QIBA Newsletter

Quantitative Imaging Biomarkers Alliance RSNA

April 2015 • Volume 7, Number 2

In This Issue:

QIBA MISSION

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

QIBA CONNECTIONS

QIBA Wiki

QIBA CONTACT

Contact Us

Daniel C. Sullivan, MD
RSNA Science Advisor

IN MY OPINION

The Importance of QIBA Profiles and Claims in Clinical Trials

Eric S. Perlman, MD

The RSNA QIBA initiative (RSNA.org/QIBA) provides value to the healthcare system in several ways. First, it offers a structured forum for subject matter experts to engage in a focused dialogue on the methodology to advance quantitative imaging and the use of imaging biomarkers in clinical trials and clinical practice. Second, it defines a concrete primary deliverable—the QIBA Profile—for each biomarker work group. The Profile is a document which identifies the performance requirements across the entire workflow of site and scanner qualification, subject preparation, image acquisition, image reconstruction and image analysis and interpretation tasks.

A key feature of the Profile is the statement of a Claim relevant to a specific clinical use context. From a radiologist's perspective, the Profile defines acceptable thresholds for each performance requirement in the chain of the workflow which, if met, would result in achieving the Claim. Following these performance requirements can therefore be a powerful tool to support the new federal Precision Medicine Initiative. Additionally, during Profile creation, the working groups identify inconsistencies and gaps in current knowledge and, through the National Institute of

Biomedical Imaging and Bioengineering (NIBIB/NIH) funding, perform groundwork projects to address these gaps.

QIBA's Relevance to Healthcare

So, how do current QIBA activities fit into the broader context of healthcare and what additional activities are relevant to this goal? Viewed as a scientific experiment, a central hypothesis of the QIBA initiative posits that developing quantitative imaging as an assay has value in drug development research and in clinical practice.

Developing clinical indication-specific imaging performance requirements is well underway as additional biomarker working groups have started creating Profiles each year. Once a Profile is finalized, the next step is to define a methodology which can prospectively qualify facilities as capable of achieving Profile performance requirements and then assess compliance of the imaging performed at these sites.

Developing standardized site qualification guidelines and processes to efficiently assess Profile compliance is a critical path item. The routine use of standardized acquisition, reconstruction and image interpretation at qualified academic and community-based imaging facilities is an achievable short-term goal. But what will facilitate this implementation? A model for a site qualification process for quantitative imaging distinct from a certified accreditation process has not yet been developed for clinical trials research, but such a model could be created through collaborative effort with current accreditation organizations.

In parallel to the site qualification effort, there is a need for a data warehouse with appropriate image sets for retrospective analysis. This will ultimately be necessary to test the hypothesis that quantitative imaging assays have value. The data warehouse can be used both for software (algorithm) challenges as well as assessing clinical outcomes correlations. As demonstrated by the QIBA Quantitative Image Data Warehouse (QIDW), RSNA.org/QIDW, this requires technology and administrative infrastructure, including permission control and cataloguing of case material. This could be a robust tool for retrospectively assessing how quantitative imaging performed in compliance with QIBA standards vs. non-compliance might alter surrogate endpoint evaluation. Ideally, this would also be linked to non-imaging data, such as genomic and clinical outcomes data.

The knowledge base necessary to create an infrastructure to perform the appropriate imaging for a given patient at a given time and to use quantitative imaging biomarkers to determine the treatment pathway is available. Thanks in part to advancements made by device manufacturers and to professional radiology organizations through creation of standardized protocols, analytics and care strategies, there is a logical convergence of clinical practice and clinical research. It is time to make available a mature infrastructure to facilitate the translation of knowledge and practice demanded by clinical trials imaging into the clinical practice community. This will result in better data from which to make not only better individual patient decisions, but also provide more consistently acquired data for population-based analyses. By working together, professional imaging organizations, through processes like QIBA, can instill quantitative imaging rigor into the daily clinical workflow of radiology practices.

 *Eric S. Perlman, MD, (Perlman Advisory Group, LLC), an imaging consultant for clinical trials and clinical practice, is a diagnostic radiologist with nuclear medicine and internal medicine board certifications who spent 13 years in radiology practice at Princeton Radiology Associates, Princeton, N.J., and has over 15 years of experience working with imaging core labs. Dr. Perlman is vice-chair of the QIBA Nuclear Medicine Coordinating Committee and co-chair of the QIBA Amyloid-PET Biomarker Committee.*

Back to Top

PUBMED

PubMed Search on: "The Importance of QIBA Profiles and Claims in Clinical Trials"

Each issue of ***QIBA Newsletter*** features a link to a dynamic search in PubMed, the National Library of Medicine's interface to its MEDLINE database. Link to articles on**:** "The Importance of QIBA Profiles and Claims in Clinical Trials."

Back to Top

ANALYSIS TOOLS & TECHNIQUES

Goals, Challenges, and Value of Developing Digital Reference Objects for fMRI
James T. Voyvodic, PhD

Creating a physical reference object (phantom) for functional MRI (fMRI) is problematic because brain function is a complex dynamic process involving both the spatial distribution of MR properties of the brain (e.g. T1, T2, T2* relaxations) as well as the temporal fluctuations of those properties (e.g. brain activity, head motion, physiological oscillations). To address the problem, QIBA's fMRI Biomarker Committee has begun developing digital reference objects (DROs) consisting of synthetic fMRI image data sets with realistic known signal qualities and noise features derived from empirical fMRI data sets.

A typical fMRI DRO consists of a whole-brain set of faceless high-resolution (e.g. 1x1x1 mm) T1-weighted images, plus one or more lower-resolution T2*-weighted fMRI image time series made up of multiple discrete temporal signals (**Figure 1**). Each fMRI scan includes a series of T2* brain images with "background" noise characteristic of a healthy brain at rest without specific task or head motion, to which is added another series of images where only selected clusters of "active" brain voxels have image intensity signals oscillating around zero (emulating the timing and spatial distribution of real brain signals during typical speech or motor fMRI tasks). DROs can also be made to include variable amounts of image motion, inconsistent task performance, and disease-related tissue pathology. Importantly, each of these discrete components is modeled based on empirical data obtained from existing fMRI scans. The result is realistic sets of brain images (~5,000 images per DRO) in which each individual signal component, including "true" brain activity,

is known. Using digital phantoms, any signal component can be manipulated. Moreover, the technical performance of image analysis methods can be measured by comparing the results obtained for each DRO to its “true” brain signals.

The goal of our DRO project is to make standard reference data sets to evaluate how different sources of signal variance affect the reproducibility and bias of our fMRI QIBA Profile Claims and which fMRI algorithms and analysis methods are capable of providing quantitative results consistent with those Claims. To this end, we have thus far generated 20 fMRI empirical DROs, which have been uploaded in both DICOM and NIFTI image formats to QIBA’s Quantitative Imaging Data Warehouse (QIDW), RSNA.org/QIDW, and then downloaded by QIBA fMRI members at seven different institutions. Each site has then performed fMRI analysis using their own standard automated analysis methods and emailed their brain map results back for comparison. Preliminary analysis of these results demonstrate: 1) sites were able to download and import DRO images into different clinical and research fMRI analysis software; 2) all sites produced brain activity maps that were qualitatively similar but quantitatively highly variable across sites; 3) post-hoc application of the AMPLE normalization algorithm (Voyvodic, 2006[1]) greatly reduced intersite variability.

Having established the infrastructure for creating and distributing fMRI DROs, we are now systematically comparing different sources of signal variance and analysis methods to finalize our first QIBA Profile. Long-term, we expect that well-documented DROs publically available via the QIDW will be invaluable for improving fMRI as a quantitative biomarker of brain function.

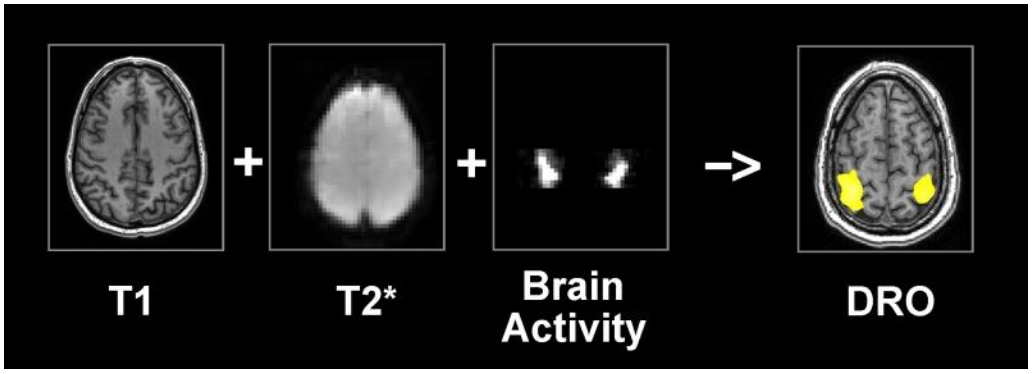

Figure 1

 *James Voyvodic, PhD, is an associate professor of radiology and neurobiology and technical director of clinical fMR at Duke University Medical Center, Durham, N.C. He leads the clinical fMRI research effort aimed at improving sensitivity, specificity, and reproducibility of diagnostic fMRI with particular interest in developing improved algorithms for real-time image analysis, quantitative imaging, and data quality assessment. He is a member of QIBA’s fMRI Biomarker Committee, Metrology Working Group, and MR Coordinating Committee.*

Reference

1. Voyvodic, J.T. Activation mapping as percentage of local excitation (AMPLE): fMRI stability within scans, between scans, and across field strengths. *Magnetic Resonance Imaging*; 2006; 24:1249-1261.

Back to Top

FOCUS ON

Growth Spurs QIBA Reorganization

Within the last six months, the QIBA Biomarker Committees have grown from six to **eight**, with additional Task Forces created to support Profile ground work and development.

The eight active Biomarker Committees are:

- CT Volumetry
- FDG-PET
- fMRI
- Lung Density
- MRE
- Perfusion, Diffusion and Flow – MRI
- PET-Amyloid
- Ultrasound - Shear Wave Speed
- SPECT (proposed)

The Biomarker Committees are open to all interested persons.

QIBA meeting summaries, the *QIBA Newsletter* and other documents are available on the QIBA website RSNA.org/QIBA and wiki qibawiki.rsna.org. Please contact QIBA@rsna.org for more information.

Due to this recent growth, modality-based Coordinating Committees have been created to better define deliverables and oversee timelines of QIBA projects.

QIBA Coordinating Committees Leadership Roster

CT Coordinating Committee

Chair:	Gregory Goldmacher, MD, PhD	(ICON Medical Imaging Inc.)
Vice-Chair:	Lawrence Schwartz, MD	(New York Presbyterian Hospital/Columbia University)

Nuclear Medicine (NM) Coordinating Committee

Chair:	Richard Wahl, MD	(Mallinckrodt Institute of Radiology, Washington University)
Vice-Chair:	Eric Perlman, MD	(Perlman Advisory Group, LLC)

MR Coordinating Committee

Co-Chairs:	Alex Guimaraes, MD, PhD	(Oregon Health Sciences University)
	Gudrun Zahlmann, PhD	(Roche Pharmaceuticals)
Vice-Chair:	Cathy Elsinger, PhD	(NordicNeuroLab, Inc.)

US Coordinating Committee

Chair:	Timothy J. Hall, PhD	(Univ. of Wisconsin, Madison)
Vice-Chair:	Brian Garra, MD	(Washington DC VA Medical Center/FDA)

Process Coordinating Committee

Chair:	Kevin O'Donnell, MASc	(ToshibaMedical Research Institute USA, Inc.)
Vice-Chair:	Daniel Sullivan, MD	(Duke University Medical Center)

The Process Coordinating Committee is unique in that its charge is comprehensive, focusing on document standardization, operational procedures, guidelines, best practices, etc.

Back to Top

QIBA IN THE LITERATURE

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.

Back to Top