The appearance of the apparent diffusion coefficient in complex fiber architecture

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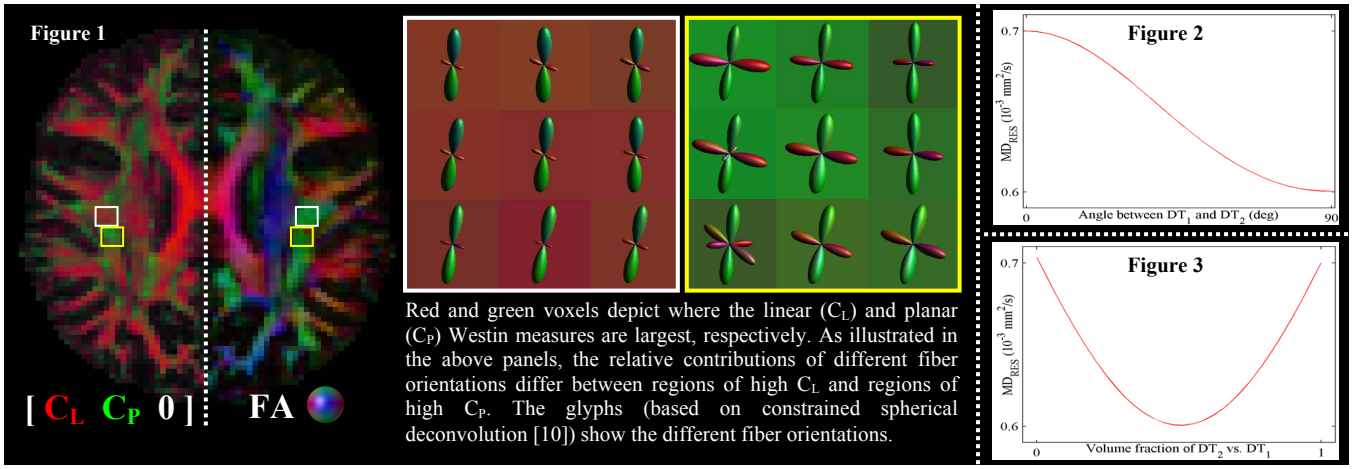
Introduction

Diffusion tensor imaging (DTI) is sensitive to structural changes in the human brain. Changes in fractional anisotropy (FA) or mean diffusivity (MD) can often be ascribed to underlying changes of the tissue. In patients with neurodegenerative disorders such as Alzheimer's disease, for instance, a decrease in FA is often observed compared to healthy subjects [1]. In order to determine the true differences, such as between subject groups (e.g., healthy vs. diseased subjects), a correct classification of underlying processes that result in these diffusion changes is important. A recent study highlighted that the interpretation of observed diffusion changes is non-trivial, as they demonstrated that *"a change in AD can cause a fictitious change in RD and vice versa in voxels characterized by crossing fibers"* [2]. As the amount of voxels with multiple fiber orientations has recently been estimated to lie around 90% of all WM voxels [3], this observed effect has a major influence on the interpretation of diffusion measures, and the interpretation of axial (AD) and radial diffusivity (RD) in particular. In this work, we show that not only the directionally dependent diffusion measures (e.g., FA, AD, and RD) are affected by the 'crossing fibers' issue, but that the MD also changes in crossing fiber voxels. Independent of the MD of the two crossing fiber bundles, we show that: (i) MD values are reduced in crossing fiber voxels compared to the MD values of single fiber voxels, (ii) the angle at which two bundles intersect modulates the MD, and (iii) the relative contribution of crossing fibers in one voxel affects the MD of that voxel.

Methods

Simulations: To examine the effect of the angle between crossing fiber populations, two identical prolate diffusion tensors (DT) were defined with FA=0.9 and MD=0.7×10^{-3} mm^2/s [4]. One tensor (DT_1) was then rotated over a range of 0-90° with respect to the second tensor (DT_2), and after rotation the two tensors were combined into one DT, with both tensors contributing equally to the resulting tensor (D_{RES}). The underlying diffusion weighted intensities (b-value=1200s/mm^2) from the individual tensors were averaged and used to estimate D_{RES}, from which the MD of the resulting tensor (MD_{RES}) was calculated (assuming the two populations are in a slow exchange regime [5]). In a second experiment, the relative contribution of crossing fiber populations in one voxel was varied. Two perpendicular tensors with FA=0.9 and MD=0.7×10^{-3} mm^2/s were calculated, but the contribution of both tensors to the resulting voxel varied from 100 through 0%, corresponding to a voxel populated completely by the second population (DT_2) and a voxel populated completely by the first population, DT_1 (where D_{RES} was calculated identically to the first experiment). Again, MD_{RES} was calculated from D_{RES}.

In vivo data: A cardiac-gated DTI dataset was acquired from one male subject (age 32.5 years), on a 3T MR system using an SS-SE EPI sequence with 60 gradient directions (distributed uniformly over the sphere [6]) and 6 B0-images (see [7] for further details). Whole brain tractography was performed using ExploreDTI [8], and the cortico-spinal tracts (CST) and the superior longitudinal fasciculus (SLF) were manually segmented. All voxels visited by these tracts where the planar Westin measure (C_P) is largest (i.e., larger than the linear, C_L, and spherical, C_S, Westin measures [9]) were classified as crossing fiber voxels and all voxels where C_L was largest were classified as single fiber voxels (Figure 1). The average MD values of those planar and linear regions (MD_{CP} and MD_{CL}, respectively) were calculated. For both fiber bundles, the non-parametric Mann-Whitney U-test was used to test for differences between MD_{CP} and MD_{CL}.



Results

Simulations: Figure 2 shows that the MD_{RES} value of a voxel with two crossing fiber populations is not solely dependent on the MD of the underlying DTs, but also depends on the angle of intersection between these two fiber populations. When both underlying tensors are parallel, the MD_{RES} of the resulting voxels equals MD_{IND}, but MD_{RES} decreases with increasing angle between the two populations until they are perpendicular. Similarly, Figure 3 shows that the MD_{RES} value of a voxel depends on the relative contribution of two crossing tensors to the resulting DT of that voxel. When only one individual tensor contributes to D_{RES}, MD_{RES} equals MD_{IND}; when a second tensor starts to contribute, MD_{RES} decreases until both tensors contribute equally (as in Figure 2), where MD_{RES} decreases roughly 14%.

In vivo data: Similar to the simulations, the MD values of crossing fiber voxels are lower than those of single fiber voxels in both the CST ($MD_{CP}=0.70\times10^{-3}$ mm^2/s vs. $MD_{CL}=0.76\times10^{-3}$ mm^2/s, $p<0.001$) and the SLF ($MD_{CP}=0.72\times10^{-3}$ mm^2/s vs. $MD_{CL}=0.78\times10^{-3}$ mm^2/s, $p<0.001$).

Discussion

In DTI, the issue of crossing fibers is well-known. However, the effect of crossing fibers on the estimation of MD has not been studied previously, as no effect would be expected intuitively. Using simulations, we demonstrate that in voxels with crossing fibers the MD decreases, and that this decrease depends on the angle of fiber intersection. Our simulations also show that the MD is dependent on the volume fractions of each of the fiber populations in a voxel. Our experimental results in the CST and SLF confirm these simulations, inasmuch that the MD was lower in voxels where there is a tendency towards multiple fiber populations (indicated by high C_P values) than in voxel with predominantly one population. These results further our understanding about the 'crossing fibers' issue by demonstrating the effect of crossing fiber populations on a non-directional diffusion measure, i.e., the MD.

References

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