REPRODUCIBILITY OF FRACTIONAL ANISOTROPY AND MEAN DIFFUSIVITY IN DIFFUSION TENSOR IMAGING AT 3.0 T

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Introduction Diffusion tensor imaging (DTI) [1] is increasingly used to provide connectivity information complementary to assessments of brain function via functional MRI (fMRI). A key requirement for employing these neuroimaging techniques in longitudinal studies is reproducibility of the measurements. Whereas reproducibility of fMRI has been investigated [2,3], little is known regarding that of DTI. Previous work [4,5,6] has used one-way ANOVA and region-of-interest analysis to investigate the systematic bias of FA and diffusivity obtained at 1.5 T. In the present study, voxel-by-voxel analysis based on the more rigorous Fisher-Pitman permutation test is performed to test the hypothesis whether there exists significant difference as well as to locate the regions with the difference between two independent DTI scans of the same subject acquired at 3.0 T.

Methods Thirty subjects were scanned twice (average 15 ± 2 days apart) on a 3.0 T scanner using the identical DTI protocol (single-shot spin-echo diffusion-weighted EPI sequence, TR = 8 s, TE = 120 ms, b =1000 s/mm^2, 12 diffusion encoding gradient directions). Six DTI datasets of the 3D brain volume ($128 \times 128 \times 60$) were repeated each time without signal averaging. In post-processing, eddy-current distortions were corrected using mutual information-based affine transformation for each diffusion-weighted image [7]. Diffusion tensors were then calculated along with FA and mean diffusivity. Within each subject, rigid-body registration was performed to place DTI images into a common coordinate system. Statistical tests were performed using the 6 measurements of FA and diffusivity per scan per subject. For each voxel, the Fisher-Pitman permutation test was used to compute the probability distribution function of the mean difference under the null hypothesis, and P value was calculated to determine significance of the difference. Due to the large number of voxels involved and spatial correlated nature of FA and mean diffusivity, the P values were corrected using false discovery rate (FDR) [8] procedure. With 95% confidence interval, regions with FDR of 5% were considered to be significantly different between scans.

Results Figure 1 shows representative T2 images, FA and mean diffusivity maps, for both scan times, and corresponding FDR-corrected P value maps, where locations with significant difference using 95% confidence were highlighted, from the same subject and brain slice. The significant difference maps are consistent with the DTI images and show little difference between the two scans. Quantitatively, the number of significant different voxels in the FA and mean diffusivity images respectively represented 13.2% and 6.8% of the entire brain volume. Histograms of the voxels as function of the FA (not shown) reveal that majority of the voxels occur at low FA area. For "white matter" (i.e., FA > 0.3) areas, only 4.1% and 1.3% of the voxels had significantly different FA and mean diffusivity values, respectively, between the scans.

Discussion and Conclusions The Fisher-Pitman permutation test was chosen because a student t test, with its associated standard Gaussian assumption requires 30 or more samples (per subject) to apply [9], which is not practical due to the long scanning time required. The results indicate excellent consistency of FA and mean diffusivity measurements obtained at 3.0 T, despite stronger susceptibility artifacts than 1.5 T. Most of the voxels in which significant difference was observed for FA or mean diffusivity are either located at the brain periphery or have FA values less than 0.3. This suggests that most of these voxels are attributable to residual registration error (in either eddy-current distortion correction or intra-subject rigid-body alignment), or partial volume effect between dissimilar tissues. Therefore, DTI measurements obtained at 3.0 T can be treated as highly reproducible.

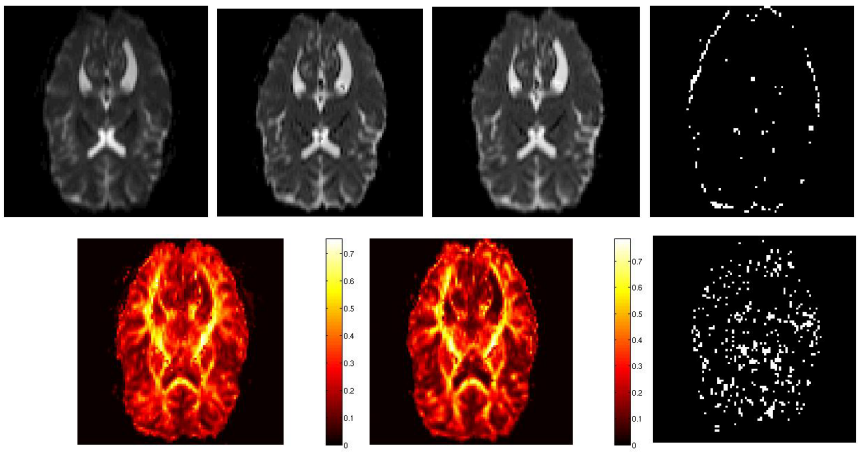

Figure 1. Representative T2-weighted image (top left), and averaged diffusivity (top row) and FA (bottom row) obtained 14 days apart. Voxels that show statistically significant difference between the scans are shown to the right.

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