Can Spherical Deconvolution give us more information beyond fibre orientation? Towards novel quantifications of white matter integrity

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Introduction

In recent years Spherical Deconvolution (SD) methods have been applied to diffusion imaging to improve the visualization of multi-fibre orientation in brain regions with complex white matter organization [1][2][3]. However, the potential to quantify white matter integrity with SD has not been explored. Previous simulations have shown that the variation of fibre diffusion properties affects the amplitude of the recovered fibre orientation density function but not its orientation [1][2]. This suggests that the amplitude of the fibre orientation can provide additional information about fibre microstructure. In this study we investigate, using a model of restricted diffusion inside a cylinder, how the variation in the axonal diameters affects the fibre response profile and consequently the amplitude of the estimated fibre orientation.

Methods

The attenuation of the diffusion signal was estimated first along the radial direction of the fibre for different axonal diameters (from 2 μm to 40 μm) with an intra-axonal diffusivity assumed equal to $D_{fibre}=1.5x10^{-3}$ mm^2/s. A Pulsed Gradient Spin Echo sequence was simulated imposing a diffusion gradient setup close to a real sequence adopted for acquiring SD data on a clinical scanner (Δ=40 ms, δ=30 ms, Gradient Amplitude=40 mT/m, b-value ~3000 mm^2/s). In order to include the effects of finite diffusion gradient pulses, two signal models of restricted diffusion were taken into account: the model proposed by Van Gelderen [4] based on the Gaussian Phase Approximation (GPA) and the Multiple Correlation Function (MCF) approach introduced by Grebenkov [5].

Assuming a statistical independence of the net displacement of water molecules along the axis and the radial direction of the fibre, the fibre signal profile for different axonal diameters was then estimated as $E_{fibre}(\mathbf{q},\Delta)=E_{//}(\mathbf{q}_{//},\Delta)E_{\perp}(\mathbf{q}_{\perp},\Delta)$ according to [6]. $E_{//}(\mathbf{q}_{//},\Delta)$ is the signal attenuation along the axis of the fibre and it is modelled as free 1D-Gaussian diffusion; $E_{\perp}(\mathbf{q}_{\perp},\Delta)$ is the signal attenuation measured perpendicular to the fibre orientation and it is modelled with the previous restricted diffusion models. Here, $\mathbf{q}_{//}$ and $\mathbf{q}_{\perp}$ are the components of the **q**-vector decomposed along the parallel and the perpendicular direction of the fibre.

To remove scaling factors in fibre responses each fibre signal profile was normalized to its corresponding maximum signal amplitude. SD was performed according to [3] on the original fibre signal profiles by imposing as fibre response both the exact normalized signal profile and an arbitrary normalized fibre response assumed with a fixed axonal diameter.

Finally, spherical deconvolution was performed on a fibre-crossing configuration where, for one of the two fibres, different axonal diameters (fibre1=6, 12, 18 μm, fibre2=12 μm) and different volume fractions (fibre1=0.7 0.5 0.3, fibre2=0.3 0.5 0.7) were assumed.

Results

Figure 1 shows that with the chosen experimental setup the two models of restricted diffusion (GPA and MCF) provide similar signal attenuations. Larger differences between the two models appear for larger axonal diameters when the signal is also close to the noise floor level typically measured on clinical scanners ($SNR_{b=0}$ =15).

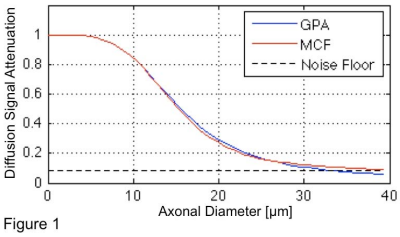

Figure 1

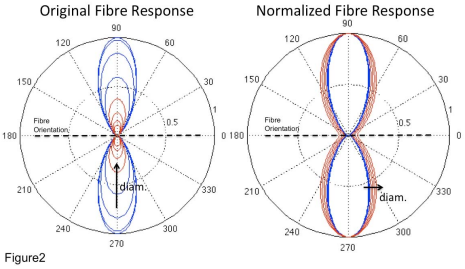

Figure2

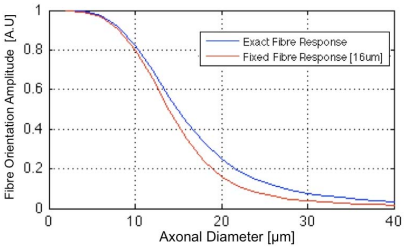

Figure 3

Figure 2 shows that the original 2D-fibre signal profiles exhibit a large decrease in the signal amplitude along the radial direction of the fibre for increasing axonal diameters. On the contrary, the normalized fibre response profiles show little differences for diameters smaller than 16 μm (blue profiles) while "fatter" profiles become evident for larger diameters (red profiles). This result suggests that for smaller diameters signal differences are mainly related to the scale of the signal profiles more than its shape.

Figure 3 shows the maximum amplitude of the fibre orientations obtained deconvolving the signal from fibres with increasing axonal diameter by imposing both the exact and the fixed (axonal diameter=16 μm) fibre responses. By applying normalized fibre responses the amplitude of the recovered fibre orientation is rescaled showing a monotonic decrease for increasing axonal diameters. The choice of a fixed fibre response produces similar results, although the amplitude for large diameters is underestimated compared to the exact fibre response.

Figure 4 shows the amplitudes of the recovered fibre orientation for the fibre-crossing configuration for different volume fractions and axonal diameters. The amplitude of the recovered fibre orientation increases with increasing volume fraction of the fibre or with decreasing fibre diameter.

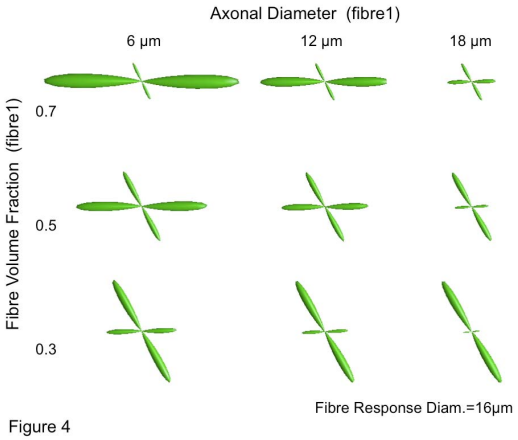

Figure 4

Discussion and conclusion

This study suggests that variations in the amplitude of the recovered fibre orientation can reflect not only differences in the volume fraction of the fibre but also changes in the intrinsic structural properties of the fibres, such as the axonal diameter. The amplitude of the recovered fibre orientation could provide, therefore, useful clinical information in several white matter conditions including motor neuron disease, Wallerian degeneration and in demyelinating disorders where the increased displacement of water molecules due to the myelin degeneration might also be seen, in first approximation, as an "apparent" increase of the axonal diameter [7]. In all these conditions, changes in white matter properties will be also reflected as changes in the amplitude of the corresponding fibre orientation.

Moreover, in comparison with previous indices of white matter integrity that provide only an average description from each voxel, the amplitude of the recovered fibre orientation is also specific to the single fibre orientation and therefore less susceptible of partial volume effects.

In conclusion assuming a fibre response function based on a restricted diffusion model may lead to a better interpretation of spherical deconvolution results, relaxing the requirement of an exact knowledge of the fibre response and possibly help the development of new fibre specific indices of white matter integrity.

References: [1] Tournier JD *et al*. NeuroImage 23:1176-1185 (2004); [2] Anderson AW, MRM 54:1194-1206, (2005); [3] Dell'Acqua F *et al.* IEEE TBME 54(3):462-472, (2007); [4] Van Gelderen P *et al*. J Magn Reson Ser B 103:255–260 (1994); [5] D. S. Grebenkov, Rev. Mod. Phys. 79, 1077 (2007); [6] Assaf Y *et al*. MRM 52:965–978 (2004); [7] Assaf Y *et al.* MRM 23:703 – 710 (2005).