QIBA Perfusion/Diffusion/Flow MRI Biomarker Committee: Overview

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Quantitative Imaging Biomarkers Alliance — RSNA

SUMMARY AND GOALS OF THE PDF COMMITTEE

The RSNA QIBA Perfusion, Diffusion, and Flow (PDF) MRI Biomarker Committee is composed of scientists representing imaging device manufacturers, image analysis laboratories, biopharmaceutical industry, academia, government research organizations, and professional societies. The goal of the committee is to define basic standards for MRI acquisition procedures and quality control that enable consistent and reliable imaging for determination of physiologic measures related to perfusion, diffusion, or blood flow in normal and abnormal tissues.

The efforts of the PDF MRI Biomarker Committee are motivated by the emergence perfusion/diffusion/flow measures as a means of diagnosing pathologies, determining disease aggressiveness, and evaluating responsiveness to therapy. Despite variance in imaging techniques, parameter choices, vendor specifications, and analytic methods, the application of these physiologic measures in clinical medicine, translational research and pharmaceutical studies continues to grow. Thus, there appears to be a promising future of these techniques for both clinical research and in routine clinical practice. However, in order to fulfill this promise, it is essential that common quantitative endpoints are used and that results are independent of imaging platforms, clinical sites, and time.

In the early development of the QIBA groups, the PDF MRI Committee (initially the DCE-MRI Committee) began with a single focus on the use of DCE-MRI for evaluating tumor response to certain vascular targeted therapies. However, in recent years, the committee has expanded its task list to include other methods for tissue vascular assessment (*e.g.*, dynamic susceptibility contrast, or DSC), as well as diffusion methods, including isotropic diffusion imaging (for apparent diffusion coefficient [ADC] measurement) and anisotropic diffusion tensor imaging (DTI) to determine the status of white matter tracts in the central nervous system. In addition, in order to capitalize on the scientific expertise of committee members, the PDF MRI Biomarker Committee has undertaken a new endeavor (co-sponsored by the QIBA Ultrasound Shear Wave Speed Technical Committee) to investigate the reliability of MR-based elastographic measures for non-invasive measurement of hepatic fibrosis.

Summary of PDF MRI Biomarker Committee Goals

To develop consensus standards based on existing literature regarding the appropriate acquisition strategies for reliable and robust quantitative MR imaging, so as to produce reproducible quantitative MR imaging biomarkers of normal and diseased tissues.

PROFILES AND WRITING GROUPS

The Profile forms the main output of the QIBA biomarker committees. Profiles are intended to serve as guidance documents to the various stakeholders in the imaging, medical, pharmaceutical, and scientific communities. In its essence, the Profile contains a "claim", which indicates the type of imaging biomarker to which the Profile is dedicated. The Profile underscores the degree of precision expected when undertaking the measurement of a certain imaging metric, outlines the conditions (including target subject populations) to which the Profile claim language applies, and provides the clinical and/or scientific context for the Profile claim.

Claim language example (from the DCE-MRI Profile v1.0):

> Quantitative imaging biomarkers reflecting 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 1.5T 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.

In this DCE-MRI Profile, the specified use case is patients with malignant tumors greater than 2 cm, and the clinical context is to gauge therapeutic response via altered tumor vascularity. A 20% within-subject coefficient of variation is based on a conservative estimate from the peer-reviewed literature. In general, this suggests that a minimum change of approximately 40% is required in a single subject to be considered physiologically significant.

QIBA Profiles provide users with guidance on imaging methodologies and practices required to ensure success in obtaining the metric(s) in question (at the proposed level of reproducibility). These areas of guidance include scanner quality assurance requirements, descriptions or test phantoms for scanner QC, imaging subject preparation and handling, imaging procedures and parameters, contrast requirements and use (when applicable), image post-processing, software requirements for image analysis, and digital reference objects to test software performance. In all cases, statements in the QIBA Profile are based on existing knowledge from the published scientific literature, data from groundwork projects funded by RSNA QIBA, or consensus opinion of the Biomarker Committee members (when published literature is lacking on a specific aspect of the imaging science).

The PDF MRI Biomarker Committee Supports a number of writing groups, each of whose goal is to complete a Profile document regarding the imaging biomarker(s) to which the Profile is dedicated. Currently, the PDF MRI Biomarker Committee supports the following Writing Groups:

- Dynamic Contrast-Enhanced (DCE-) MRI Task Force Group (initiated in 2010)
- Isotropic Diffusion Weighted Imaging Task Force group (initiated in 2012)
- Diffusion Tensor Imaging Task Force Group (initiated in 2014)
- Dynamic Susceptibility Contrast (DSC-) Task Force Group (initiated in 2014)
- *Magnetic Resonance Elastography (MRE) Task Force Group (initiated in 2014)
  (*Sponsored jointly by the PDF and the US Shear Wave Speed Biomarker Committees)

The PDF MRI Task Force Groups are composed of members of the PDF MRI Biomarker Committee; each group works to complete the writing of a Profile. Current Profile activity of the PDF MRI Biomarker Committee includes:

- DCE-MRI Profile v1.0 (circulated for public comment in 2012)
- DCE-MRI Profile v1.1 (with compliance documentation, in preparation for public comment submission in 2015)
- Isotropic DWI Profile v1.0 (in preparation for public comment submission in 2015)

GROUNDWORK PROJECTS

Groundwork projects are specific investigational activities funded by National Institute of Biomedical Imaging and Bioengineering (NIBIB), to aid in the implementation of PDF MRI Biomarker Committee areas of investigation. Groundwork projects seek to provide material resources (*e.g.*, phantoms, digital reference objects, software) to aid investigators seeking to obtain reproducible quantitative imaging biomarkers, or to provide data from field testing of the robustness of quantitative imaging biomarkers when applied to data acquisition (phantom or human data) in a multi-institutional framework. Groundwork projects are not themselves designed to test specific aspects of biological or pharmaceutical phenomenon reflected by the quantitative imaging metrics. Rather, they serve to spur development of these quantitative imaging biomarkers through development of tangible products to aid in imaging quality assurance, or to demonstrate robustness of the quantitative imaging biomarker(s) in practice.

Currently, the QIBA PDF MRI Biomarker Committee has undertaken groundwork projects in all three initial rounds of QIBA funding. Round IV groundwork projects have just recently been awarded. Past and current groundwork projects supported through the PDF MRI Biomarker Committee are detailed below.

Round I

- DCE-MRI Phantom Fabrication, Data Acquisition and Analysis, and Data Distribution
  - PI: Edward Jackson, PhD
  - Institution: MD Anderson Cancer Center
  - Initiated: 2011
  - Status: Complete (Figure 1)
- Software Development for Analysis of QIBA DCE-MRI Phantom Data
  - PI: Edward Ashton, PhD
  - Institution: VirtualScopics, Inc.
  - Initiated: 2011
  - Status: Complete (Figure 1)
- Digital Reference Object for DCE-MRI Analysis Software Verification
  - PI: Daniel Barboriak, MD
  - Institution: Duke University
  - Initiated: 2011
  - Status: Complete (Figure 2)

Figure 1: DCE-MRI Phantom and Analysis

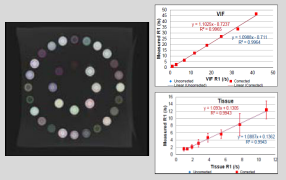
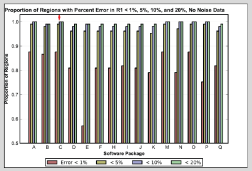


Figure 2: DCE-MRI DRO Software Analysis



Round II

- Test-retest Evaluation of Repeatability of DCE-MRI and DWI in Human Subjects
  [with the American College of Radiology Imaging Network (ACRIN)]
  - PI: Mark Rosen, MD, PhD
  - Institution: University of Pennsylvania
  - Initiated: 2012
  - Status: In progress (Figure 3)

Round III

- DW-MRI ADC Phantom
  - PI: Michael Boss, PhD
  - Institution: Nat'l Inst. of Standards and Technology, Boulder, CO
  - Initiated: 2013
  - Status: In progress (Figure 4)
- Software Development for Analysis of QIBA DWI-MRI Phantom Data
  - PI: Thomas Chenevert, PhD
  - Institution: University of Michigan
  - Initiated: 2013
  - Status: In progress
- Development of a Tool to Evaluate Software Using Artificial DCE-MRI Artificial DCE-MRI Data and Statistical Analysis
  - PI: Hendrik Laue, PhD
  - Institution: Fraunhofer MEVIS, Germany
  - Initiated: 2013
  - Status: In progress
- DCE-MRI Phantom Study to Evaluate the Impact of Parallel Imaging and B_1 Inhomogeneities at Different MRI Field Strengths of 1.0T, 1.5T, &3.0T
  - PI: Thorsten Persigehl, MD
  - Institution: University of Cologne, Germany
  - Initiated: 2013
  - Status: In progress

Figure 3: DCE-MRI Study

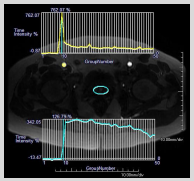
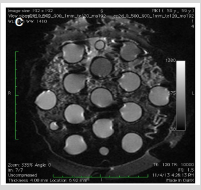


Figure 4: DWI Phantom Image



Round IV

- RSNA DCE-MRI Phantom Automated Analysis Software Package Development
  - PI: Edward Jackson, PhD
  - Institution: University of Wisconsin-Madison
  - Initiated: 2014
  - Status: In progress
- Digital Reference Object for DCE-MRI Analysis Software Verification 2
  - PI: Daniel Barboriak, MD
  - Institution: Duke University
  - Initiated: 2014
  - Status: In progress

INTERNATIONAL COLLABORATIONS

The PDF MRI Biomarker Committee has recently completed a Memorandum of Understanding (MOU) with the Innovative Medicine Initiative (IMI) European partnership to support their project on validation of tumor ADC as a biomarker of tumor response to chemotherapy. The "Quantitative Imaging in Cancer: Connecting Cellular Processes with Therapy" (QuIC-ConCePT) project, an undertaking with the European Organization for Research and Treatment of Cancer (EORTC), will seek to identify quantitative reproducibility of tumor ADC measures in liver metastases from colorectal carcinoma, and use of ADC early after chemotherapy to predict tumor response. The project will be undertaken under the umbrella of the EORTC 40091 study of targeted therapy in metastatic colorectal carcinoma. Under this trial, participating sites will undergo scanner qualification utilizing the DW-MRI phantom developed through the QIBA PDF Round III groundwork project (M Boss, PI).

The schema of the clinical trial is shown in Figure 5 below:

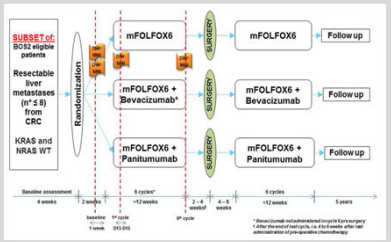


Figure 5: Schema of the EORTC 40091 trial evaluating targeted therapy in metastatic colorectal carcinoma. The QuIC-ConCePT project will evaluate the utility of early post-therapy DWI to predict pathologic response of tumors to combination therapy. The study design includes duplicative repeatability assessment prior to initiation of treatment. Site qualification for quantitative tumor ADC determination will be undertaken utilizing the DW-MRI phantom design from the QIBA Round III groundwork project

HIGHLIGHTS AND ACCOMPLISHEMENTS

To date, the PDF MRI Biomarker Committee has achieved a number of accomplishments in the course of both Profile development and technical groundwork projects. These include:

- Completion of the DCE-MRI Profile, with invitation for public comment in 2011 with release of the "publicly reviewed" version in 2012.
- Successful completion of all Round I groundwork projects with deliverables including:
  - Completion of the version 1.0 and version 2.0 DCE-MRI phantoms and testing in multi-site environment.
  - Public dissemination of the DCE-MRI phantom analysis software
  - Completion of the DCE-MRI digital reference object, with testing of more than 15 distinct software platforms, and reporting metrics of software performance.
- Successful initiation of the Phase II human test-retest study of DCE-MRI and DWI repeatability in human subjects with prostate carcinoma. Progress to date includes completion of all initial milestones under the Round II grant:
  - Clinical trial protocol (ACRIN 6701) submission and approval by CTEP.
  - Qualification of eight distinct institutions (representing all three major MRI vendors) for the study, utilizing DWI and DCE-MRI phantoms and software developed under the Round I groundwork projects. A ninth center is currently undergoing qualification procedures.
  - Successful trial initiation and opening. To date,15 subjects (out of projected total of 30) have been enrolled and undergone dual time point DWI and DCE-MRI. Subjects have been enrolled from six distinct centers.

PUBLICATIONS AND PRESENTATIONS

- Guimaraes, *et al.*: "QIBA DCE-MRI Technical Committee: DCE-MRI Profile v. 1.0", RSNA 2011.
- Jackson, *et al.*: "QIBA Perfusion, Diffusion, & Flow MRI Technical Committee: Current Status" RSNA 2012.
- Bosca *et al.*: RSNA Quantitative Imaging Biomarker Alliance (QIBA) DCE-MRI Phantom: Goal, Design, and Initial Results. Proceedings of the 98th Scientific Assembly and Annual Meeting of the RSNA (Oral Presentation), 2012
- Boss *et al.*: "QIBA Perfusion, Diffusion, & Flow MRI Technical Committee: Current Status" RSNA 2013.
- Barboriak and Price: "Digital Reference Objects for Dynamic Contrast-enhanced MRI" QIBA Quarterly (2013).
- Cron *et al.*: "Bias and Precision of Three Different DCE-MRI Analysis Software Packages: A Comparison Using Simulated Data" ISMRM 2014, Milan.
- Huang *et al.*: "Variations of dynamic contrast-enhanced magnetic resonance imaging in evaluation of breast cancer therapy response: a multicenter data analysis challenge", Transl Oncol, 7:153-166 (2014).

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