QIBA Perfusion, Diffusion, & Flow MRI Technical Committee: Current Status

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Quantitative Imaging Biomarkers Alliance — RSNA

Brief Summary of Activities in 2013

The PDF Technical Committee made significant progress in several areas in 2013, and initiated an active international collaboration for diffusion phantom and profile development with the Innovative Medicines Initiative (IMI) QuIC-ConCePT project. Primary areas of focus were: 1) development of the isotropic Diffusion-Weighted MRI Profile, 2) design, construction and initial round-robin testing of the NIST/QIBA/NCI isotropic diffusion phantom, 3) statistical analysis of test results using a DCE-MRI Digital Reference Object (DRO), and 4) site qualification for the test-retest field test of the v1.0 DCE Profile (ACRIN 6701 clinical trial). In addition, funding was obtained from NIBIB/RSNA for four new groundwork projects focusing on phantom-based assessments of DCE- and DW-MRI, the development of compliance tools for DCE analysis packages, and analysis software for use with the DW-MRI phantom.

DW-MRI Profile

The PDF committee has dedicated much effort to the development of a diffusion-weighted MRI Profile. This Profile aims to allow investigators to gain insight into microstructure and composition in tumors using precise measurements of the apparent diffusion coefficient (ADC) for robust tissue characterization and longitudinal tumor monitoring. As the optimal imaging parameters needed across different tissues differ, we decided to approach profile writing on a region- and organ-specific basis, with protocols prescribed for each organ. We conducted an extensive literature review under this paradigm, with an eye towards research addressing repeatability and reproducibility to strengthen the Profile claim in the settings of abdomen, bone, brain, breast, kidney, liver, lymphoma, prostate, and whole body diffusion-weighted imaging. Substantial contributions were made to the motion compensation, quality control (QC), ROI selection, image analysis, and artifacts sections of the profile. The profile claims have been reformatted to comply with QIBA's profile claim template developed by the QIBA Metrology Group. The working draft of the DW-MRI profile and related materials can be found at:

http://qibawiki.rsna.org/index.php?title=Perfusion%2C_Diffusion_and_Flow-MRI_tech_ctte

We have entered into a collaboration with the IMI QuIC-ConCePT project, with mutual interest in development of ADC as a biomarker for use in diagnosis and treatment monitoring. The collaboration has accelerated development of the profile, in particular for the liver, which is a focus of QuIC-ConCePT clinical trials. The QuIC-ConCePT team also has experience working with ice-water phantoms for DW-MRI QC, and has been instrumental in the deployment and initial round-robin testing of the NIST/QIBA/NCI isotropic diffusion phantom. The PDF committee is working closely with QuIC-ConCePT to determine the optimal analysis methods for data collected using the phantom.

Isotropic Diffusion Phantom

In order to promote the use of ADC as a quantitative imaging biomarker, it is necessary to establish the repeatability and reproducibility of ADC measurements. To date, this has been best accomplished by use of an ice-water phantom: tubes of water are maintained at 0 °C with an ice-water bath, removing temperature fluctuations as a source of variability. This results in an ADC of 1.1 x 10^{-3} mm^2/s, and has been verified at magnet isocenter in MR scanners. However, *in vivo* ADC values range from 0.4 to 3.0 x10^{-3} mm^2/s, limiting the utility of ice-water phantoms when assessing scanner performance at the limits of this range.

In the interest of measuring ADCs spanning a broad range of physiological values, we designed a phantom containing polyvinylpyrrolidone (PVP) in aqueous solution as a means of tuning ADC. This non-toxic polymer has a short T2 and does not appreciably contribute signal in DW-MRI; water protons in PVP solutions exhibit Gaussian diffusion, with monoexponential decay at low and high *b*-values (Figure 1), making this system ideal for an isotropic diffusion phantom.

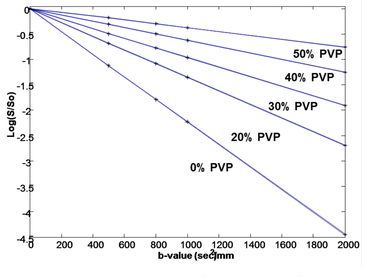


Figure 1: Monoexponential decay of signal in vials of PVP as a function of b-value. The data indicate that the diffusion is Gaussian over the full range of PVP concentrations, making these materials excellent choices for a diffusion phantom.

Our phantom design is novel in that it not only addresses a wide range of ADC values, but is temperature-controlled by means of an ice-water bath, fits into all commercially-available head coils, and can characterize off-isocenter performance by means of vials placed near the edge of the phantom (Figure 2). Its largest exterior dimension is 194 mm, allowing it to be rotated along any axis to enable coronal, axial or sagittal imaging. Our initial prototype was 3D printed to maintain low costs using ABS and polycarbonate, assembled at NIST with vials containing 0, 10, 20, 30, 40 and 50% PVP by mass, and sent to our QuIC-ConCePT partners in the UK and France for round-robin testing at three sites. The phantom was scanned across two days at each site, using a standard EPI protocol in the coronal plane at *b*-values of 0, 500, and 900 s/mm^2.

Acquired data were uploaded to the QIBA Quantitative Imaging Data Warehouse (QIDW) for easy access and analysis. Initial results at 0 ºC indicate excellent reproducibility across sites with the exception of the most viscous solutions. At 0 ºC and at bore temperature, PVP solutions enable a wide range of physiologically-relevant ADC values (Figure 3). Current plans are to assess repeatability and reproducibility of ADC values by a combination of coffee-break acquisitions in all 3 imaging planes, and day-to-day scans (see chart below). A second prototype is being designed to address the feedback received on the first phantom, with plans to scan at sites in the U.S. Over the next year, we hope to upgrade the production process to facilitate inexpensive fabrication of the phantom and dissemination of a larger number of copies to sites for QC use in clinical trials.

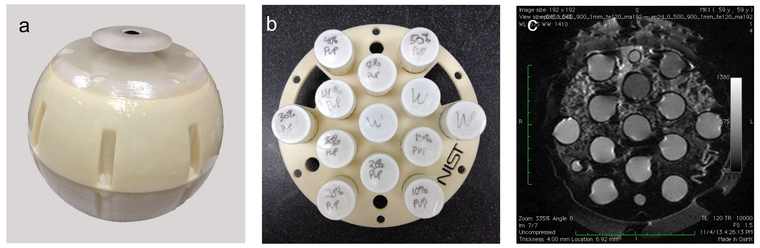


Figure 2: Isotropic diffusion phantom. a) The assembled phantom. Fill port caps at the poles of the phantom are removed to easily fill the interior with ice. A small secondary fill port in the handle of the fill port cap allows for removal of air bubbles, important for non-coronal imaging. b) Polypropylene vials of PVP at the center of phantom: a vial of DI water is placed in the middle to assess isocenter performance of ADC measurement. The vials have a diameter of approximately 26 mm, and a length of 60 mm. c) Diffusion-weighted image of the vials (b_{900}) at 1.5 T. Small susceptibility artifacts can be seen, but do not adversely affect the measurement of ADC.

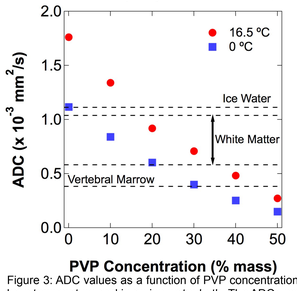


Figure 3: ADC values as a function of PVP concentration at bore temperature and in an ice-water bath. The ADCs cover a physiologically-relevant range, including that of white matter.

DAY 1:

1. Coronal DWI scans at b= 0, 500 and 900 s/mm^2
2. Reposition phantom, axial scans at b= 0, 500 and 900 s/mm^2
3. Reposition phantom, sagittal scans at b= 0, 500 and 900 s/mm^2
4. Reposition phantom, coronal scans at b= 0, 500 and 900 s/mm^2
5. Reposition phantom, axial scans at b= 0, 500 and 900 s/mm^2
6. Reposition phantom, sagittal scans at b= 0, 500 and 900 s/mm^2

DAY 2: REPEAT

The PDF committee gratefully acknowledges the contributions of our colleagues at IMI-QuICConCePT and NIST towards phantom development and testing: John C. Waterton, David M. Morris, Hossein Ragheb, Alan Jackson, Nandita deSouza, David J. Collins, Bernard E. van Beers, Philippe Garteiser, Sabrina Doblas, Stephen E. Russek, and Kathryn E. Keenan.

Summary Statistics from DRO Evaluation

With the goal of evaluating software package performance, sets of R1 relaxometry DROs, both with and without noise, were generated by Dr. Daniel Barboriak. R1 measurement results were used to generate figures of merit. Fifteen different software package implementations were tested; a preliminary example of the summary statistics is shown in Figure 4. These summary statistics were presented in an anonymized fashion in order to encourage participation while at the same time allowing comparison of a given package's performance *vs.* the other packages. Discussion of these preliminary results has led to an effort to narrow the analysis to the range of parameter combinations most relevant to clinical use cases in order to provide a more useful comparison of the software packages.

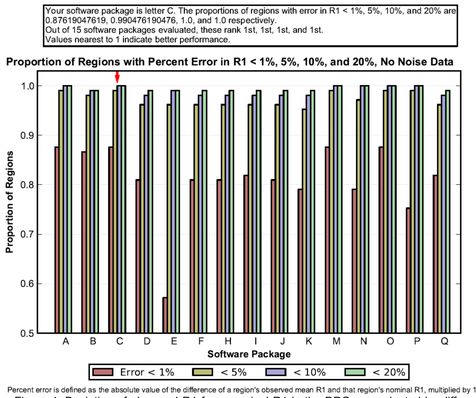


Figure 4: Deviation of observed R1 from nominal R1 in the DRO as evaluated by different analysis packages.

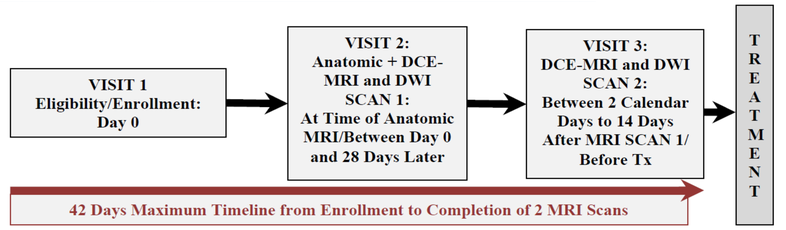
This work was geared towards evaluation of metrics used in DCE-MRI. However, it is readily apparent how DROs can be extended into other MR parameters of interest, such as ADC.

Test-Retest Data: ACRIN 6701

The ACRIN 6701 trial, led by Dr. Mark Rosen, implements the QIBA PDF DCE-MRI Profile v1.0 to assess the limits of reproducibility of quantitative MRI metrics, specifically K^{trans} and $IAUCGC90_{bn}$, in the prostate. There are small deviations from profile recommendations in order to align with patient needs: these include acquiring data at 3.0 T instead of 1.5 T, the use of parallel imaging, and an axial imaging plane rather than the coronal imaging specified in the Profile. It also seeks to acquire test-retest data for ADC in the whole prostate and in the dominant tumor nodule, and examines test-retest data acquired via the coffee-break approach (same day) vs. data acquired on different days Quality control will be established by use of the QIBA DCE-MRI phantom and an ice-water phantom for DWI. Two 3 T MRI studies temporally separated by 2 to 14 days will be performed on participants, selected by recent diagnosis of adenocarcinoma by use of TRUS-guided biopsy and other criteria.

Currently, 8 sites in the US and Europe have agreed to participate in the study, representing three different MRI vendors, with plans to initiate data acquisition by Q1 2014. To date, 5 of these sites are fully qualified by use of the DCE and DWI phantoms, with the remaining three sites needing to qualify DCE scans. More information may be found at:

http://www.acrin.org/PROTOCOLSUMMARYTABLE/PROTOCOL6701.aspx



New NIBIB-funded Projects

Four new groundwork projects previously submitted to NIBIB were funded in October 2013:

1. DCE-MRI phantom study to evaluate the impact of parallel imaging and B_1 inhomogeneities at different MR field strengths of 1, 1.5, and 3 T (T. Persigehl, H. Laue)
This project aims to acquire T1 maps obtained from variable flip angle data with the QIBA DCE-MRI phantom across several different sites, field strengths and vendors. B1 maps will be acquired to correct for flip angle error on a pixel-by-pixel basis. T1 data will be acquired with and without parallel imaging, and analyzed with and without B1 correction.

2. Development of a tool to evaluate software using artificial DCE-MRI data and statistical analysis (H. Laue)
There is a need to statistically compare DCE-MRI analysis packages to properly assess variability. Test data will be synthesized, with associated DCE-MRI reference parameters maps. These data will then be evaluated by different software packages to generate parameter maps. A software tool will be developed using the open source Python environment to compare via difference and ratio plots the reference and software-generated parameter maps.

3. DW-MRI ADC Phantom (M. Boss)
Building on the current isotropic diffusion phantom prototype, this work will further refine phantom design and scale up the number of available phantoms. Standardization of DW imaging protocol and ROI selection will enable identification of error sources and scanner-to-scanner variation in ADC measurements. 3D printing technology will be employed for prototyping and will lead into a mold-based production method. Moving past the ice-water paradigm, *in situ* thermometry techniques will be evaluated to enable bore-temperature scanning, widening the range of obtainable ADC values, as seen in Figure 3.

4. Software Development for Analysis of QIBA DW-MRI Phantom Data (T. Chenevert)
The software deliverable for this project will take in DW-MRI phantom data in DICOM format and output ADC values for regions-of-interest (ROIs), as well as provide signal-to-noise ratio estimates. It will determine optimal *b*-value selection for ROIs and provide summary statistics for all parameters of interest. The software package will directly feed into the QC section of the QIBA DW-MRI profile.

The timeline for completion of each of these projects is one year.

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