Isotropic Diffusion Weighting Provides Insight on Diffusion Compartments in Human Brain White Matter In vivo

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TARGET AUDIENCE: Researchers interested in biophysical basis of diffusion weighted signal.

INTRODUCTION: Understanding diffusion-weighted MR signal in brain white matter (WM) has been a long-sought-after goal. However, accurate estimation of the diffusivities in different tissue compartments have not yet been well established. Using isotropic DWI, we experimentally address two common assumptions made in different models: (i) the presence of isotropically restricted water compartment [1] and (ii) the relation between ADC of extra and intra-axonal water in single fiber bundles [2].

METHODS: Measurements were performed on an informed volunteer in a human scanner (Siemens PRISMA, max gradient strength: 80 mT/m, 32 channel receive coil). The imaging parameters were FOV = 25.6 cm, 4 mm isotropic resolution, TE = 123 ms and 9 slices. An isotropic-weighted diffusion protocol was run for 10 b-values incremented linearly between 0.05 and 5.4 ms/μm^2. The number of averages were increased with increased b-values. A simple DWI sequence was also applied for 3 b-value shells of 0.05, 1 and 2 ms/μm^2 and 64 directions in each shell. For single bundle WM, only voxels with an FA>0.55, were used.

$$S(b) = (1-v)e^{-bD_{a||}\cos(\theta)^2} + v\,e^{-bD_{e||}\cos(\theta)^2 - bD_{e\perp}\sin(\theta)^2} - (1)$$

From the DWI sequence, the four parameters a two compartment model (Eq.(1)) were estimated [2,3]. Using this model the radial extraaxonal diffusivity $D_{e\perp}$, and volume fractions can be uniquely derived from the radial diffusivity and kurtosis [2]. But, since the axial kurtosis only suggests the squared difference between $D_{a||}$ and $D_{e||}$, the axial measures define $D_{a||}$ and $D_{e||}$, with an ambiguity. The two conditions (i) [$D_{a||} < D_{e||}$] (ii) [$D_{a||} > D_{e||}$] result in drastically different diffusivities (Table 1 for the results presented below). We resolve this ambiguity using the isotropic encoding, whose kurtosis is sensitive to the squared difference between the mean ADC of the two compartments rather than their axial components.

RESULTS: Fig.1 shows normalized signal for 3 images at different b-values obtained from the isotropic weighted sequence. The contrast between gray and white matter is low. For WM voxels (FA>0.55), nearly monoexponential decay is observed until the remaining signal at b = 5.4 ms/μm^2 is around 2.7%. Fig 2. shows the mean normalized signal attenuation obtained from isotropic DWI for single bundle WM voxels.

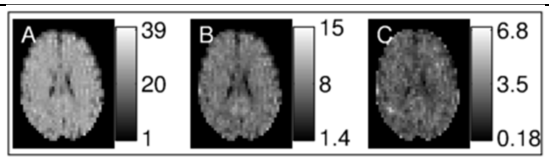

Fig1: Normalized signal for isotropic DWI at b-values of 1.8, 3.6 and 5.4 ms/μm^2 (left to right). At the highest b-factor, the average remaining signal is only around 2.7% of the initial signal.

Condition	$D_{a\|\|}$	$D_{e\|\|}$	$Tr(D_a)/3$	$Tr(D_e)/3$	K_{iso}
$D_{a\|\|} < D_{e\|\|}$	1.0±0.4	2.4±0.6	0.3±0.1	1.3±0.3	0.94
$D_{a\|\|} > D_{e\|\|}$	2.6±0.8	0.8±0.3	0.9±0.3	0.8±0.2	0.06

Table 1: Parameters of Eq.(1) for the two conditions. K_{iso} is the estimated kurtosis for the isotropic weighting.

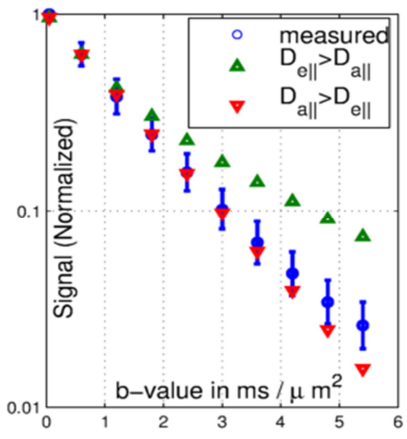

Fig 2: Decay curves for isotropic encoding scheme. The blue dots with error bars are log averaged data for all WM voxels measured with the isotropic encoding sequence. The upper and lower triangles are the estimated curves from the two fitting conditions.

From the two-compartment model [4,3], the volume fraction of the extra-axonal water was found to be 0.6±0.1 and the $D_{e\perp}$ was 0.7±0.3 μm^2/ms. Axial diffusivities estimated for the two different conditions are shown in Table 1. The condition [$D_{a||} < D_{e||}$] results in the extraaxonal trace, $Tr(D_e)$, to be significantly larger than $Tr(D_a)$, whereas they are very similar for [$D_{a||} > D_{e||}$]. Fig. 2 shows the attenuation for the isotropic weighting that is expected from these two conditions. It is seen that that [$D_{a||} > D_{e||}$] can better explain the data.

DISCUSSION: The nearly monoexponential decay of the isotropically weighted diffusion data suggests that presence of isotropically restricted water pool in WM (dot using the terminology of Ref.[4]) is negligible. Its presence would have resulted in a strongly nonlinear diffusion decay curve similar to those obtained with a conventional unidirectional encoding. This additional information is helpful for resolving the parameter ambiguity in the two-compartment model, Eq.(1) suggesting the relation $D_{a||}>D_{e||}$, which is opposite to the previously made assumption [3].

REFERENCES: [1] Alexander et al., NeuroImage 2010:52(4) 1374-1389 [2] Fieremans et al., NMR Biomed 2010:23 711-724 [3] Fieremans et al., NeuroImage 2011:58(1) 177-188 [4]Panagiotaki et al., NeuroImage 2012:59(3) 2241-2254