DIFFUSION GRADIENT CALIBRATION IN DSI USING A CYCLOOCTANE PHANTOM

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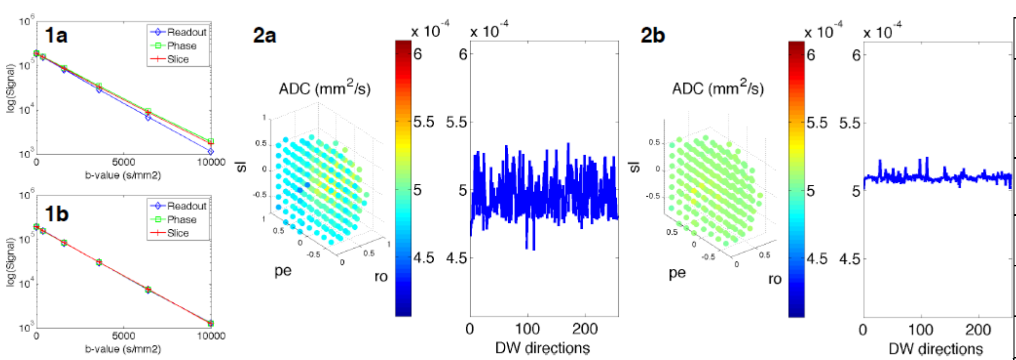
Target Audience Clinicians, researchers and technologists involved in diffusion spectrum imaging (DSI) and q-space imaging (QSI).

Purpose Gradient calibration is vital to accurate and precise measurements in diffusion MRI. This mitigates the bias in q-space sampling that leads to errors in estimation of the probability density function and relevant parameters. Small errors in gradient strength could be magnified. For example, the measured apparent diffusion coefficient (ADC) depends on the square of the gradient amplitude. One method adjusts the strength of the diffusion weighting (DW) gradients in a phantom filled with a solution of known diffusivity at a given temperature [1]. Phantoms filled with water have been used [1, 2], however its relatively high diffusivity makes it suitable only for calibration at lower b-values. To obtain calibration data at higher b-values, as required in DSI [3] and QSI in general, we used a phantom filled with cyclooctane. We compared corrected and uncorrected DSI data in the phantom and one ex-vivo rat heart.

Methods A 3cm long plastic tube was filled with 99% cyclooctane (Sigma-Aldrich, MO, USA). MRI was performed using a 9.4T preclinical scanner (Agilent Technologies, Santa Clara, CA). Uncorrected DSI data were acquired of the phantom with a 3D echo planar imaging sequence with Stejskal-Tanner DW, where TR = 1000 ms, TE = 23.7 ms, resolution = 375^3 μm^3, G_{max} = 728 mT/m, δ = 5 ms, Δ = 12 ms, 257 diffusion encoding vectors, B_{max} = 10000 s/mm^2. The ADC was calculated for each point in q-space based on fitting a monoexponential decay curve. The temperature of the phantom was measured as 21°C before and after the scan. The reference diffusivity at 21°C was calculated by fitting a 2nd-order polynomial to a range of reference diffusivity data [4]. Gradient calibration factors (α) were calculated using $\alpha = (D_t/D_p)^{0.5}$ where D_t is the reference diffusivity and D_p is the uncorrected diffusivity [1], and applied to obtain corrected DSI data. A region-of-interest (ROI) was specified in the central 5^3 voxels. Subsequently, an ex-vivo rat heart was prepared [5] and scanned using both uncorrected and corrected DSI. Here a 40-voxel ROI was specified in the myocardium in a middle transverse slice.

Results Figures 1a & 1b plot signal S(ROI) vs b-value in q-space in the uncorrected and corrected data respectively, showing that the decay is monoexponential through the full range of b-values. Figures 2a & 2b present the ADC (ROI) reconstructed at each point in q-space in the uncorrected and corrected data, and the results are shown in Table 1. The accuracy and precision of the mean ADC (ROI) estimates are improved post-correction. The lower generalized fractional anisotropy and mean excess kurtosis post-correction are consistent with the isotropic, non-restricted diffusion one would expect in the phantom. Subtle differences are revealed in the heart post-correction. Our previous work (unpublished) with bootstrap diffusion tensor imaging in ex-vivo rat heart yielded improvements in precision of the fractional anisotropy and 95% cone of uncertainty by 18% and 20% respectively post-correction.

Discussion Cyclooctane possesses a number of properties that make it suitable for gradient calibration at high b-values, including isotropic diffusion, relatively low diffusivity and high viscosity, and a single proton resonance. Conversely, water fails as a calibration substrate due to severe signal attenuation at higher b-values. Gradient calibration is critical to accurate sampling of q-space, particularly for applications like DSI that rely on a precise relationship of q-space samples. We present the novel use of a phantom for gradient calibration in DSI and other high b-value QSI applications.



Figures 1a, b. Semilog plot of the signal S(ROI) vs b-value along the readout (blue), phase (green) and slice (red) axes in q-space in the uncorrected and corrected phantom data respectively; **Figures 2a, b.** ADC (ROI) representation in 3D q-space and plotted against DW direction in uncorrected and corrected phantom data; **Table 1.** Comparison of mean apparent diffusion coefficient (ADC), generalized fractional anisotropy (GFA) and mean excess kurtosis (MK) shows improvements post-correction.

Table 1

Reference	**Phantom**	**Heart**
Mean ADC ($\times 10e^{-4}$ mm^2/s)	5.08	-
Uncorrected		
Mean ADC ($\times 10e^{-4}$ mm^2/s)	4.96 ± 0.16	8.30 ± 0.44
GFA	0.0611 ± 0.0015	0.220 ± 0.043
MK	0.251 ± 0.011	0.93 ± 0.14
Corrected		
Mean ADC ($\times 10e^{-4}$ mm^2/s)	5.095 ± 0.028	8.59 ± 0.44
GFA	0.00692 ± 0.00083	0.199 ± 0.035
MK	0.1358 ± 0.0098	0.88 ± 0.13

References [1] Nagy Z., et al. MRM. 2007; [2] Malyarenko., et al. JMRI. 2013; [3] Wedeen V.J., et al. MRM. 2005; [4] Tofts P.S., et al. MRM. 2000; [5] Plank G., et al. Phil Trans Series A. 2009.

Acknowledgements This work was supported by the EPSRC, UK (EP/J013250/1) and the British Heart Foundation (FS/11/50/29038).