

Summary of Activities in 2014

2014 was an active year for the PDF committee's efforts in diffusion-weighted MRI. The committee oversaw the prototyping and testing of an isotropic diffusion phantom, with a goal of providing a quality control object for characterizing measurement of the apparent diffusion coefficient (ADC) a quantitative biomarker. QIBA PDF members received prototype copies, leading to data that culminated in the submission of multiple abstracts and presentation of results. A finalized phantom design has been provided to 12 QIBA PDF member/collaborator institutions, and has attracted interest from a clinical trial. In parallel, a NIBIB-funded project to develop an analysis package for phantom data was completed.

Due to the increasing number of topics of interest within the PDF committee, members have formed task force groups to focus on specific problems. Within diffusion MRI, the committee now has a Diffusion-Weighted Imaging task force group that focuses on measurement of isotropic diffusion, primarily via ADC, as well as a Diffusion Tensor Imaging group, focusing on metrics for assessment of anisotropic diffusion, primarily in the brain. Each of these task force groups is dedicated to developing a profile document.

Isotropic Diffusion Phantom

In late 2013, an initial isotropic diffusion phantom prototype was conceptualized (Fig 1a, b) and 3D-printed (Fig 1c) by the PDF Committee, using resources provided by NIST and the National Cancer Institute. It consisted of a spherical shell compatible with all known commercial multi-channel head coils, and employed aqueous solutions of the polymer polyvinylpyrrolidone (PVP) (Fig 1d), whose use was pioneered by researchers at NIH^{1,2}. Higher concentrations of PVP result in lower ADC values. Due to the temperature-sensitivity of diffusion, the phantom incorporated an ice-water bath as a means of temperature stabilization, eliminating thermal variability across test sites and time. This first prototype (Fig 1e) underwent round-robin testing at 3 sites within the IMI-QuICConCePT consortium institutions, located in the UK and the EU, leading to the submission and presentation of a successful ISMRM abstract³.

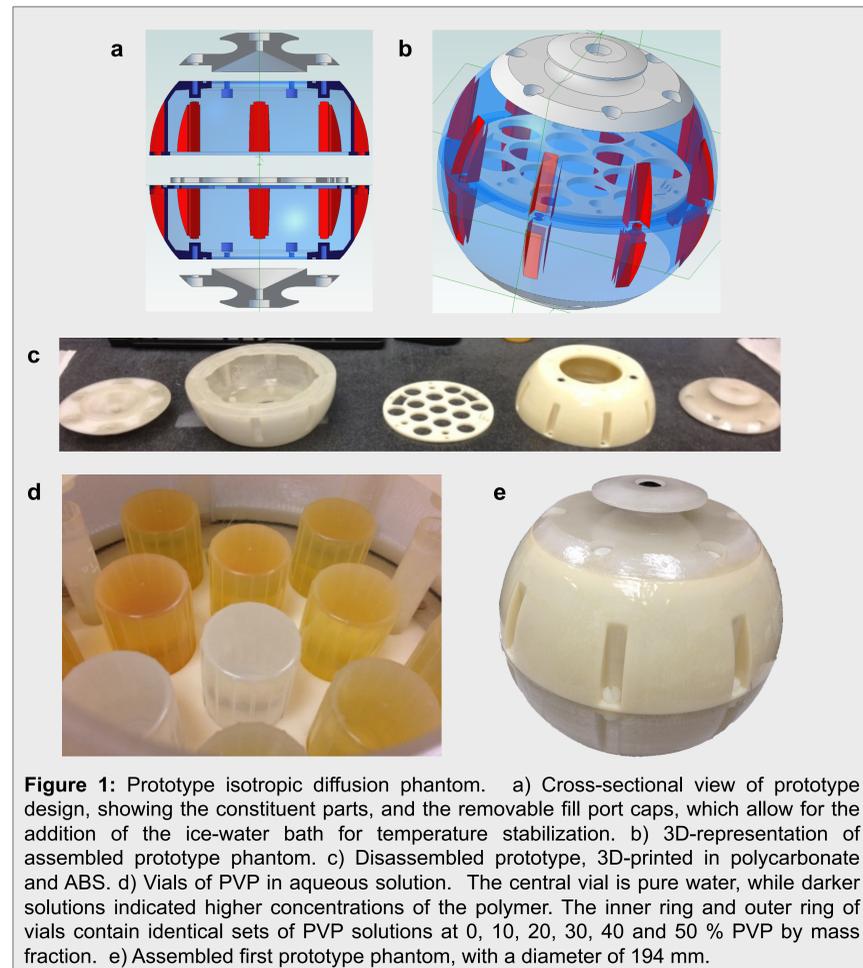


Figure 1: Prototype isotropic diffusion phantom. a) Cross-sectional view of prototype design, showing the constituent parts, and the removable fill port caps, which allow for the addition of the ice-water bath for temperature stabilization. b) 3D-representation of assembled prototype phantom. c) Disassembled prototype, 3D-printed in polycarbonate and ABS. d) Vials of PVP in aqueous solution. The central vial is pure water, while darker solutions indicated higher concentrations of the polymer. The inner ring and outer ring of vials contain identical sets of PVP solutions at 0, 10, 20, 30, 40 and 50 % PVP by mass fraction. e) Assembled first prototype phantom, with a diameter of 194 mm.

This early success generated interest within the diffusion MRI community, and a second prototype copy was provided to the TRACK-TBI clinical trial. TRACK-TBI sites assessed this prototype and provided data to the PDF committee for comparison with results from our EU collaborators. The first prototype copy continued to be assessed within the 3 IMI-QuICConCePT sites for determination of longitudinal reproducibility of results, as well as at Cologne, where QIBA PDF members Drs. Dennis Hedderich and Thorsten Persigehl oversaw experiments. These data were collected, analyzed, and presented at the AAPM meeting in July 2014⁴, with representative data shown in Fig. 2. Concurrently, Round 3 funding from NIBIB allowed for further development and testing of the phantom. A third, modified prototype was sent to Dr. Chen Lin at Indiana University, where Dr. Lin's team performed experiments elucidating off-isocenter effects on the measurement of ADC, resulting in an abstract submission for ISMRM 2015. These results informed the phantom design, usage, and inherent variability in assessing ADC.

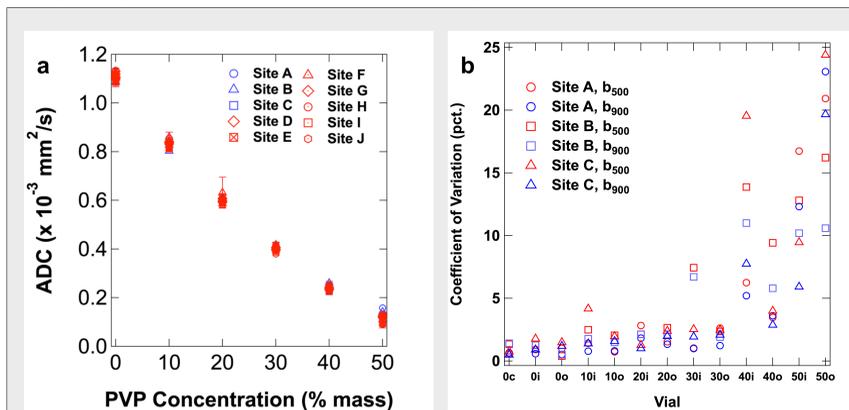


Figure 2: Prototype phantom data. a) Aggregate data from IMI-QuICConCePT and TRACK-TBI sites, demonstrating the range of ADC values achieved by use of PVP at 0 °C, as well as the reproducibility of these values across sites and time. b) Breakdown of data acquired at IMI sites in initial round robin. Vial nomenclature represents the PVP concentration and the vial location: central (c), inner ring (i), or outer ring (o). Red data points are from ADC values measured using b_0 and b_{500} , while blue data points were measured with b_0 and b_{900} . The data show that the higher b-value experiments result in lower coefficients of variation, and have informed imaging protocol choice. The high CoV's seen for the low ADC vials are likely due to insufficiently high b-value, and the recommended protocol for imaging these vials now includes b_{2000} .

After prototyping and initial testing, a finalized phantom design was produced by a commercial manufacturer (Fig. 3). This design incorporated lessons learned from the prototyping stage, and was produced in transparent polycarbonate by means of injection molding, keeping costs down, and allowing optimal use of NIBIB Round 3 funds. Further research will acquire data with 12 copies of the ADC phantom provided to QIBA PDF and IMI-QuICConCePT institutions:

1. NIST, Boulder CO
2. University of Michigan
3. University of Wisconsin
4. University of Pennsylvania
5. Massachusetts General Hospital
6. University of Southern California
7. University Hospital Cologne, Germany
8. AIM Medical Imaging, Vancouver
9. Memorial Sloan Kettering, NY
10. The Institute of Cancer Research, UK
11. University of Manchester, UK
12. INSERM, France

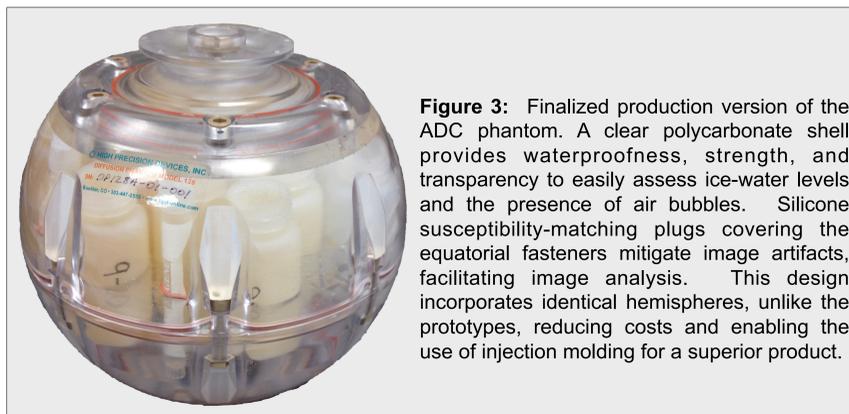


Figure 3: Finalized production version of the ADC phantom. A clear polycarbonate shell provides waterproofness, strength, and transparency to easily assess ice-water levels and the presence of air bubbles. Silicone susceptibility-matching plugs covering the equatorial fasteners mitigate image artifacts, facilitating image analysis. This design incorporates identical hemispheres, unlike the prototypes, reducing costs and enabling the use of injection molding for a superior product.

DWI Phantom Analysis Software

Dr. Thomas Chenevert successfully completed a Round 3 NIBIB-funded project to develop an analysis package for the ADC phantom, "QIBaphan". The software automates calculation and analysis of ADC and SNR maps to characterize scanner performance and allow for cross-site comparison of scanners using the phantom. It reads in DICOM images of the phantom and provides a full exam series catalog, checks for acquisition protocol compliance ($b = 0, 500, 900$ and 200 s/mm^2), generates diffusion-weighted images and ADC maps for user-directed region-of-interest (ROI) placement, and provides summary statistics within the ROIs in the form of a CSV file. The software eliminates variation in analyzed results due to any possible differences in ADC calculation from the DW-images, determining ADC within an ROI rather than on a pixel-by-pixel basis. QIBaphan greatly complements the phantom, and will facilitate the coordination of multi-site experiments to elucidate sources of bias and variation, e.g. gradient non-linearity, as well as better enabling consistent quality control when employing the QIBA DWI profile.

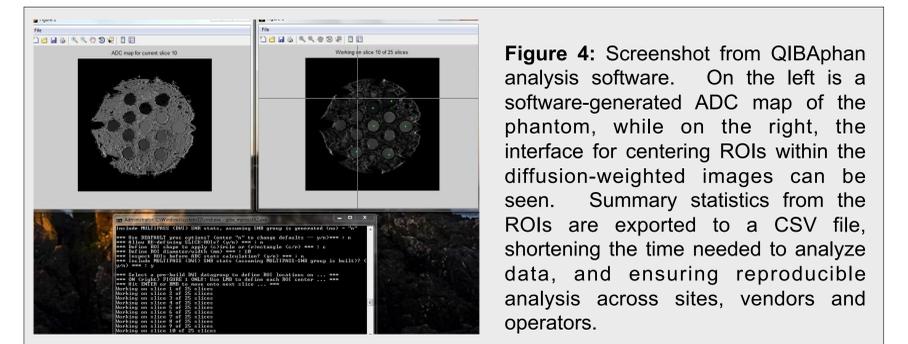


Figure 4: Screenshot from QIBaphan analysis software. On the left is a software-generated ADC map of the phantom, while on the right, the interface for centering ROIs within the diffusion-weighted images can be seen. Summary statistics from the ROIs are exported to a CSV file, shortening the time needed to analyze data, and ensuring reproducible analysis across sites, vendors and operators.

Formation of Task Force Groups

With the rapid increase in profile writing activities within the PDF committee, it is necessary to have dedicated task force groups (TFGs), composed of a small number of individuals, to focus on a particular profile. Within PDF's diffusion activities, this change has resulted in a dedicated isotropic group (DWI), and a corresponding group for anisotropic diffusion (DTI). These groups anticipate accelerated development of profiles as a result, while simultaneously addressing the wider breadth of PDF biomarkers of interest.

The DWI group is co-chaired by Michael Boss and Tom Chenevert. Contributing members are Amita Dave, Dennis Hedderich, Marko Ivancevic, Mark Rosen, and Ona Wu. The DTI group is led by Drs. James Provenzale and Walter Schneider, with support from Michael Boss and Ed Jackson. These groups will meet on their own, and report their progress to the wider PDF committee on a periodic basis.

Diffusion Activities in 2015

The DWI TFG anticipates completion of the DWI profile for public comment by the end of 2014. This will enable implementation of the profile in clinical trials, in the US and beyond. With a substantial number of production ADC phantoms in the hands of QIBA members and collaborators in the UK and the EU, the TFG hopes to characterize scanner performance over a relevant physiological range of ADC across scanners, operators, and time. During the lifetime of the phantoms, NIST will provide ground truth values of ADC and other relevant MR parameters. These activities will establish a baseline for scanner performance and shed light on the intrinsic measurement error when assessing isotropic diffusion. Simultaneously, the DTI TFG will continue its efforts into 2015, capitalizing on lessons learned from previous PDF profile efforts, and aiming to better standardize the assessment of anisotropic diffusion, most notably in the brain.

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¹C Pierpaoli et al., Proc. 17th Ann. Meeting ISMRM, Abstract 1414 (2009)

²C Pierpaoli et al., US Patent application 13/146,058

³M Boss et al., Proc. 22nd Ann. Meeting ISMRM, Abstract 4505 (2014)

⁴M Boss et al., AAPM Annual Meeting, Abstract TU-C-12A-8 (2014)

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