In vivo pore size estimation in white matter with double wave vector diffusion weighting

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INTRODUCTION

Diffusion weighting with two gradient pulse pairs of independent direction (double wave vector diffusion weighting, DWV, see Fig. 1) [1] can provide tissue structure information which is not easily accessible otherwise, such as cell size or shape. For free diffusion, it is irrelevant whether the diffusion gradients in the two weightings are parallel or antiparallel with respect to each other. Both situations should yield the same result. In restricted diffusion, differences between these situations occur at short mixing times, τ_m. This difference, predicted in 1995, was observed in phantoms and biological samples [2-5]. However, experimental data is still scarce, in particular for *in vivo* applications. Here, a DWV sequence with short mixing time is used to estimate the pore size in the human corticospinal tracts (CST) *in vivo*, and analytical expressions for cylindrical pores are used for data analysis.

METHODS

The signal from randomly oriented pores should depend on the angle θ between the two diffusion gradients of equal strength as [1]

$$S/S_0 \approx 1 - \left\langle R^2 \right\rangle \frac{1}{3} \gamma^2 \delta^2 G^2 (2 + \cos\theta) \qquad (1)$$

if $q = \gamma\delta G$ is small and if the time lag τ_m between the two weighting periods is negligible. The mean squared radius of gyration $\langle R^2 \rangle$ increases with pore size. It is also assumed that $\delta \ll \tau_D \ll \Delta$ holds, with τ_D being the mean time required for diffusion across a pore. Equation (1) implies that the diffusion-induced signal loss varies by a factor of 3 between parallel and anti-parallel gradient orientations. An analytical expression for restricted diffusion in parallel cylinders that does not make assumptions on the size of δ and Δ,

$$S/S_0 \approx \exp\left[-\gamma^2 D_0 \delta^2 (\Delta - \delta/3)\left(g_1^2 + g_2^2\right)\right]\left[1 - (2A + B\cos\theta)G^2 + Ag_1^2 + Ag_2^2 + Bg_1g_2\right], \qquad (2)$$

was derived by Özarslan [6], where $g_i = \mathbf{G}^{(i)} \cdot \mathbf{u}$ is calculated from the unit vector $\mathbf{u}$ along the cylinder axis, and A and B are functions of δ, Δ, τ_m, and the cylinder radius, a. D_0 is the free diffusion coefficient. A DWV-prepared double spin echo-echo planar imaging sequence (Fig. 1) with short τ_m was applied to eight healthy volunteers on a 3 T whole-body MR system (Magnetom Trio, Siemens, Erlangen/Germany). For $\mathbf{G}^{(1)}$ and $\mathbf{G}^{(2)}$, the parallel and antiparallel combinations of the 4 directions with $|G_x| = |G_y|$ and $G_z = 0$ were used, approximately perpendicular to the CST (20 axial slices, 3×3×3 mm³ nominal resolution, $\delta = 7.36$ ms, $\Delta = 62.36$ ms, $\tau_m = \delta + 0.6$ ms, $q = 100.4$ mm⁻¹, $TE = TE_1 + TE_2 = 165$ ms, 20 averages). In an additional measurement, the diffusion gradients were applied along the directions of a truncated icosahedron in order to determine the diffusion tensor ($\delta = 10.4$ ms, $\Delta = 65.4$ ms, $q = 100.4$ mm⁻¹, $TE = 176$ ms, 2 averages). In a region of interest (ROI) defined by a signal threshold and covering the CST, $\langle R^2 \rangle$ was calculated from Eq. (1), and a and $|g_i|$ were determined by independently fitting Eq. (2) to both $\mathbf{G}^{(1)} = \pm\mathbf{G}^{(2)}$ result pairs.

RESULTS

The antiparallel-parallel difference $S(q,\pi) - S(q,0)$ decreases upon increasing the mixing time, as predicted. Averaged over the ROI, the equations (1) and (2) yield $\langle R^2 \rangle \approx 3.4$ μm² and a cylinder diameter $2a \approx 13.0$ μm, respectively. These values are on the correct order of magnitude, given that extracellular compartments may contribute. The size of the z component of the fitted cylinder direction, $\mathbf{u}$, agrees reasonably well with that of the diffusion tensor eigenvector corresponding to the largest eigenvalue, $|e_z^{(1)}|$ (Fig. 3). In all volunteers, comparable ROI mean values were measured. The results suggest that a DWV-based estimation of compartment sizes *in vivo* provides results on the correct order of magnitude.
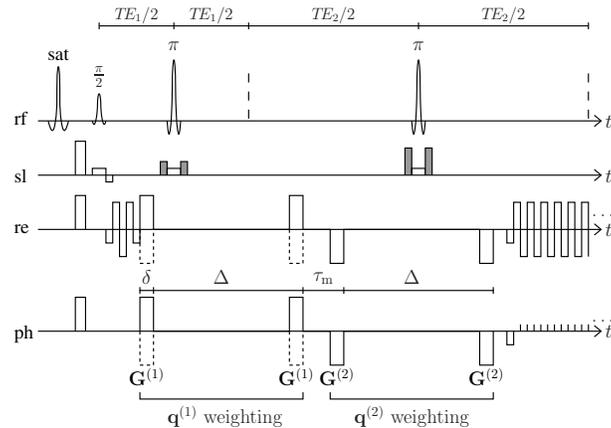

Fig. 1: DWV-prepared EPI sequence. Vertical dashed lines mark spin echo positions. The echo at the last shown position was acquired. $G = |\mathbf{G}^{(1)}| = |\mathbf{G}^{(2)}|$. Diffusion gradients shown by a solid line correspond to $\theta = \pi$. The fat saturation rf pulse is labeled by "sat."
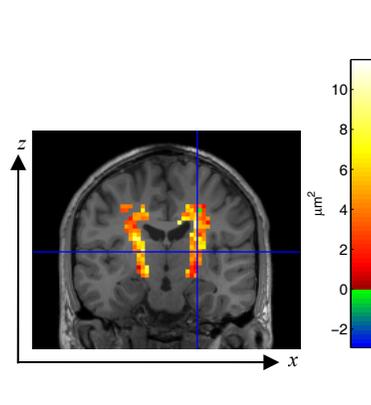
Fig. 2: Color map of $\langle R^2 \rangle$, overlaid on corresponding T_1-weighted image. Color suppressed where $S(q,\pi) < 3.8\,N$ (N: mean background signal).
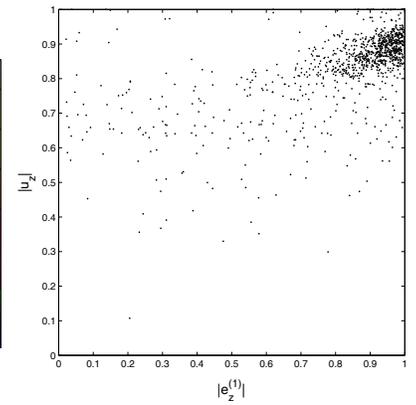
Fig. 3: Fitted cylinder direction compared to the dominant fiber direction indicated by the diffusion tensor: $|u_z|$ versus $|e_z^{(1)}|$ in all ROI voxels.

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