Calibrating high q-value diffusion MRI methods with a novel anisotropic phantom

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Introduction: Diffusion MRI (DI) comprises a growing number of methods that utilize anisotropic water diffusion to detect distinct features of tissue microstructure. In order to test, calibrate, and validate these methods an anisotropic diffusion phantom such as one employing Glass Capillary Arrays (GCA) (1) should be used as a gold standard to vet a wide array of high q-value DI methods. Typically, these advanced DI methods require applying high q- or b-values that "crush" the free water signal. To achieve comparability with real tissue, a suitable phantom would contain a solute whose free diffusion coefficient would be an order of magnitude smaller than that of free water at the same temperature. To this end, we propose using a GCA phantom filled with a low diffusivity silicon oil. Moreover, an analytical framework needs to be employed that incorporates the phantom's known pore morphology to predict the diffusion weighted (DW) signal intensity for any prescribed DW pulse sequence. Here, this phantom and a novel analysis pipeline were used to test and validate High angular resolution diffusion imaging (HARDI) and double pulsed-field gradient (d-PFG) MRI methods.

Materials and Methods: The GCA phantom (fig.1) consists of eight stacked fused silica wafers (13mm OD) filled with Decamethylcyclopentasiloxane ($C_{10}H_{30}O_5Si_5$). The wafers' microcapillaries have nominal pore diameters of 5, 10, and 25 μm. For pores with cylindrical symmetry the MRI signal $S(\mathbf{q})$ can be written as,

$$S(\mathbf{q}) = S_0 E_{circle}\left(q\sin\theta; \frac{a}{\sqrt{D\Delta}}, \frac{\delta}{\Delta}\right)\exp\left(-(2\pi q\cos\theta)^2\left(\Delta - \frac{\delta}{3}\right)D\right) \qquad (1)$$

where S_0 is the signal without diffusion attenuation, $\mathbf{q}$ is the diffusion sensitization vector, $q = |\mathbf{q}|$, θ is the angle between $\mathbf{q}$ and the cylinders' axes, δ is the diffusion gradient pulse width, Δ is the diffusion pulse separation, a is the radius of the pores, and D is the bulk diffusivity of the medium. For a given pulse sequence, the transverse attenuation function, E_{circle}, can be computed using the multiple correlation function (MCF) method (2). HARDI data were acquired using a sagittal 2D spin-echo DWI sequence with the following parameters: TE/TR=57.286/4000 ms, 1 ave., FOV=16x16 mm^2 coronal slice thickness = 1 mm, and spatial res. = 125x125x2000 μm^3. Diffusion MR parameters: δ = 3 ms, Δ = 50 ms. The q-vectors lay in the plane of the free-restricted diffusion directions, with G = 123, 205, 342, 580 mT/m. To calibrate HARDI methods (e.g., Q-ball or spherical deconvolution) or multi-shell q-space MRI experiments, we determined whether they could generate the correct estimate of the radius of the GCA's cylindrical pores. D-PFG filtered data were acquired using a 2D spin echo MRI sequence with the following parameters: τ_m = 0 (3), TE/TR=8/5000 ms, 2 ave., FOV=16x16 mm^2 sagittal slice thickness = 1 mm and spatial resolution = 125x125x1000 μm^3. D-PFG MR parameters: δ = 3 ms, Δ = 30 ms, ϕ the angle between the two PFG blocks varied from 0° to 360° with intervals of 30° in the restricted plane and G = 221.4, 295.2, 369, 442.8, 516.6, 590.4, 664.2 mT/m. The d-PFG experiment results in an MR signal attenuation from the microcapillaries with radius R that is expressed as $E_{rest}(G_1, G_2, \phi, R)$. Since the phantom only consists of fused glass capillaries, a free diffusion compartment was not modeled. The restricted signal was calculated (for each value of G_1, G_2, ϕ, and R) using the MCF method (2), which was later extended to describe d-PFG MR experiments (4).

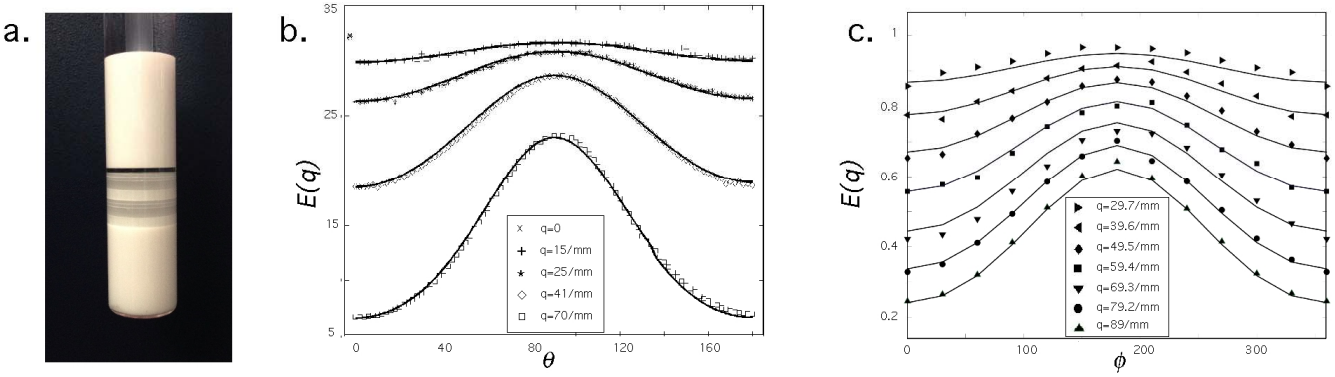

Figure 1: a.) Picture of the GCA phantom. b.) HARDI and c.) dPFG fits for one of the 5μm GCA wafers.

Table 1. Phantom pore diameter measured using HARDI and D-PFG vs. nominal pore diameter

Nominal	5.0 μm	10.0 μm	25.0 μm	5.0 μm	10.0 μm	25.0 μm
HARDI	5.42 μm	9.92 μm	30.4 μm	5.1 μm	9.88 μm	30.0 μm
d-PFG	5.28 μm	10.06 μm	25.45 μm	5.28 μm	10.12 μm	26.03 μm

Results and Discussion: Figure 1 shows a good agreement between the theoretical predictions and experimental data. Table 1 shows the resulting pore diameters predicted by the HARDI and d-PFG models. Most of the estimated pore diameters are very close to the nominal pore diameters. The HARDI method over-estimates the pore diameter for the 25 mm wafers. The cause of this bias is currently being investigated.

Conclusion: The silicon oil-filled GCA phantom is suitable to test, calibrate, validate and reveal limitations of high q-value MRI methods.

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