QIBA Perfusion, Diffusion, and Flow (PDF-MRI) Biomarker Committee: 2017 Overview

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Quantitative Imaging Biomarkers Alliance — RSNA

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. There are now five Profiles in development, with the addition of ASL in 2017, each with a corresponding task force. 2017 also saw the release of the DWI Profile for public comment.

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.

Summary of PDF-MRI Biomarker Committee Goals

To develop consensus technical performance standards (QIBA Profiles), based on existing literature and 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.

ORGANIZATIONAL UPDATES, PROFILE AND CONFORMANCE PROGRESS

PDF-MRI

Co-Chairs: Dan Barboriak, Michael Boss, John Kirsch

DCE Task Force

Co-Chairs: Caroline Chung, Hendrik Laue

The main clinical impact DCE is the identification and staging of various tumors. As a quantitative biomarker, K^{trans} is of special interest in treatment monitoring of antiangiogenic therapies.

The DCE TF developed preliminary claims for K^{trans} for two different tumor types:

Claim 2a: A measured change of K^{trans} in brain tumors (GBM) of 21.33 % or larger indicates that a true change has occurred with 95 % confidence.

Claim 2b: A measured change of K^{trans} in prostate tumors of 50.7 % or larger indicates that a true change has occurred with 95 % confidence.

The claim definitions for prostate and brain are based on test-retest data from Alonsi[1] et al., 2010 and Jackson[2] et al., 2003, respectively. The claims will be updated with new, soon-to-be-published test-retest data.

1 Jackson, A., Jayson, G. C., Li, K. L., Zhu, X. P., Checkley, D. R., Tessier, J. J. L., & Waterton, J. C. (2003). Reproducibility of quantitative dynamic contrast-enhanced MRI in newly presenting glioma. British Journal of Radiology, 76(903), 153–162. http://doi.org/10.1259/bjr/70653746

2 Alonzi, R., Taylor, N. J., Stirling, J. J., d'Arcy, J. A., Collins, D. J., Saunders, M. I., et al. (2010). Reproducibility and correlation between quantitative and semiquantitative dynamic and intrinsic susceptibility-weighted MRI parameters in the benign and malignant human prostate. Journal of Magnetic Resonance Imaging : JMRI, 32(1), 155–164. http://doi.org/10.1002/jmri.22215

The DCE task force has recently completed extensive literature searches in three main body sites, informing our profile with regards to scan parameters and reproducibility metrics.

Brain: Comprehensive Search Results: 2490 papers Papers reviewed for profile content: 403 papers	
Outcome measures	K^{trans}; V_e, $V_p > V_e$, K_{ep}; Ki; AUGC, AUC; rCBV, CBV, CBF MTT, Max SI, max SI rate/slope
Field strength	0.5 T: 2 (on MS); 1.5 T: 29; 3 T: 21
Acquisition parameters for brain tumors	TR: 3.8-11.9ms (majority 3.8-6ms); TE: 1-4.2 ms FA: 6-30° Temporal resolution: 1-60 s (majority 1.25-6.5 s) Slice thickness: 2.5-6 mm Overall scan time: 1.5 – 12 min (majority 2.8-6.5 min)

Head and Neck: Comprehensive Search Results: 672 papers Papers reviewed for profile content: 127 papers	
Outcome measures	K^{trans}, V_e, $V_p > V_e$, K_{ep}, Ki; AUGC, AUC; rCBV, CBV, CBF MTT, Max SI, max SI rate/slope, max Slirate/slope, peak height, time to peak, relative max enhancement, relative washout ratio, vascular permeability, leakage space, contrast index, tumor blood volume, tumor blood flow, VVF
Field strength	1.5 T: 55; 3 T: 47; 4.7 T: 2; 9.4 T: 1
Acquisition parameters for H&N tumors	TR: 2.3-20 ms for GRE (majority 2.3-9 ms); TE: 0.9-4.2 ms for GRE Temporal resolution: 0.95-40 s (majority between 0.95-10 s) Slice thickness: 1-10 mm Overall scan time: < 1-10 min (majority 1.5-6 min)

Prostate: Comprehensive Search Results: 395 papers Papers reviewed for profile content: 202 papers	
Outcome measures	K^{trans}, V_e, $V_p > V_e$, K_{ep}, Ki, AUGC, AUC, rBV, BV, BF, MTT, Max SI, max SI rate/slope, wash-in/wash-out
Field strength	1.5 T: 79; 3 T: 94; 1.5 T + 3.0 T mixed: 11
Acquisition parameters for prostate tumors	TR: 3.8-11.9 (majority between 3.8-6ms) TE: 1-4.2 ms FA: 5-70° Temporal resolution: 1-90 s(majority 1.25-6.5 s) Slice thickness: 2.5-6 mm Overall scan time: 1.5 – 12 min (majority 2.8-6.5 min)

ASL Task Force

Co-Chairs: Xavier Golay (WG1), Rik Achten (WG2), Matthias Günther (WG3)

The QIBA Steering Committee approved the formation of the ASL task force, in conjunction with ESR's EIBALL. This task force has organized 3 working groups: WG1 focuses on statistics and technical definition of the claims; WG2 on the clinical aspects of the claims; WG3 addresses phantom usage and sequence parameters.

DSC Task Force

Co-Chairs: Brad Erickson, Ona Wu

The clinical application of the DSC profile is characterization of brain tumors. The TF has recently completed two ground work projects to develop a physical phantom and DRO generation tool. A literature search of relevant articles yielded 2472 articles in 2015; an additional 562 articles have been added since. The draft profile is presently being updated to the latest QIBA profile template.

DTI Task Force

Co-Chairs: Jim Provenzale, Walt Schneider

The DTI TF is in the process of drafting its Profile. The TF has conducted an initial literature review regarding the reproducibility of several different anisotropic diffusion metrics, including fractional anisotropy and mean diffusivity. In parallel, the TF has scanned a phantom with anisotropic components consisting of hollow polypropylene fibers with inner and outer diameters on the scale of micrometers to determine optimal scan protocols and reproducibility of metrics with existing clinical protocols (see groundwork project).

DWI Task Force

Co-Chairs: Michael Boss, Tom Chenevert

The DWI TF successfully released v1.0 of its profile for Public Comment, and began work on a checklist to facilitate profile use. The claims for prostate are shown below:

Claim 3a: A measured change in the ADC of a prostate lesion of 47% or larger indicates that a true change has occurred with 95 % confidence.

Claim 3b: A 95% CI for the true change in ADC of a prostate lesion is given below, where Y_1 and Y_2 are the ADC measurements at the two time points:

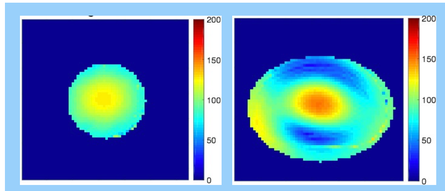
$$(Y_2 - Y_1) \pm 1.96 \times \sqrt{(Y_1 \times 0.17)^2 + (Y_2 \times 0.17)^2}.$$

The TF received about 100 comments, and created a spreadsheet to track user-submitted proposals and the final TF-approved resolution; examples are shown below.

Name	New Line	Old Line	Section	Issue	Proposal	Priority	Resolution
Anon	896	344	3.6.2	stated TE does not match PI-RADS	TE < 90 ms	H	ADTL/CDM: Change to "Acceptable <= 90ms" (will match PIRADS)
Anon	896	344	3.6.2	stated maximal b-value does not match PI-RADS	maximal b-value of at least 1,400 (stated in PI-RADS in numerous locations); 500-1,000 is not sufficient	H	ADTL/CDM: Leave unchanged to agree with primary pubs and emphasis on ADC (not DWI).

GROUNDWORK PROJECTS

Groundwork projects are specific investigational activities, often 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. Recently groundwork projects in PDF include:



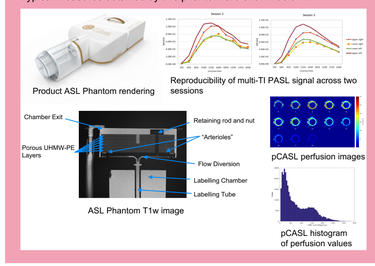
RF Transmit Calibration for DCE-MRI, PI: K. Nayak

We have developed head and torso phantoms for the evaluation of RF transmit homogeneity, which match relevant conductivity and T_1 range. We have measured and compared the spatial RF transmit inhomogeneity across different scanners, vendors, and sites in the greater Los Angeles area. The top figures contains sample RF transmit maps from one scanner (GE 3T HD23). We are in the process of completing a 2-month test-retest study, and evaluation of vendor-recommended protocols for RF measurement that can be used to improve quantitative DCE-MRI analysis. This will inform the claims and protocol guidance in the next DCE-MRI profile.

ASL Phantom Development, PI: Xavier Golay

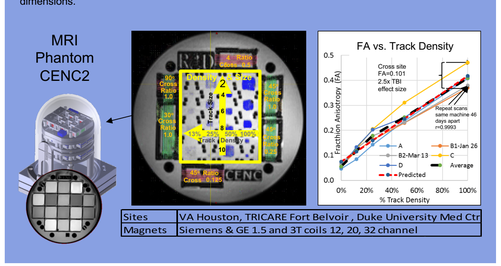
The ASL TF did not benefit from an NIH-sponsored project, but is currently building its profile together with members of ESR's EIBALL on the basis of a ground work developed through the EC-funded COST Action BM1103 on "ASL in Dementia", running from 2011-2015, including more than 200 people from 17 EU countries, leading to the publication, together with the ISMRM Perfusion Study Group of the "Recommended Implementation of Arterial Spin-Labeled Perfusion MRI for Clinical Applications: A Consensus of the ISMRM Perfusion Study Group and the European Consortium for ASL in Dementia" paper, by D. Alsop et al, Magn Reson Med, 73, 102-116 (2015). Another outcome of that COST Action was the creation by the PI (XG) of a company to make an ASL Phantom (Gold Standard Phantoms Ltd).

As of October 2017, a first series of pre-production phantoms is being distributed to 10 sites (funded by a grant from UK's SBRI) to perform stability studies of ASL on multiple platforms. Typical measures obtained by this phantom are shown below.



Measurements of Reproducibility of DTI Metrics on Clinical MR scanners using a DTI Phantom, PI: James Provenzale

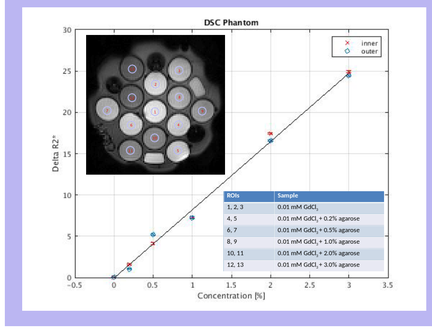
This groundwork project utilizes a hollow-fiber phantom developed in the Chronic Effects of Neurotrauma Consortium. The fibers are of uniform size (outer diameter of ~20 µm, inner diameter ~12 µm), and their packing density can be controlled in order to change the degree of anisotropic diffusion behavior. The goal of the project is to investigate the reproducibility of fractional anisotropy (FA), mean diffusivity, radial diffusivity, and axial diffusivity across scanners at Duke University, utilizing a protocol that can be run on all scanners, with a limited number of gradient directions and diffusion-weighting, as well as a research protocol utilized at sites within Department of Veterans Affairs (VA) hospitals and TRICARE sites. Initial data comparing scanners at Duke, the VA Hospital in Houston, and Fort Belvoir indicate good intrasite reproducibility, but substantial inter-scanner variability, as well as deviation from expected FA values given the density of fibers and their dimensions.



Sites	VA Houston, TRICARE Fort Belvoir , Duke University Med Ctr
Magnets	Siemens & GE 1.5 and 3T coils 12, 20, 32 channel

Dynamic susceptibility contrast MRI phantom, PI: Ona Wu

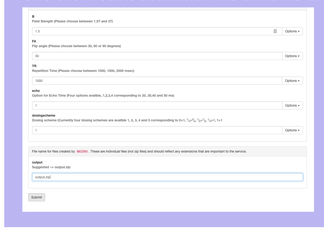
The DSC phantom effort coordinates resources and personnel from MGH, NIST, Leiden University, and the Mayo Clinic. The project delivered a test object that can be easily shipped between sites, allowing for evaluation of the measurement of T_2^*, while maintaining physiologically-relevant ratios of T_2^* to T_1. The phantom used solutions of $GdCl_3$ and agarose to generated differences in T_2^*, repurposing the NIST-QIBA diffusion phantom shell for multi-vendor compatibility. Example data acquired with this phantom is shown below.



A web-based tool for creating DSC Digital Reference Objects, PI: Brad Erickson

On the QIBA website (http://www.rsna.org/QIDW/)

One of 3 models available: The BNI DRO image generator



PUBLICATIONS

1. EM Palacios, AJ Martin, MA Boss, et al. *Towards Precision and Reproducibility of Diffusion Tensor Imaging: A Multicenter Diffusion Phantom and Traveling Volunteer Study*, AJNR **38**:537-545; **https://doi.org/10.3174/ajnr.A5025**
2. SJ Hectors, M Wagner, I Corcuera-Solano, et al. *Comparison Between 3-Scan Trace and Diagonal Body Diffusion-Weighted Imaging Acquisitions: A Phantom and Volunteer Study*; Tomography **2**:411-420; **https://dx.doi.org/10.18383/j.tom.2016.00229**
3. D Malyarenko et al. *Toward uniform implementation of parametric map DICOM in multi-site quantitative diffusion imaging studies*; J Med Imag **6**:011006; **https://doi.org/10.1117/1.JMI.5.1.011006**
4. DC Newitt, D Malyarenko, TL Chenevert, et al. *Multi-site concordance of apparent diffusion coefficient measurements across the NCI Quantitative Imaging Network*; J Med Imag **5**:011003; **https://doi.org/10.1117/1.JMI.5.1.011003**

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