Comparison of MR Diffusion Anisotropy with Axon Density

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Introduction:

In nerve fibers, water diffusion is strongly influenced by the presence of axon membranes and myelin sheaths. With diffusion tensor magnetic resonance imaging (DT-MRI)[1] rotationally invariant measures of diffusion restriction such as fractional anisotropy (FA) can be obtained. Here we compare FA measured in axial spinal cord specimen sections with the density of axons determined from corresponding histological sections.

Methods:

Image data with diffusion-weighting along six non-collinear and non-coplanar directions were acquired with LSDI[2] in four sections of a spinal cord specimen, which had been excised from a deceased patient without known spinal cord disease. In-plane resolution was set to 625 µm, and the slice thickness to 3 mm. Sixteen signal averages were performed. After the MRI scan, the specimen was fixed and histological sections were obtained at locations corresponding to the position of the scanned sections and then stained according to Bielschowski's method of silver impregnation. The histology sections were scanned with a light microscope at 0.53 µm resolution. With manually drawn outer boundaries as reference, both diffusion-weighted image data and histology data were co-registered to concurrently acquired T2-weighted fast-spin echo images via an affine transformation. To automatically identify through-plane axons in the histology data, they were processed with a combination of segmentation algorithms. On this particular stain, through-plane axons appear as dark, round objects, with a bright halo that shows the myelin around the nerve fibers. Morphological operators were applied to enhance the contrast and watershed segmentation was used to separate merged axons. Finally, intensity thresholding and shape-based filtering were applied to eliminate any non-axon candidates. The end result of this procedure is the localization of individual axons (see Figure 1, where automatically-identified axons are outlined in pink) as well as estimates of axon number and axon area for each pixel of the original MR scan matrix. Axon density, i.e., the number of axons divided by the pixel area, was then directly compared with the corresponding pixel FA value.

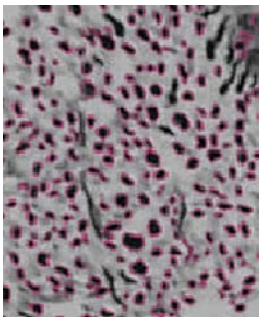

Figure 1

Results:

An FA map of one spinal section is shown in Figure 2 and the corresponding computed axon density map in Figure 3 (both maps have been interpolated). One histology section was excluded from further analysis, since it contained areas with relatively severe non-uniform deformation, which could not be corrected by the affine transformation. In all histology sections, there were some minor local discontinuities that originated either from the complex anatomy along the dorsal fissure, vessels, or small imperfections from the microtome cut. In the MR FA maps there were some artifactual high FA values along the specimen border, which were the result of minor mismatches between diffusion-weighted images. Here, our results focus on the results obtained from two of the sections. A correlation plot of axon density vs. FA for one section is presented in Figure 4. Pearson's correlation coefficient between FA and axon-density values is 0.77 for this section, and 0.76 for another section respectively.

Discussion:

Results show, there is a high positive linear correlation between FA maps and corresponding computed axon density maps. We can assume that such correlation also applies to other white matter structures in the brain. However, this must be verified, since different white matter structures exhibit different axon sizes and degree of myelination. The dorsal running tract of epicritical and proprioceptive sensation fibers is clearly visible as a superior triangular-shaped area of high amplitude in corresponding locations in both FA and axon density images. Gray matter is characterized by low FA values and low axon density.

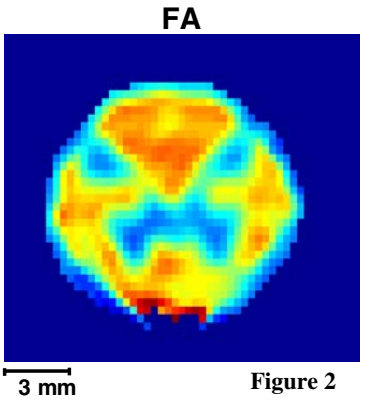

Figure 2

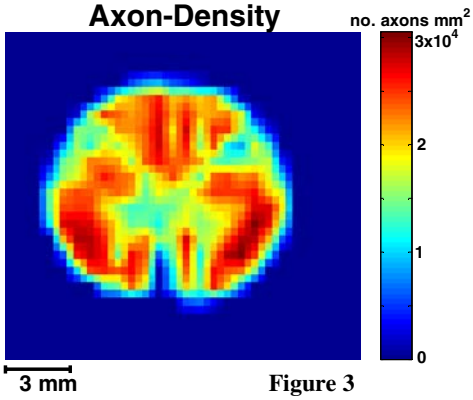

Figure 3

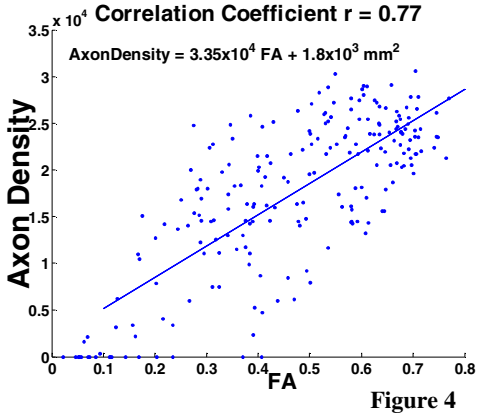

Figure 4

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[1] Basser, P.J., Pierpaoli C. Microstructural and physiological features of tissue elucidated by quantitative-diffusion-tensor MRI *J Magn Reson B* vol.111, pp. 209-219, 1996

[2]The Gudbjartsson H, Maier SE, Mulkern RV, Morocz IA, Patz S, Jolesz FA. Line scan diffusion imaging. *Magn Reson Med* 1996;36:509-519