

QIBA Perfusion, Diffusion, and Flow (PDF-MRI) Biomarker Committee: Overview

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SUMMARY AND GOALS OF THE PDF-MRI BIOMARKER COMMITTEE

The RSNA QIBA Perfusion, Diffusion, and Flow MRI Biomarker Committee (PDF-MRI BC) is composed of scientists representing imaging device manufacturers, image analysis laboratories, biopharmaceutical industry, academia, government research organizations, imaging core labs, and professional societies. The goal of the PDF-MRI BC is to define technical performance standards (QIBA Profiles) for data acquisition, data processing, and quality control procedures that enable consistent and reliable quantitative imaging biomarkers for assessment of physiologic measures related to perfusion, diffusion, and/or blood flow in normal and abnormal tissues.

The efforts of the PDF-MRI BC are motivated by the emergence of perfusion/diffusion/flow quantitative imaging biomarkers as a means of diagnosing pathologies, staging disease, 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, particularly in the era of precision medicine. However, in order to fulfill this promise, it is essential that common quantitative endpoints are used and that results are reproducible and unbiased across imaging platforms, clinical sites, and time.

In the early development of the QIBA groups, the PDF-MRI BC (initially the DCE-MRI Technical Committee) began with a single focus on the use of Dynamic Contrast Enhanced (DCE) MRI for evaluating tumor response to certain vascular targeted therapies. However, in recent years, the PDF-MRI BC has expanded its scope to include other methods for tissue vascular assessment (i.e., dynamic susceptibility contrast, or DSC), as well as diffusion methods including isotropic diffusion-weighted imaging (DWI, 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.

Summary of PDF-MRI Biomarker Committee Goals
To develop consensus technical performance standards (QIBA Profiles), based on existing literature and groundwork projects, regarding the appropriate data acquisition, data processing, and quality control procedures necessary to provide reproducible quantitative MR imaging biomarker measures of normal and diseased tissues.

TASK FORCES: DCE, DWI, DSC AND DTI PROFILE WRITING ACTIVITIES

A Profile forms the main output of a QIBA Biomarker Committee. Profiles serve as guidance documents to the various stakeholders in the imaging, medical, pharmaceutical, and scientific communities. In its essence, the Profile contains a "claim" that indicates the type of imaging biomarker or metric 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 to which the Profile claim belongs.

DCE (Hendrik Laue & Caroline Chung):

The DCE-MRI profile was one of the first profiles made available to the public and will now be adapted to 3 T and parallel imaging. The profile v1.0 claim was:

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 1.5 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.

Profile 1.0 described the appropriate determination of the transfer constant (K^{trans}) and blood normalized initial area under the gadolinium concentration curve ($IAUGC_{BN}$), quantitatively reflecting changes in tumor vasculature. This initial profile was limited to 1.5 T applications without the use of parallel imaging.

Profile 2.0: Reflecting changes in practice, we are completing a literature review and groundwork projects necessary to have the profile include 3.0 T and parallel imaging, with organ-specific recommendations.

DCE Task Force Literature Review Strategy Summary

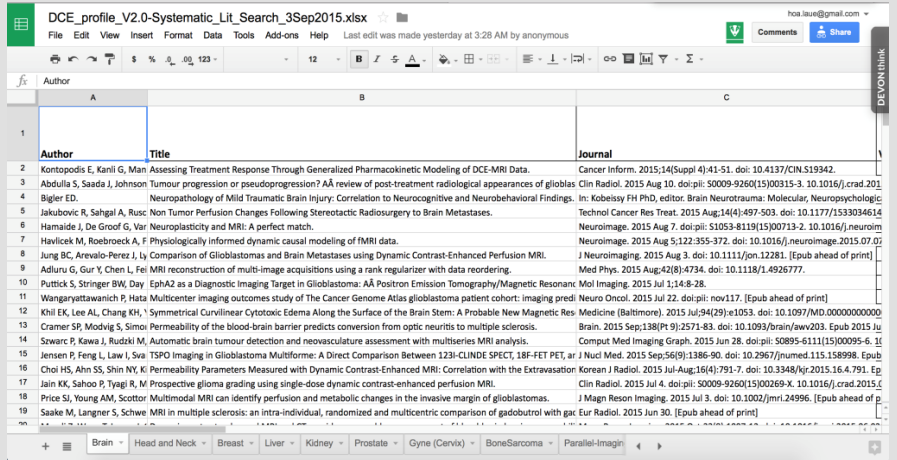
Databases: Pubmed, for initial search. MedLine and EMBASE may be added, if needed
Search Strategy: (in Pubmed under 'advanced' setting):

(((DCE-MRI[Title/Abstract] OR MRI[Title/Abstract] AND (dynamic[Title/Abstract] OR contrast enhanced*[Title/Abstract])) AND (INSERT BODY PART[Title/Abstract]))

(((DCE-MRI) OR (MRI AND (dynamic OR contrast enhance*)) AND (INSERT BODY PART FROM LIST BELOW))

Body Part keywords:

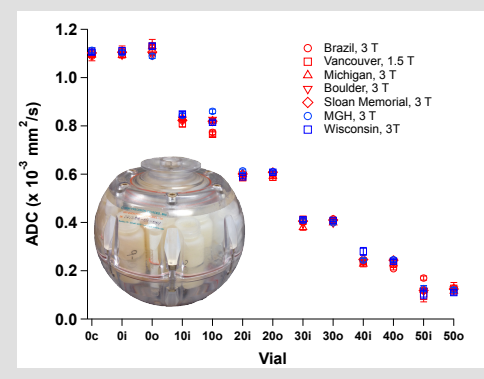
liver*, breast*, kidney*, OR renal*, cervix*, prostate*, Head AND neck (head OR neck), Brain*, Parallel



DWI (Thomas Chenevert & Michael Boss): 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:

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



DSC (Ona Wu & Bradley Erickson):

Quantitative imaging biomarkers reflecting microvascular properties, specifically leakage coefficient (K_2) and blood normalized initial area over the susceptibility signal intensity curve (IAOSSIC), can be measured from DSC-MRI data obtained at 1.5 T and 3.0 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.

DSC has an ongoing literature search using cloud-based tools to sort through the large volume of literature to support the above claim.

DTI (Walter Schneider & James Provenzale):

The DTI task force is conducting a literature search, focusing on the use of axial diffusivity, radial diffusivity, fractional anisotropy and mean diffusivity as quantitative imaging biomarkers.

OTHER ACCOMPLISHMENTS

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

- Completion of the v1.0 DCE-MRI Profile, including incorporation of public comments
- Successful completion of all Round 1-4 groundwork projects with deliverables including:
 - Completion of the RSNA QIBA DCE-MRI phantoms and testing in a multi-site, multi-vendor environment.
 - Completion of the DCE-MRI digital reference object (DRO), with testing of more than 15 distinct software platforms, and reporting metrics of software performance.
 - Initiation of the ACRIN 6701 clinical trial, which incorporated key aspects of the v1.0 DCE-MRI Profile.
 - Completion of groundwork projects needed to generalize the v1.0 DCE-MRI Profile to include 3.0 T field strengths and parallel imaging.
 - Development and distribution of software for analysis of DCE-MRI DRO data.
 - Development of a DWI ADC Phantom and associated data analysis software.
 - Development and distribution of an automated software analysis package for use with the RSNA QIBA DCE-MRI phantom.
 - Development and distribution of an extended DCE-MRI DRO addressing additional variables, including 3.0 T, variable cardiac output, etc.

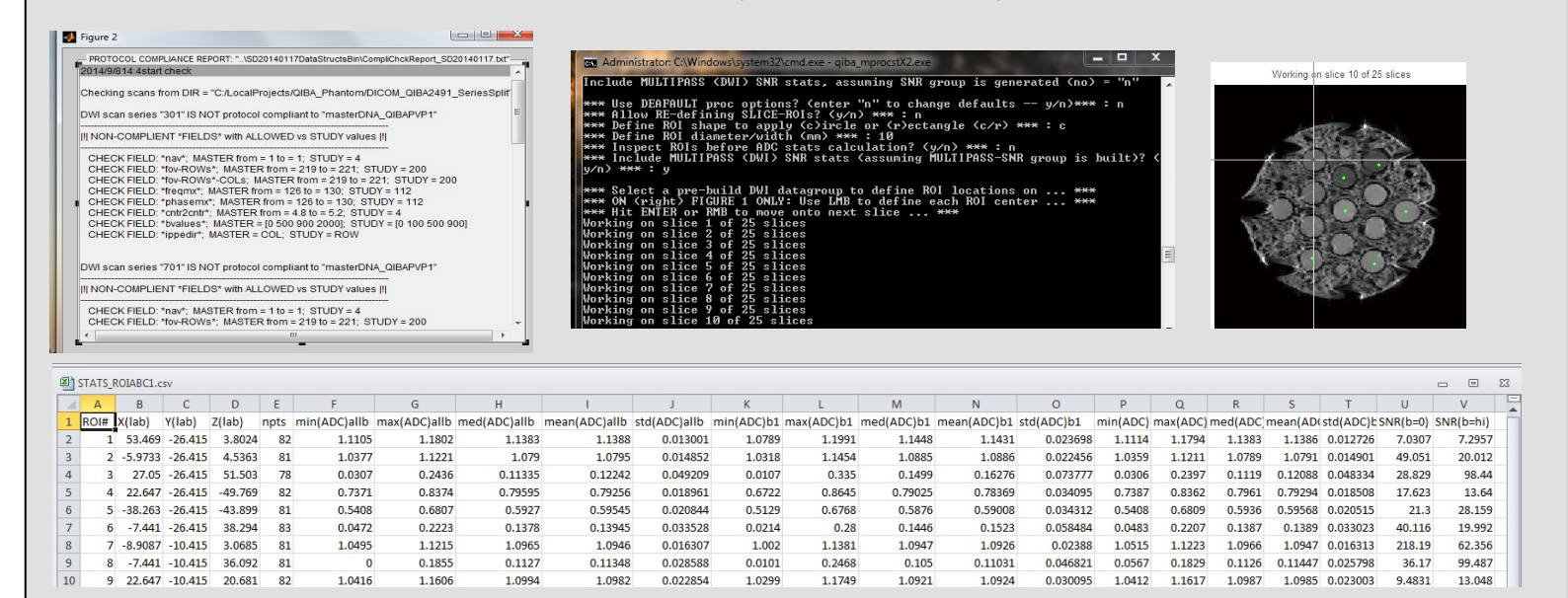
GROUNDWORK PROJECTS

Groundwork projects are specific investigational activities, funded by the National Institute of Biomedical Imaging and Bioengineering (NIBIB), to aid in the implementation of PDF-MRI BC 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 phenomena reflected by the quantitative imaging biomarkers. Rather, they enable development of tangible products to aid in Profile development or revision, to allow demonstration of conformance with such Profiles, and to demonstrate robustness of the quantitative imaging biomarkers(s) in practice. Examples of recently completed and upcoming groundwork projects include, but are not limited to:

Round 3 and 4 Completed Projects

DW-MRI Phantom Software Analysis, PI Thomas Chenevert:

Project goal was automated derivation and analysis of key system DWI performance metrics for cross-vendor/site certification and quality control utilizing NIST PVP DWI Phantom data.



QIBAphan" SW Functionality:

- Read-in DW-MRI multi-vendor multi b-value classic DICOM images of the PVP DWI Phantom
- Output scan series with acquisition protocol compliance check
- Visualization of DWI and derived ADC maps for user-supervised ROI loci definition
- Tabulation of ROI summary statistics for ADC, DWI and SNR for individual b-values and repeat scans

Upcoming Round 5 Projects

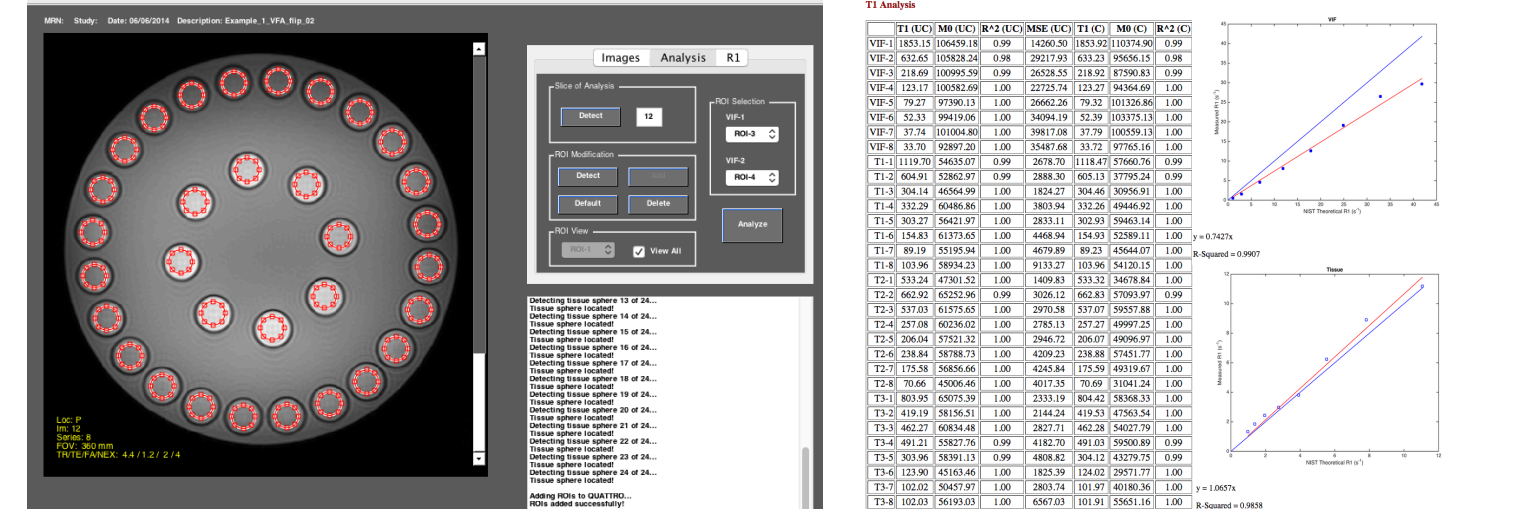
DWI-DRO Development for ADC Analysis, PI Dariya Malyarenko:

This project will provide a DWI-DRO for a relevant range of tissue diffusion values and Rician noise utilizing standard diffusion DICOM attributes for software testing and acquisition optimization.

Further information can be found on the QIBA DRO Poster.

DCE-MRI Phantom Software Analysis, PI Edward Jackson:

A DCE-MRI Phantom for site qualification, conformance testing, and ongoing QC was developed as a Round-1 QIBA/NIBIB project. To eliminate bias and variance in results introduced by analyzing phantom data using differing algorithms, an automated analysis package was developed in MATLAB, with executables created for Windows and MacOS. The software, user manual, and example data and reports from GE, Philips, and Siemens scanners are available on the RSNA Quantitative Imaging Data Warehouse (www.rsna.org/qidw) in the DCE-MRI WG community.



Digital Reference Object for DCE – MRI Analysis Software

Verification 2, PI Daniel Barboriak: Further information can be found on the QIBA DRO Poster.

DSC Susceptibility Phantom, PI Ona Wu:

This project will create a physical phantom with multiple specified levels of magnetic susceptibility. This phantom will be scanned in multiple MR scanners, including different vendors at both 1.5 T and 3.0 T. Based on those scans, the reproducibility of susceptibility measurements can be estimated, and that in turn will inform an estimate of reproducibility of DSC measurements.

PUBLICATIONS AND PRESENTATIONS

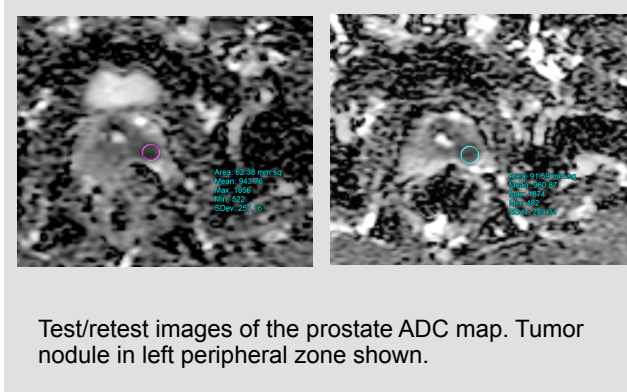
- Guimaraes, et al: "QIBA DCE-MRI Technical Committee: DCE-MRI Profile v. 1.0", RSNA 2011.
- Jackson, et al: "QIBA Perfusion, Diffusion, & Flow MRI Technical Committee: Current Status" RSNA 2012.
- Boss et al: "QIBA Perfusion, Diffusion, & Flow MRI Technical Committee: Current Status" RSNA 2013.
- Barboriak 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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Reasons for non-analyzable data for DWI:

- poor image quality (2)
- incorrect protocol (1)



Reasons for non-analyzable DCE-MRI data:

- poor image quality (2)
- incorrect protocol (3)
- incorrect temporal resolution (1)
- SAR limits on flip angle (2)

