its own standard fMRI processing and analysis workflow. The activation map results accompanied by data analysis forms describing workflow were collected from each site. For the period through September 2015, generation and testing of advanced DROs for head motion in fMRI were performed. These include DROs from various combinations of selected empirical and synthetic datasets wherein amplitude and spatial distribution of task-related fMRI signals and associated fMRI noise were controlled. By fully specifying "ground truth" in this way, subsequent post-processing and display methods can be tested for the ability to accurately recover the original signal distributions and to quantify any inaccuracies that might be present. These DROs, containing realistic task signal and noise variability (including motion, performance, and neurovascular uncoupling sources of variance), have been uploaded to the QIDW. Detailed reports of fMRI DRO projects were submitted to QIBA leadership.

DROs from various combinations of task-related fMRI signals of known ground truth and containing realistic task and noise variability (including motion, performance, and neurovascular uncoupling (NVU) sources of variance) have been uploaded to the QIDW. These can be used for trial and comparison of fMRI analysis and correction methods for coping with the variance of the BOLD signal in the primary motor cortex as a function of presence or absence of NVU.

Members of the Biomarker Committee contribute to the DICOM Working Group 16 fMRI task force. The proposed DICOM work item will build on recent quantitative imaging support added to the standard, with new elements created as necessary to represent fMRI acquisition, activation maps, and task paradigms. The functional requirements incorporated by WG-16 fMRI were drawn from work done in the QIBA fMRI Biomarker Committee.

Funded projects

Round 1 of funding (2011-2012):

Project title: Quantitative Measures of fMRI Reproducibility for Pre-Surgical Planning

PI/Institution: Edgar DeYoe, PhD (Medical College of Wisconsin)

Status: Completed

Posters:

- DeYoe E, Voyvodic JT, Elsinger C, et. al., Reproducibility of Functional MRI – Progress Towards Profile Development. RSNA Annual Meeting 2011, Chicago. (QIBA Poster)
- DeYoe E, Voyvodic JT, Pillai J, et. al., Establishing A More Quantitative Approach for Clinical Application. RSNA Annual Meeting 2012, Chicago. (QIBA Poster)

- DeYoe, E, Voyvodic JT, Pillai J, et. al., BOLD fMRI – Establishing a More Quantitative Approach for Clinical Application. American Society of Functional Neuroradiology Annual Meeting, 2013, Charleston.

Other: Data sets are being uploaded to an fMRI Community on the QIDW.

Project title: Quantitative Measures of fMRI Reproducibility for Pre-Surgical Planning-Development of Reproducibility Metrics

PI/Institution: James Voyvodic, PhD (Duke University)

Status: Completed

Publications:

- Voyvodic JT. Reproducibility of Single-Subject fMRI Language Mapping with AMPLE Normalization. *J. Magn. Reson. Imaging*, 2012; 36:569-80.

Posters:

- DeYoe E, Voyvodic JT, Elsinger C, et. al., Reproducibility of Functional MRI–Progress Towards Profile Development. RSNA Annual Meeting 2011, Chicago. (QIBA Poster)
- DeYoe E, Voyvodic JT, Pillai J, et. al., Establishing A More Quantitative Approach for Clinical Application. RSNA Annual Meeting 2012, Chicago. (QIBA Poster)
- DeYoe, E, Voyvodic JT, Pillai J, et. al., BOLD fMRI – Establishing a More Quantitative Approach for Clinical Application. American Society of Functional Neuroradiology Annual Meeting, 2013*,* Charleston.

Round 2 of funding (2012-2013):

Project title: Validation of Breath Hold Task for Assessment of Cerebrovascular Responsiveness and Calibration of Language Activation Maps to Optimize Reproducibility

PI/ Institution: Jay J. Pillai, MD (Johns Hopkins)

Status: Completed

Publications:

- Zacà D, Jovicich J, Nadar SR, et. al., Cerebrovascular Reactivity Mapping in Patients with Low Grade Gliomas Undergoing Pre-surgical Sensorimotor Mapping with BOLD fMRI. *J Magn Reson Imaging;* 2013.

Posters:
- DeYoe E, Voyvodic JT, Pillai J, et. al., Establishing A More Quantitative Approach for Clinical Application. RSNA Annual Meeting 2012, Chicago. (QIBA Poster)
- Zacà D, Nadar SR, Jovicich J, Pillai JJ. Cerebrovascular Reactivity-based Calibration of Presurgical Motor Activation Maps to Improve Detectability of the BOLD Signal in Patients with Perirolandic Brain Tumors. International Society for Magnetic Resonance in Medicine, 2013 Annual Meeting (April 20-26, 2013, Salt Lake City, Utah).

Project title: fMRI Digital Reference Objects for Profile Development and Verification

PI/Institution: Edgar DeYoe, PhD (Medical College of Wisconsin)

Status: Completed

Meeting Presentations:

- DeYoe E & Voyvodic J; fMRI Digital Reference Objects. ASFNR Annual Meeting 2015, Tucson, AZ.
- DeYoe E, Elsinger C, Kalnin A et al. fMRI Biomarker Development: Progress Report 2015. RSNA Annual Meeting 2015, Chicago. (QIBA Poster)

Posters:

- Mohamed F, Soltysik D, DeYoe E, et. al., Creation of fMRI Digital Reference Objects with Multiple Sources of Signal Variance. RSNA Annual Meeting 2013, Chicago. (QIBA Poster)

Collaborations:

- DICOM WG-16 - 5/2014 WG-16 fMRI task force established. Goal is to prioritize information which can be expressed in DICOM to enhance storage and transmission of fMRI data.

Round 4 of funding (2014-2015):

Project title: Generation and Testing of Advanced Digital Reference Objects for fMRI

PI/Institution: Edgar DeYoe, PhD (Medical College of Wisconsin)

Status: Completed

Round 5 of funding (2015-2016):

Project title: Quantitating Clinical fMRI Mapping of Language

PI/Institution: James Voyvodic, PhD (Duke University)

Status: In progress

Magnetic Resonance Enterography (MRE) Biomarker Committee – Est: January, 2015

Co-Chairs:

- Patricia Cole, PhD, MD - (Takeda Pharmaceuticals)
- Richard Ehman, MD – (Mayo Clinic)

Purpose: To establish a set of standards to allow for meaningful assessment of longitudinal changes in studies using MRE.

Activities and Deliverables

MRE Profile development is beginning.

Nuclear Medicine (NM)

QIBA FDG-PET / CT Biomarker Committee - Est: June 2008

Co-Chairs:

- Rathan Subramaniam, MD, PhD, MPH - (Johns Hopkins University School of Medicine)
- John J. Sunderland, PhD - (University of Iowa)
- Scott D. Wollenweber, PhD - (GE Healthcare)

Purpose:

Foster adoption of pragmatic standards for accurate and reproducible longitudinal quantitation of biologic parameters with clinical relevance, such as SUV on FDG-PET scans

Activities and Deliverables

FDG-PET UPICT Protocol – *Public review*

http://rsna.org/uploadedFiles/RSNA/Content/Science_and_Education/QIBA/UPICT_FDG-PET_Protocol_ver08July2014.pdf

FDG-PET Profile – *Public review*

QIBA Profile: QIBA Profile: FDG-PET/CT as an Imaging Biomarker Measuring Response to Cancer Therapy (Publicly Reviewed Version)

Claim: Measure Change in SUV

If Profile criteria are met, tumor glycolytic activity as reflected by the maximum standardized uptake value

(SUVmax) should be measurable from FDG-PET/CT with a within-subject coefficient of variation of 10-12%.

1. An FDG-PET/CT Profile Field Test was performed to thoroughly examine the feasibility and practicality of the QIBA Profile in the specific context of three academic PET imaging centers using imaging equipment from three different manufacturers. The field test resulted in Profile revisions and identified impractical or ambiguous specifications, and initiated discussion regarding how to formalize this QIBA profile revision workflow procedure.
2. **Checklist:** A reduced list of 36 specifications was extracted from the QIBA FDG PET Profile that can serve as a simple checklist for imaging sites to determine their QIBA conformance. This distillation from the much longer set of QIBA Profile specifications was based on feasibility and relevance to quantitation. Profile specifications relevant to PET/CT devices were sent to the four manufacturers to evaluate their own system's compatibility with the Profile.
3. A follow-up field test was initiated, in which the site-relevant Profile specifications were evaluated for feasibility at 11 sites (academic and non-academic).   Additional incompatibilities between Profile specifications and imaging site practices were identified. From this, follow-up discussion amongst committee members was held to determine whether individual specifications should be modified to be more compatible with sites' practices, or whether sites should be encouraged to modify their practices.
4. A QIBA/NIBIB funded DRO extension project increased the functionality of the previous PET-CT DRO in efforts to test for (a) PET/CT display alignment (b) SUVpeak calculation and (c) Region of Interest (ROI) fidelity.
5. Profile and Uniform Protocols in Clinical Trials (UPICT) Protocol revisions were made in Q1 2015 regarding the control mechanism for lean body mass (LBM) based on public review comments and field-test findings. Future QIBA Profile updates being discussed include structured reporting inclusion/reference, clinical outcomes data, and biomarker qualification efforts. A summary document of the UPICT FDG-PET/CT Protocol was published in the Journal of Nuclear Medicine in April 2015.

Funded projects

Round 1 of funding (2011-2012):

Project title: *Meta-analysis to Analyze the Robustness of FDG SUV Changes as a Response Marker, Post and During Systemic and Multimodality Therapy, for Various Types of Solid Extra-cerebral Tumors*

PI/ Institution: *Otto Hoekstra, MD, PhD (VU Medical Center, The Netherlands)*

Meeting Presentations:

- *Abstract #1325408, Vincent A, RizviN, Tinteren H, Riphagen, Hoekstra O, "Towards qualification of FDG PET as a biomarker of response to cancer therapy: A meta-analysis." SNMMI 2012.*

- *Abstract # 1633580, Oo JH, Leal J, Tahari A, Baker L, Wahl RL, "Early treatment response by FDG PET in patients with the Ewing sarcoma family of tumors predicts survival." SNMMI 2013.*

Project title: *QIBA FDG-PET/CT Digital Reference Object Project*

PI/Institution: *Paul Kinahan, PhD (University of Washington)*

Publications: Larry A. Pierce II, Brian F. Elston, David A. Clunie, Dennis Nelson, Paul E. Kinahan *A Digital Reference Object to Analyze Calculation Accuracy of PET Standardized Uptake Value.* Radiology, Nov 2015, Vol. 277:538–545

Meeting Presentations: Poster and display station presentations at the Quantitative Reading Room, RSNA 2012; oral presentation at 2012 SNMMI meeting.

Project title: Analysis of SARC 11 Trial PET Data by PERCIST with Linkage to Clinical Outcomes

PI/Institution: Richard Wahl, MD (Johns Hopkins University School of Medicine)

Publications: Manuscript submitted to JCO

Meeting Presentations: Oral presentation, SNMMI 2013 Vancouver

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Round 2 of funding (2012-2013):

Project title: Personnel Support for FDG-PET Profile Completion (Profile Editor)

PI/Institution: Eric Perlman, MD (Perlman Advisory Group)

Meeting Presentations: 2014 SNM meeting

Posters: SNMMI 2014, St. Louis

Project title: Evaluation of the Variability in Determination of Quantitative PET Parameters of Treatment Response Across Performance Sites and Readers

PI/Institution: Richard Wahl, MD (Johns Hopkins University School of Medicine)

Meeting Presentations: RSNA 2013, oral presentation

Posters: SNMMI 2014, St. Louis

Project title: PERCIST Validation

PI/Institution: *Otto Hoekstra, MD (VU Medical Center, The Netherlands)*

Status: *Manuscript in progress.*

Project title: *Evaluation of FDG-PET SUV Covariates, Metrics, and Response Criteria*

PI/Institution: *Jeffrey Yap, PhD (Dana-Farber Cancer Institute)*

Status: *Manuscript in progress.*

Round 3 of funding (2013-2014):

Project title: *FDG-PET/CT Profile Field Test*

PI/ Institution: *Timothy Turkington, PhD (Duke University)*

Status: *Completed*

Project title: FDG-PET/CT Digital Reference Object (DRO) Extension

PI/ Institution: Paul Kinahan, PhD (University of Washington)

Status: Completed

Collaborations:

Joint workshop with Society of Nuclear Medicine and Molecular Imaging (SNMMI) to develop the FDG-PET UPICT Protocol.

The NCI Quantitative Imaging Network (QIN) is using the FDG-PET/CT Digital Reference Object as a test step during a grand challenge project for PET segmentation.

Round 4 of funding (2014-2015):

Project title: FDG-PET/CT Profile Multi-Center Field Test

PI/Institution: Timothy Turkington, PhD (Duke University)

Status: Completed

Project title: Biologic and Reader Repeatability of FDG and CT Volumetric Parameters (ACRIN 6678 & MERCK)

PI/Institution: Rathan Subramaniam, MD, PhD, MPH (Johns Hopkins University)

Status: In progress

Project title: A PET-Metabolic Tumor-Volume-Digital Reference Object (PET-MTV-DRO)

PI/Institution: Paul Kinahan, PhD (University of Washington)

Status: In progress

Project title: A Procedure to Facilitate Greater Standardization of PET Spatial Resolution

PI/Institution: Martin Lodge, PhD (Johns Hopkins University)

Status: In progress

Related Publication:
Gillies RJ, Kinahan PE, Hricak H. **Radiomics: Images Are More than Pictures, They Are Data.**
DOI: http://dx.doi.org/10.1148/radiol.2015151169   (Ahead of print)

QIBA FDG-PET Reporting Standards Writing Group - Est: March, 2014

Co-Chairs:

- Paul E. Kinahan, PhD, FIEEE - (University of Washington)
- Paul Marsden, PhD - (King's College London, UK)

Purpose:

To summarize the study characteristics that would need to be reported for a PET quantitative imaging biomarker in order for the study to be repeated and/or usefully included as part of a future meta-analysis.

Activities and Deliverables

This is a multi-group activity, involving members from QIBA, QIN, Cancer Research UK, and ECOG-ACRIN

and others.

The committee is planning two deliverables:

1. A guideline listing what data that should be reported as part of a quantitative imaging biomarker study
2. A companion paper that provides the following: motivation, rational for data to be reported, proposed methods of adoption.

These activities are intended to extend to other quantitative imaging biomarkers.

A presentation was made at the 2014 AAPM Annual Meeting, Austin.

QIBA PET Amyloid Biomarker Committee - Est: December, 2013

Co-Chairs:

- Satoshi Minoshima, MD, PhD - (University of Utah)
- Eric S. Perlman, MD - (Perlman Advisory Group, LLC)
- Anne M. Smith, PhD - (Siemens Medical Solutions USA, Inc.)

Purpose: To develop a QIBA Profile for quantitative assessment of amyloid protein burden in the brain using 18F-PET imaging agents.

Activities and Deliverables

The QIBA Amyloid PET Biomarker Committee (BC) has made substantive progress in drafting a Profile whereby 18F-Amyloid tracers may be used in clinical trials for assessing subjects with cognitive impairment. The Profile is based on a longitudinal claim and uses the change in SUVR as the measurand. The draft Profile is currently undergoing the final phase of internal BC review. The claim language is being revised based on current literature citations reviewed by a Task Force within the BC. The Profile is slated for distribution for public review during the 1Q2016.

There continues to be excellent participation on the teleconferences by members of all 18F-PET radiotracer manufacturers and equipment manufacturers as well as key subject matter experts from clinical, academic, imaging core lab, medical physics and systems engineering backgrounds.

One of the NIBIB Round 4 (2014-2015) projects was for co-development of a first generation digital reference object (DRO) and physical phantoms for quantitative assessment of amyloid tracers. The Amyloid BC felt that amyloid imaging, in particular, and the field of neuro-PET imaging in general, would significantly benefit from a well-designed quantitative brain phantom. Co-development has been completed for (1) a PET Brain DRO with separate gray and white matter anatomic compartments plus CSF, with well-defined reference regions for SUVR calculations, and (2) a precision physical brain phantom with anatomic

compartments identical to the DRO. The physical phantom has been successfully imaged on a PET scanner.

Based on BC discussions, scientific gaps which were identified during Profile development for which several groundwork projects were submitted for Round 5 NIBIB funding consideration. Listed below are projects for which funding was granted (Round 5) as well as a listing of prior years' projects.

Collaborations:

RSNA QIBA is now an affiliate of GAAIN (Global Alzheimer's Association International Network)

Round 5 of funding (2015-2016):

Project title: Analysis to Support Amyloid Imaging Profile Development

PI/Institution: Dawn Matthews (ADM Diagnostics, LLC)

Status: In progress

Project title: Amyloid Brain PET Test-Retest Meta-Analysis

PI/Institution: Rathan Subramaniam, MD, PhD, MPH (Johns Hopkins University)

Status: In progress

Project title: A Procedure to Facilitate Greater Standardization of PET Spatial Resolution

PI/Institution: Martin Lodge, PhD (Johns Hopkins University)

Status: In progress (joint project with Amyloid-PET and FDG-PET benefits)

Round 4 of funding (2014-2015):

Project title: Amyloid Profile Continued Support with Physical Brain Phantom Development

PI/Institution: John Sunderland, PhD (University of Iowa)

Status: Completed

Project title: Amyloid Profile Continued Support with DRO Brain Phantom Development

PI/Institution: Paul Kinahan, PhD (University of Washington)

Status: Completed

QIBA SPECT Biomarker Committee - Est: May, 2015

Co-Chairs:

- Yuni Dewaraja, PhD - (University of Michigan)
- P. David Mozley, MD - (Endocyte, Inc.)
- John Seibyl, MD - (Yale/ Institute for Neurodegenerative Disorders)

Purpose: To develop a QIBA Profile for SPECT.

Activities and Deliverables

SPECT Profile

Driven by mounting evidence that quantification adds value to SPECT, and the accelerating production of commercial software packages to capture that value, a large group of physicians and scientists, from industry, academia, and governmental agencies have now begun developing a SPECT Profile. International enthusiasm for participating has been particularly strong from Japan and several European Union states.

The initial focus will be on dopamine transporter brain scans to assist in the evaluation of patients with parkinsonian symptoms. Use cases that are expected to follow include quantification of trans arterially administered macro aggregated albumin for radiotherapy planning in patients with liver metastases, and targeted theranostics for selecting candidates for treatment with companion therapeutics in the emerging fields of antibody and small molecule drug conjugates.

Three co-chairs with relevant experience have been selected, 4 task groups led by deep subject matter experts have been formed, and regular meetings to define the first Profile are under way. As this is a relatively new initiative, there is uncertainty about the time-line to completion of the first profile, but active collaboration with the FDG and amyloid groups seems to be expediting initial progress.

QIBA Process Committee – Est: March, 2015

Co-Chairs:

- Kevin O'Donnell, MASc – (Toshiba Medical Research Institute-USA, Inc.)
- Daniel Sullivan, MD – QIBA External Relations Liaison (Duke University)

Purpose: *To:*

- Drive consistent content & format of QIBA Profiles
- Develop common Templates & Processes
- Support & mentor adoption of above
- Support infrastructure for QIBA Committees

Activities and Deliverables

1. Worklist (Activities)

   a) Revise QIBA Profile Template and Guidances
   b) Harmonize Conformance procedures across Profiles
   c) Draft QIBA Conformance Statements
   d) Standardize conventions for Profile editions/versions
   e) Formalize a change-tracking process
   f) Improve Wiki layout with a focus on Process page
   g) Review/improve criteria for Profile categories of "Technically Confirmed" and "Clinically Confirmed"
   h) Formalize publication process for official QIBA documents (CC approval vote, send to RSNA Staff)
   i) Create an on-boarding/indoctrination process for new committees
   j) Propose process/best practices for initial literature search around a new biomarker/profile

2. Deliverables: Items "a" through "f" above have been "delivered".

[QIBA Profile Template](#)

[QIBA Claim Guidance](#)

Draft Conformance Statements [URL]

Ultrasound Shear Wave Speed (SWS)

QIBA Ultrasound Shear Wave Speed (SWS) Biomarker Committee - Est: March 2012

Co-Chairs:

- Brian Garra, MD - (Washington DC VA Medical Center/FDA)
- Timothy J. Hall, PhD - (University of Wisconsin, Madison)
- Andy Milkowski, MS - (Siemens)

Purpose: To create and support implementation of a QIBA Profile for an ultrasound shear wave speed

(SWS) quantitative biomarker for liver disease.

Activities and Deliverables

The original goal of the SWS US Biomarker Committee was to develop a QIBA Profile for a single biomarker: ultrasound shear wave speed as a measure of liver stiffness which correlates with the degree of liver fibrosis/cirrhosis present. Major efforts center on completing groundwork studies and publishing results, continuing to understand and account for sources of bias in SWS estimation with ultrasound imaging systems, continuing to determine sources of variance in these estimates, minimizing those contributions, and finalizing the draft Protocol and Profile documents.

The three areas of groundwork efforts completed during 2013-2015 were: (1) Validation of simulations and phantoms mimicking elastic and viscoelastic properties of liver, (2) Comparison of SWS measurements in uniform liver-mimicking phantoms using ultrasound imaging systems, the established US non-imaging system, and, initially, MR elastography, and (3) Sources of measurement variability in shear-wave elasticity techniques. It is anticipated that the physical and digital phantoms will be part of these efforts, as well as of the conformance procedures.

Appropriate viscoelastic phantoms were not available commercially so had to be developed. This work was substantially complete as of November 2014. Independently establishing the viscoelastic response of these materials (estimating the complex shear modulus) is challenging. Although excellent agreement between dynamic mechanical testing and acoustic radiation force shear wave techniques has been demonstrated for media ten times stiffer than liver, the differences among measurements among various dynamic mechanical tests for very soft materials (about 1 kPa) is larger than the differences among shear wave speed estimates among ultrasound imaging systems. Further development of dynamic mechanical test methods is needed to estimate bias in shear wave speed estimates.

The objective of the phase II phantom study is to compare SWS measurements between commercially-available systems using calibrated phantoms that have viscoelastic behavior similar to that observed in normal and fibrotic liver. CIRS fabricated three phantoms using a proprietary oil-water emulsion of their Zerdine hydrogel that were matched in viscoelastic behavior to healthy and fibrotic human liver data. Phantoms were measured at academic, clinical, government, and vendor sites using different systems with curvilinear arrays at multiple focal depths (3.0, 4.5 & 7.0 cm). The results of this study show that current-generation ultrasound SWS measurement systems are able to differentiate viscoelastic materials that span healthy to fibrotic liver. The lowest combined system variability existed for the shallowest focal depth in the softest phantom (8.4%), while the greatest variability existed in the deepest focal depth in the stiffest phantom (22.2%). Median SWS estimates for the greatest outlier system in each phantom/focal depth combination ranged from 12.7–30.0%. Future efforts will include performing more robust statistical analyses of these data, comparing these phantom data trends with viscoelastic digital phantom data, providing vendors with study site data to refine their systems to have more consistent measurements, and integrating these data into the QIBA ultrasound shear wave speed measurement profile.

Simulation data sets have been developed and posted on the QIDW for use by research groups and manufacturers. The goal is to find approaches that allow different ultrasound systems to achieve the same SWS results from data generated using appropriate simulated visco-elastic materials. Simulated data representing elastic (lossless) and viscoelastic (tissue-mimicking) media have been released for download by interested parties, and several manufacturers have begun to look at the materials to determine if it is technically and economically feasible to analyze test data using their proprietary software. A

comprehensive comparison of simulation results obtained with two common commercial finite element modeling software has been performed, and the corresponding code to process the data are available on GitHub. If this plan is successful, use of digital reference objects (DROs) to analyze ways to achieve better agreement in SWS values will become a real possibility.

Clinical data has been acquired to investigate sources of variance from comorbidity, biological variability, and measurement methods that might affect shear wave speed estimate correlation with fibrosis. Studies were based on the literature analysis of 1548 publications from which 102 SWS papers included a study of one or more confounding factors. Detailed summary of the findings in these 102 papers were compiled into an Excel spreadsheet. The confounders and sources of variation were ranked according to type and importance. A further analysis of the potential for steatosis and/or inflammation to affect the correlation of SWS with liver fibrosis was performed using results obtained for 242 subjects. Data were de-identified, and upload into the QIDW has begun.

A standardized plan for archiving clinical and phantom data into the QIDW is being devised and will be included as an appendix to the QIBA Profile.

A first draft of the QIBA ultrasound Profile "SWS Estimation of Liver Fibrosis" has been created. Distribution within and approval by the Biomarker Committee is pending while the Profile document is converted to the new document template provided by the Process Committee and system-dependent methods descriptions are provided by the participating manufacturers. A standardized SWS data collection report form has been developed for inclusion in the Profile appendices.

Funded projects

Round 3 of funding (2013-2014):

Project title: Phase 2 Phantom Study with Inelastic, SWS-dispersive Media

PI/ Institution: Timothy J. Hall, PhD (University of Wisconsin, Madison)

Status: Completed

Project title: A Pilot Study of the Effect of Steatosis and Inflammation on Shear Wave Speed for the Estimation of Liver Fibrosis Stage in Patients with Diffuse Liver Disease

PI/Institution: Anthony Samir, MD, MPH (Massachusetts General Hospital)

Status: Completed

Project title: Numerical Simulation of Shear Wave Speed Measurements in the Liver

PI /Institution: Mark Palmeri, MD, PhD (Duke University)

Status: Completed

Meeting Presentations:

Emelianov S, Hall TJ, Bouchard R, Ultrasound Elasticity, Educational Course, AAPM Annual Meeting, 2014 Austin, TX, Med Phys, WE-E-9A-1.

Garra, B, (2013). Ultrasound Measurements and FDA Criteria for Display of New Quantitative Measures. RSNA 2013 (p. abstract only), Short Course RC825A. Retrieved from *rsna2013.rsna.org/program/details/?emID=12020945.*

Hall TJ, Milkowski A, Garra B, et. al., RSNA/QIBA: Shear Wave Speed as a Biomarker for Liver Fibrosis Staging, *Proc. IEEE Ultrason. Symp. Proceedings* 397-400, ISSN: 1948-5719, 2013. Prague, Czech Republic, 2013. (also a poster)

Hall TJ, Garra B, Milkowski A, et. al., QIBA Shear Wave Speed Imaging: Making It Much More Reproducible, American Institute of Ultrasound in Medicine Conference*,* 2013.

Hall TJ, RSNA Quantitative Imaging Biomarker Alliance: A Paradigm for Validating Quantitative Ultrasound Methods, International Symposium on Ultrasonic Imaging and Tissue Characterization, Arlington, Va., 2013.

Hall TJ, Quantitative Imaging in Ultrasound: Elasticity and Backscatter Related Measures. RSNA 2013, Course RC825A.

Posters:

Cohen-Bacrie C, Garra B, Hall TJ, et. al., QIBA Technical Committee for Shear Wave Speed (SWS) Measurement, RSNA 2012

Dhyani M, Palmeri M, Alam SK, Barr RG, Cosgrove DO, Sporea I, Chen S, Nightingale K, Rouze N, McAleavey S, Guenette G, Urban MW, Shamdasani V, MacDonald M, Obuchowski N, Xie H, Lynch T, Milkowski A, Wear KA, Hall TJ, Carson PL, Garra B, Samir AE, "RSNA/QIBA Ultrasound Shear Wave Speed Biomarkers Committee," 101st Sci Assembly RSNA, Radiol Soc N Am, Chicago, Poster, Learning Center, Quantitative Imaging (Nov 29 - Dec 4, 2015).

Hall TJ, Milkowski A, Garra B, et. al., RSNA/QIBA: Shear Wave Speed as a Biomarker for Liver Fibrosis Staging, RSNA 2013, poster.

Round 4 of funding (2014-2015):

Project title: Beyond Confounders: Addressing Sources of Measurement Variability and Error in Shear Wave Elastography

PI/Institution: Anthony Samir, MD, MPH (Harvard/MGH)

Status: Completed

Project title: Development and Validation of Simulations and Phantoms Mimicking the Viscoelastic Properties of Human Liver

PI/Institution: Mark Palmeri, MD, PhD (Duke University)

Status: Completed

Round 5 of funding (2015-2016):

Project title: Analysis of Sources of US SWS Measurement Inter-System Variability

PI/Institution: Mark Palmeri, MD, PhD (Duke University)

Status: In progress

QIBA Ultrasound Shear Wave Speed - System Dependencies and Phantom Development Task Force - Est: May 2012

Co-Chairs:

- Mark L. Palmeri, MD, PhD - (Duke University)
- Keith A. Wear, PhD - (FDA)

Purpose: To establish a set of standards to allow for comparison of SWS across vendors.

(**Note:** In 2014, the FDA provided funding to the Duke University investigators to support the numerical simulation effort).

Activities and Deliverables

Meeting presentations and posters

Carson P; Milkowski A; Hall TJ; et. al., RSNA QIBA Ultrasound Shear Wave Speed: Sources of Variability in Phantoms, Simulations and Humans, *Biomedical Engineering Society,* San Antonio, Texas, 2014

Hall TJ, Garra BS, Milkowski A, et. al., RSNA's QIBA Effort To Develop And Validate Cross-System Shear Wave Speed Measurements For Staging Liver Fibrosis, Eleventh International Tissue Elasticity Conference,

Deauville, France, Oct 2, 2012.

Jiang J, McAleavey S, Langdon J, Palmeri M. Development of Open-Source Tools to Validate Shear Wave Imaging: An Integrated QIBA Effort, 13th International Tissue Elasticity Imaging Conference, September 07-10, 2014 Snowbird, Utah.

Milkowski A, Hall TJ, Garra B, et. al., RSNA/QIBA Ultrasound Shear Wave Speed Estimation inelastic Phantoms: Sources and Magnitude of Variability in a Multicenter Study, American Institute of Ultrasound in Medicine Conference, March 31, 2013.

Milkowski A, Hall TJ, Andre M, et. al., Ultrasound Shear Wave Speed Estimation in Elastic Phantoms: Sources and Magnitude of Variability in a QIBA Multicenter Study, RSNA Annual Meeting, Chicago, 2013.

Palmeri M, Deng Y, Rouze N, Nightingale K. Modulation of Acoustic Radiation Force-Induced Shear Wave Spectral Content by Spatial Beamwidths and Excitation Duration, 39th International Symposium on Ultrasonic Imaging and Tissue Characterization, June 09-11, 2014.

Palmeri M, Deng Y, Rouze N, et. al., Dependence of Shear Wave Spectral Content on Acoustic Radiation Force Excitation Duration and Spatial Beamwidth, IEEE Ultrasonics Symposium, September 2014, Chicago, in Procs, IUS, 1105-1108.

   a. **Software or Datasets**

Mendeley Literature Database: http://www.mendeley.com/groups/2396601/qiba-sws/

Finite element simulation data of elastic materials corresponding to the Phase I and Phase II phantoms, simulated for a variety of excitation configurations, have been available publicly for the past year, hosted on a Duke web server (https://github.com/RSNA-QIBA-US-SWS/QIBA-DigitalPhantoms). Very recently, those data have been transferred to the QIBA QIDW. The data, posted in Matlab® format, also has accompanying documentation to allow anyone to replicate the simulations or adapt them for their specific imaging configurations.

QIBA Ultrasound Shear Wave Speed - Clinical Applications & Biological Targets Task Force - Est: May 2012

Co-Chairs:

- Anthony Samir, MD, MPH - (Massachusetts General Hospital)
- David O. Cosgrove, MD - (Imperial College/Hammersmith Hospital, London)
- Claude Cohen-Bacrie, MS - (Supersonic Imagine (SSI))

Purpose: To provide the necessary clinical perspective and data to inform development of QIBA profiles for the clinical application of sheer wave elastography for liver fibrosis staging.

Activities and Deliverables

- A UPICT protocol, based on the protocol used at Massachusetts General Hospital, is in Version 2.
- It is being converted into the new Profile template from the Process Committee and is awaiting device-specific description of measurement methods from industry for the UPICT protocol.
- A draft case report form has been developed and is currently in Version 5.
- The form covers confounders, measurements, and reference standard pathology.
- Online research registry. The draft case report form has been uploaded to REDCAP (Research Electronic Data Capture) as an online research system and has been made available to other QIBA group members and will be available to the research community later in 2014.
- Images have been uploaded into QIDW.
- A survey has been created, intended for distribution among hepatologists, to help establish clinical confounders that would likely affect SWS assessments of liver fibrosis stage. That information will be incorporated into the QIBA Profile.

Ultrasound Volume Blood Flow (VBF)

US Volume Blood Flow Biomarker Committee – Est: November, 2015 - {AIUM Supported}

Co-Chairs:

- J. Brian Fowlkes, PhD – (University of Michigan)
- Oliver Kripfgans, PhD – (University of Michigan)

Purpose: To create and support implementation of a QIBA Profile for an ultrasound volumetric blood flow (VBF) quantitative biomarker for vascular flow estimation.

Activities and Deliverables

US VBF Profile development is beginning.

The goal of the Volume Blood Flow Biomarker Committee is to develop a QIBA Profile for a cross-platform biomarker. In many clinical practices, almost every scan performed has some component of blood flow imaging using color or power Doppler, typically to show the presence or absence of flow. Very conservatively 20% of scans actually are performed where blood flow is quantified to some degree. There are about 200,000 ultrasound machines in the United States based on the 2014 Klein Report, which based on the 2013 Klein Report produce about 136 million exams. As such one can estimate that about 27 million scans ultrasound scans are performed per year in the USA where a true flow measurement might be of interest.

Currently for volume flow, a one dimensional measurement is made from a 2D image and a volume flow estimate is made by estimating the Doppler angle and assuming cylindrically symmetric flow and circular vessel cross section. This introduces considerable error and operator dependence. This QIBA effort is to establish a biomarker for volume flow that is stable, reproducible and clinically applicable.

Current efforts center on creating a realistic phantom/model for initial testing of elected methods for Volume Blood Flow estimation before clinical validation. Kidney transplant has been chosen as a clinical model that will also provide a direct comparison to an independent volume flow measurement made directly at the time of surgery.

Team members include academic institutions as well as industry partners. The co-chairs sent a general letter to a list of industry partners that produce ultrasound imaging systems that might be interested in joining this process. There are plans for such a call to industry partners involved in ultrasound phantom construction.

The team has begun monthly conference calls and the first face-to-face meeting occurred during the QIBA breakout sessions at the 2015 RSNA meeting. The meeting defined two task force groundwork activities: 1) examination of the information needed for the QIBA profile and 2) design and construction of the appropriate phantom including specifications related to conditions expected clinically.

Funding

For the initial project duration (2015-2018), the American Institute of Ultrasound in Medicine (AIUM) is providing administrative support. Subsequent funding will be sought to support specific activities as the project advances.

QIDW - Quantitative Imaging Data Warehouse

QIBA - RIC Informatics Task Force - Est: July 2011

Chair: Bradley Erickson, MD, PhD

Purpose:

To address the informatics needs of the QIBA research community, and to provide recommendations to accelerate development of industry tools to support the standardization of, and infrastructure for, quantitative imaging. In particular, to develop and implement a quantitative imaging data warehouse (QIDW).

The task force is a joint effort between QIBA and the RSNA Radiology Informatics Committee. The purpose of the QIDW is to facilitate data and algorithm sharing, and research collaboration to promote the development and adoption of quantitative imaging by the research and clinical radiology communities.

Activities and Deliverables

QIDW has been in development and pilot testing since January 2012. It officially launched as of May 15, 2013. https://qidw.rsna.org/

The QIDW currently consists of 15 communities with a total of 223 users and more than 127,600 image uploads and has been used internationally by biomedical imaging, clinician and industry research collaborators. QIDW is currently restricted to QIBA members, but plans include providing open access to

the public. Initially the QIDW has been used for phantom images and digital reference objects only, but clinical images are now being uploaded for research activities. QIDW User Agreement, Data Upload and User Access forms have been formalized. Data curation services will be provided for clinical images. Increased functionality for image data, metadata, and algorithm storage are in development, as well as analysis resources for the quantitative imaging research community.

Meeting Presentations:

"Quantitative Imaging: A Revolution in Evolution," RSNA in Association with SIIM, 2012, 2013, 2014 annual meetings.

"The Role of Informatics in Quantitative Imaging," RSNA in Association with AAPM, 2012, 2013, 2014 annual meetings.

"Introduction to Quantitative Imaging," SIIM 2013 Annual Meeting.

Funded projects

Round 1 of funding (2011-2012):

Project Title: Groundwork for QIBA image reference database - QIBA Image Reference

PI/ Institution: Gudrun Zahlmann, PhD (Roche); Rick Avila, MS (Kitware)

Status: A White Paper was created to guide the formation of the QIBA-RIC Task Force.

Round 3 and 4 of funding (2013-2015):

Project Title: Support and Development of the Quantitative Imaging Data Warehouse (QIDW)

PI/ Institution: Kitware, Inc.

Status: Completed

Round 5 of funding (2015-2016):

Project Title: Support and Development of the Quantitative Imaging Data Warehouse (QIDW)

PI/Institution: Kitware, Inc.

Status: In progress

Future Plans

During the first few years of QIBA, many of the efforts of the organization focused necessarily on developing concepts, procedures and policies for QIBA Biomarker Committee activity and deliverables. Stakeholders set out to

create and agree on a shared vision, strategic plan and operational plans to accomplish the goals of QIBA. Now that such a foundation has been firmly established, QIBA Biomarker Committees will focus on more expeditiously producing new, additional QIBA Profiles. Also, the first few Profiles that were written are being revised in light of better appreciation of the sources of bias and variance in image quantification and the development of a more rigorous and robust metrological basis for expressing QIBA Claims and structuring QIBA Profiles.

We also plan to continue to emphasize dissemination and implementation of QIBA Profiles into clinical trials or into clinical practice, depending on which is more relevant for a given Profile. Developing processes for demonstrating conformance with QIBA Profiles is another area of active work. We are also working to enhance and expand the Quantitative Imaging Data Warehouse to make it a more valuable research resource to the imaging community. Furthermore, there continues to be growing international interest in quantitative imaging biomarkers, and QIBA will continue to collaborate with interested international organizations seeking to implement quantitative imaging biomarkers in clinical trials and in patient care.

All QIBA Biomarker Committees and Task Forces are open to any interested person. More information the QIBA organizational structure, including the Biomarker Committee and Task Forces, can be obtained at www.rsna.org/qiba. Additional details, including information on QIBA Claims, Profile Templates, and groundwork projects, are available at the RSNA QIBA Wiki site, qibawiki.rsna.org. To participate, or learn more, please contact RSNA staff at QIBA@rsna.org. We look forward to hearing from you!

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QIBA Activities

RSNA Awarded Third NIBIB Contract to Support QIBA Activities

The National Institute of Biomedical Imaging and Bioengineering (NIBIB) has awarded RSNA a new two-year, $2.5-million contract to support the Quantitative Imaging Biomarkers Alliance (QIBA) and its research activities.

Quantitative imaging biomarkers (QIBs) are of considerable interest in evidence-based clinical decision making and for therapeutic development. A portion of this funding will support groundwork projects developed and led by QIBA members to help validate specific QIBs, improve QIB reproducibility, and standardize QIBs across vendor platforms.

This collaboration will produce standards documents (Profiles) informed by the groundwork activities, and physical phantoms, digital reference objects, publicly available data sets, and software applications to test the performance specifications in the Profiles and allow vendors and imaging sites to demonstrate conformance with Profile details.

This marks the third consecutive multi-year contract between NIBIB and QIBA since 2010. To learn more about QIBA, go to RSNA.org/QIBA.

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.