An Accelerated, Alternative Approach for Estimating Zero-Displacement Probability in Hybrid Diffusion Imaging

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Inroduction: Hybrid diffusion imaging (HYDI) is a diffusion-weighted (DW) technique whose encoding scheme is composed of multiple concentric (spherical) shells of constant diffusion weighting in q-space, which may be used to characterize the signal behavior with low, moderate, and high diffusion weighting [1]. The zero-displacement probability (Po) describes the probability density of water molecules that do not diffuse within the diffusion time [2], and is a measure of restricted diffusion, which may be modulated by axons and myelin in white matter diseases like multiple sclerosis (MS). In HYDI, the Po is conventionally estimated by using the signal measurements in all the shells (Po_{all}), which requires long scan time. However, the highest diffusion-weighting measurements are likely to contribute most heavily to the restricted diffusion signal. Thus, an alternative and faster approach for characterizing restricted diffusion would be to use the signal measurements only in the outermost shell, or highest diffusion weighting (Po_{outer}).

In this work, we graphically and statistically compare both Po_{all} and Po_{outer} approaches in normal appearing white matter (NAWM) from MS patients and white matter (WM) in a control group. We show that both approaches yield similar statistical properties for characterizing restricted diffusion, which suggests that the outer shell Po is both adequate and faster than using full q-space measurements.

Table 1: NAWM/WM measurements (mean ± stdev)

	Po_{outer}	Po_{all}
Patient 1	.1321 ± .0187	.7037 ± .0748
Patient 2	.1396 ± .0223	.7472 ± .0877
Patient 3	.1423 ± .0200	.7509 ± .0769
Patient 4	.1400 ± .0162	.7361 ± .0634
Patient 5	.1449 ± .0201	.7625 ± .0787
Control 1	.1368 ± .0194	.7173 ± .0752
Control 2	.1507 ± .0195	.7686 ± .0778
Control 3	.1543 ± .0169	.7870 ± .0659
Control 4	.1450 ± .0184	.7577 ± .0713

Theory: In q-space, the diffusion propagator is the 3-D Fourier transform of the DW measurements in q-space: $P(\vec{R}) = FT[E(\vec{q})]$, where $\vec{R}$ is the diffusion displacement vector and $E(\vec{q}) = S(\vec{q}) / S(0)$ is the normalized q-space signal [3]. Po is obtained upon application of the central ordinate theorem: $Po = Po_{all} = P(\vec{R} = 0) = \int E(\vec{q}) d^3\vec{q} \approx 4\pi \int_0^{q_{\max}} E(q\hat{u}) q^2 dq$, where $q_{\max}$ is the radius of the outermost shell; $\hat{u}$ is a 3D unit vector; and $q = |\vec{q}| = |q\hat{u}|$. Similarly, $Po_{outer} = 4\pi \int_{q_b}^{q_{\max}} E(q\hat{u}) q^2 dq$, where q_b is the radius of the second-to-last shell. Po_{all} was estimated by taking weighted arithmetic mean of signal across all shells while Po_{outer} by taking the arithmetic mean of signal across outermost shell only.

Materials and Methods: HYDI was performed on five MS patients and four healthy volunteers. MR images were acquired using a 3 T GE SIGNA whole body scanner. The DW pulse sequence was a single-shot, spin-echo, echo-planar imaging (SS-SE-EPI) pulse sequence with diffusion gradient pulses, dual-echo gradient refocusing to minimize distortions from eddy currents, and cardiac gating (using a photo-plethysmograph) to minimize signal fluctuations from brain pulsations. The HYDI sampling scheme consisted of 6 icosahedral shells with a total of 127 encoding directions, 50 of them in the outermost shell. MR parameters were: TR/TE = 2300/99 ms, matrix = 96x96, FOV = 24 cm, b_{max} = 6500 s/mm^2, and 15 axial 5 mm slices. Highly compact NAWM tissues for MS patients and WM tissues for control group were selected by intersecting the segmentation outputs of the FAST [4] algorithm (four clusters for both patient and control) on Po_{all} and Po_{outer} maps. Volume normalized histograms of Po were compared between patient and control. In addition, mean and standard deviation were calculated for Po of NAWM and WM (Table 1).

Results: The Po_{all} and Po_{outer} histograms are highly overlapping with similar distributions (Fig. 1a,b). The Po_{outer} and Po_{all} in both MS NAWM and healthy WM were plotted against each other. The resulting scatter plot shows a strong linear relationship between Po_{outer} and Po_{all}, with Pearson's correlation coefficient being $r^2 = 0.950$ (Fig. 1c). A two-tailed two-sample t-test for equal population variances was applied to compare the mean Po between NAWM and healthy WM. A p-value of less than 0.05 was considered to indicate a statistically significant difference. The p-value is 0.138 for Po_{outer} and 0.342 for Po_{all}. Both the histograms and scatter plot demonstrate that the characterization of restricted diffusion for each approach is about the same, which suggests that the outermost shell of the HYDI scheme is adequate for Po measurements. However, both the overlapping nature of the Po distributions between MS patients and controls and the t-test suggest that Po may not be sensitive to disease related changes. These results are inconsistent with a previous study showing reduced Po in MS NAWM [5].

Conclusions: A new approach for estimating Po involving only the encoding directions in the outermost shell is just as sensitive to restricted diffusion in WM as the full q-space approach. This demonstrates that characterization of restricted diffusion does not require measurements over all of q-space.

References: [1] Wu, Alexander Neuroimage (2007). [2] Wedeen et al. MRM (2005). [3] Callaghan et al. Nature (1991). [4] Zhang et al. IEEE Trans. Med (2001). [5] Assaf et al. MRM (2002).

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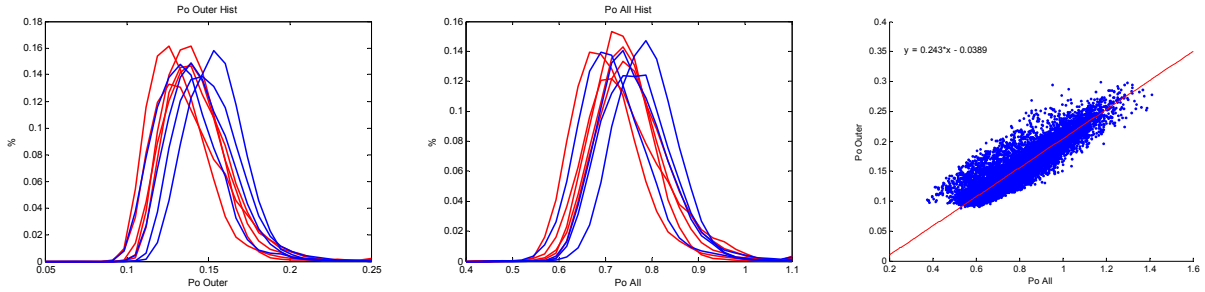

Figure 1: (a), (b) Po_{outer} and Po_{all} histograms of patients (red) and controls (blue) and (c) Po_{outer} vs Po_{all}, where red line denotes least squares linear regression.