Reproducibility measurements with an anisotropic diffusion tensor imaging phantom

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INTRODUCTION: Diffusion tensor imaging (DTI) permits the in depth study of the orientation and connectivity of fiber bundles within the brain and other tissues. DTI-derived biomarkers have been used to differentiate phenotypes of multiple sclerosis (*4*), diagnose autism spectrum disorder (*1*), and assess mild traumatic brain injury (*3*). Quantifiable measures of reproducibility obtained through phantom studies are needed to insure performance across time. We used a polyester fiber anisotropic phantom (*5*) to assess the reproducibility of DTI-metrics.

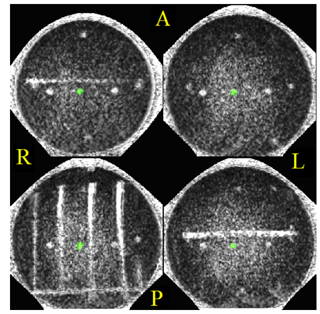

Figure 1: Examples of the ROI (green) drawn in the fiber bundle perpendicular to the plane.

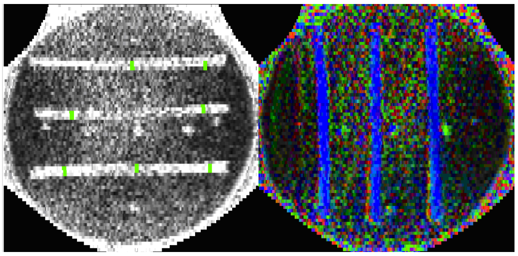

Figure 2: *Left:* Example of left-right fibers (transverse view) with regions-of interest superimposed in green, three ROIs were used for each fiber bundle (2 ROIs, upper-left and center, for the left-right fibers are out-of-plane in this view). *Right:* Example DTI image shown (coronal view) with fiber directions color-coded (red = left-right, blue = superior-inferior, green = anterior-posterior) and intensity weighted by the fractional anisotropy. Note that the fibers are neither precisely straight nor orthogonal to the imaging plane.

METHODS: An anisotropic phantom (Brain Innovations, Maastricht, NL) with somewhat orthogonal fibers was scanned once per day for five days on a 3 Tesla scanner using a conventional medium direction DTI scan (TR = 18634 ms, TE = 43.9 ms, acquisition matrix = 80x80, acquired voxel = 2x2x2 mm^3, reconstruction matrix = 320x320, reconstructed voxel = 0.5x0.5x2 mm^3, no gap between slices, 15-directions, b-value = 1000 s/mm^2, field-of-view = 160x160x160 mm^3, 5-coil loop array with 10 cm loops, transverse slice orientation). The phantom was positioned such that the fiber orientations generally matched the scanner x, y, z orientation. FSL software (*2*) was used to calculate the fractional anisotropy, mean diffusivity, eigenvectors, and eigenvalues of the tensor over the entire phantom. In order to examine the effect of slice position on DTI-derived measures, eleven regions of interest (ROIs) were drawn by hand around the center fiber aligned along the superior-inferior axis (perpendicular to the acquisition plane) in a single DTI dataset (Figure 1). The mean and standard deviation were determined for each ROI for fractional anisotropy (FA), mean diffusivity (MD), radial diffusivity (RD), and axial diffusivity (AD).

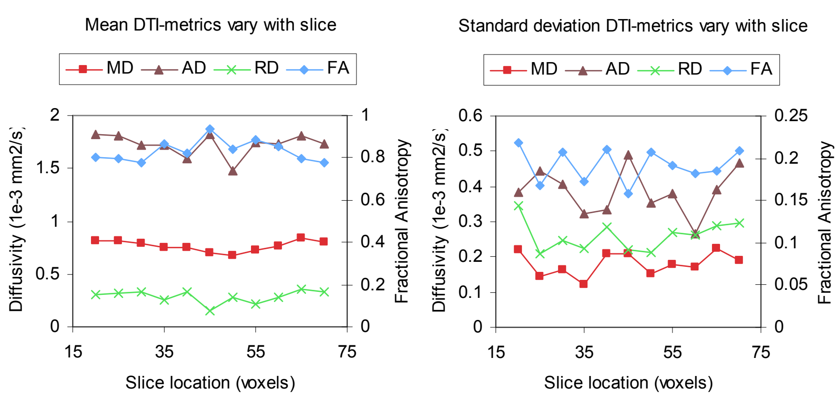

Figure 3: The variation in the mean DTI-metrics (*left*) and variability of those metrics (standard deviation, *right*) appears to be independent of slice position. Diffusivity is indicated on the left axis MD, RD, and AD while fractional anisotropy is located on the right axis.

ROIs for the reproducibility measures across days were defined over 2.5x2.5x6mm^3 (5x5x3 voxels) centered in the fibers at three locations within each fiber in a reference volume and transformed to the DTI images for each day using FLIRT in FSL (Figure 2). Within each ROI, the average FA, MD, RD, and AD were determined. ROIs were grouped according to the orientation of the fiber bundle (fiber orientation) for statistical analysis. A mixed-model two-factor (fiber orientation, day – repeated) ANOVA was used to assess differences in FA, MD, RD, and AD and implemented in the R statistical package (v2.12.1).

RESULTS: Measures of DTI obtained at various slice locations show consistent DTI-derived metrics and little slice-dependent variation (Figure 3). There was no statistically significant effect (p>0.05) of day on any of the DTI-derived metrics (FA, MD, RD, and AD) nor any interaction effects with fiber orientation and day (p>0.05). The effect of fiber orientation was statistically significant for FA (F=4.59, p=0.011), RD (F=4.19, p=0.017), and AD (F=3.67, p=0.028) (Table 1). Post-hoc comparisons (Bonferroni corrected p-values) revealed that FA was greater in fibers oriented in the superior-inferior direction than right-left (p=0.05) and anterior-posterior (p=0.044), that AD was greater in fibers oriented in the anterior-posterior than right-left (p=0.00012) and superior-inferior (p=0.037), and that RD was lower in the superior-interior orientation than the anterior-posterior (p=0.030).

Table 1: DTI-derived metrics for various fiber orientations

Mean ± SD	**Anterior-posterior**	**Right-left**	**Superior-inferior**
FA	0.857 ± 0.0953	0.858 ± 0.127	0.909 ± 0.0749
MD (1x10^{-3} mm^2/s)	0.749 ± 0.154	0.682 ± 0.139	0.664 ± 0.0856
AD (1x10^{-3} mm^2/s)	1.77 ± 0.246	1.60 ± 0.156	1.70 ± 0.162
RD (1x10^{-3} mm^2/s)	0.238 ± 0.179	0.223 ± 0.200	0.145 ± 0.117

DISCUSSION: Understanding the dependencies and validating the stability of DTI-metrics are essential steps toward using DTI as a clinical biomarker. The DTI-metrics observed in this abstract were stable across days and at various locations within the imaging volume. Our results indicate that the DTI- metrics are dependent on the fiber orientation within the acquired slice. Future studies will investigate the dependence of DTI-metrics on fiber directions and slice acquisition orientation.

REFERENCES: **1.** M. Ingalhalikar, D. Parker, L. Bloy, T. P. Roberts, R. Verma, *Neuroimage* 57, 918 (2011). **2.** M. Jenkinson, C. F. Beckmann, T. E. Behrens, M. W. Woolrich, S. M. Smith, *Neuroimage.* (2011). **3.** A. R. Mayer *et al.*, *Neurology* 74, 643 (2010). **4.** P. Preziosa *et al.*, *Radiology.* 260, 541 (2011). **5.** P. Pullens, A. Roebroeck, R. Goebel, *J. Magn. Reson. Imaging* 32, 482 (2010).