Intra-rater and inter-rater reproducibility of FA and ADC: a clinical pediatric DTI study.

D. Bonekamp[1], L. M. Nagae-Poetscher[1,2], M. Degaonkar[1,2], M. Matson[2,3], S. Mori[1,2], A. Horska[1]

[1]The Russell H. Morgan Department of Radiology and Radiological Science, Johns Hopkins University, Baltimore, Maryland, United States, [2]FM Kirby Research Center for Functional Brain Imaging, Kennedy Krieger Institute, Baltimore, Maryland, United States, [3]Department of Neuropsychology, Johns Hopkins University, Baltimore, Maryland, United States

INTRODUCTION

Diffusion tensor imaging[1] (DTI) provides unique information on brain white matter structure and organization.[2] Common measures derived from DTI are apparent diffusion coefficient (ADC) and fractional anisotropy (FA). ADC is a non-directional measure for the amount of diffusion restriction, while FA gives information about the non-sphericity of the diffusion ellipsoid. Color maps provide a combined view of directionality and anisotropy of diffusion. There is currently a great interest in evaluating white matter pathology with DTI, as demonstrated by the increasing number of such studies e.g. of schizophrenia[3], epilepsy[4] and multiple sclerosis[5]. In general two methods have most often been utilized to obtain information about changes in DTI measures: region of interest (ROI)-based[3, 6, 7] and voxelwise methods[8-11]. ROI methods have the advantage of focusing directly on regions that are expected to be abnormal, but have limited brain coverage and are time-consuming. Voxelwise methods require inter-subject registration and image smoothing, and comprise a large number of statistical tests that increase Type I errors. To provide a reliable measure of white matter water diffusion changes in healthy and pathological brain, in particular in longitudinal studies, knowledge of measurement reproducibility is essential. The goal of our study was to evaluate intra-rater and inter-rater reproducibility of ADC and FA measurements, using two different fully manual ROI drawing methods.

MATERIAL AND METHODS

DTI was performed in 10 healthy children (3 boys, age 14.3±2.8 years, age range 10-18.5 years) at 1.5 Tesla using a single-shot diffusion-weighted EPI sequence with the following parameters: TE=93.7 ms, acquisition matrix 96x96, FOV 240 mm, two b=0 $s \cdot mm^{-2}$ images, 15 independently diffusion-weighted images, maximum b=1000 $s \cdot mm^{-2}$, 24 axial slices parallel to the anterior commissure - posterior commissure plane, 5 mm slice thickness. ADC, FA and color maps were calculated from the raw data using the in-house developed software DTI Studio (http://cmrm.med.jhmi.edu/). ROIs were drawn on color coded maps and subsequently overlaid on FA and ADC images, obtaining pixel mean and standard deviation for each ROI. In this initial investigation we focused on pathways with different fiber organization, to test the reliability of our method under different conditions, and we simultaneously concentrated on pathways with well known anatomy, and thus with easily identifiable structure: cerebral peduncle, anterior limb and posterior limb of internal capsule, genu of the corpus callosum, superior corona radiata, and cingulum (Fig. 1). All measurements were performed in both hemispheres, at a fixed level for each structure. Two different approaches were compared: a) drawing a polygonal outline of the color-coded area and b) drawing a predefined number of evenly distributed elliptical ROIs (encompassing 16 pixels each). For the evaluation of intra-rater and inter-rater reproducibility, the measurements were performed five times by one rater (2400 ROIs) (with evaluations separated by 1 to 3 days) and one time by 4 raters (1920 ROIs). Reproducibility was measured using coefficients of variations (CV=standard deviation/mean).

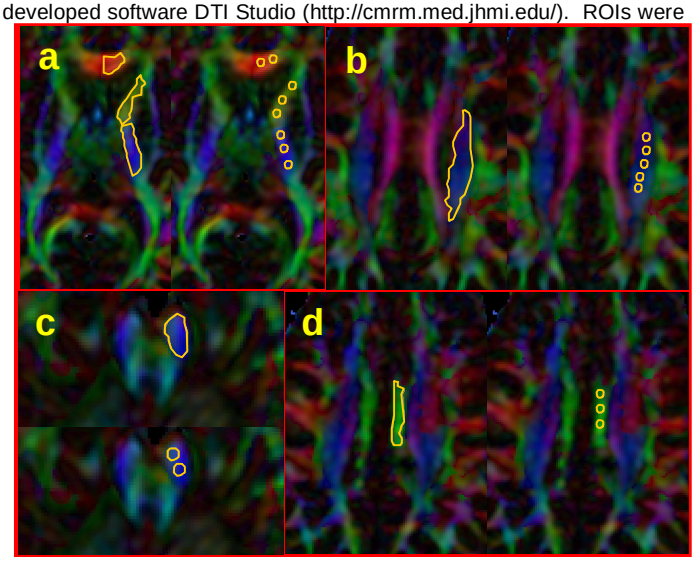

Figure 1: Polygon and ellipse ROIs in a) genu of the corpus callosum, anterior and posterior limb of the internal capsule, b) superior corona radiata, c) cerebral peduncle, d) cingulum.

RESULTS

Interhemispheric agreement of mean values was excellent for FA (differences detected in 17% of all comparisons), while ADC showed difference in 37% of all comparisons (independent t-test ($p<0.05$)). For both FA and ADC, interhemispheric agreement was better for polygons than ellipses. The reproducibility for polygonal ROI drawing and elliptical ROI drawing is presented as median (10^{th} percentile / 90^{th} percentile) of CV (in %) averaged over all regions (Table 1). The table shows that the polygonal approach generated more reproducible results than the ellipsoid approach. The best reproducibility for FA was obtained with polygons in the genu of the corpus callosum (median %CV intra-rater/inter-rater=0.53/2.16), and the lowest in the cerebral peduncle (2.25/6.53).

Table 1	Polygonal ROI		Elliptical ROI	
	ADC	FA	ADC	FA
Intra-rater	0.58 (0.18/2.98)	1.81 (0.55/3.67)	1.58 (0.64/3.74)	3.27 (1.38/7.58)
Inter-rater	0.72 (0.22/5.13)	3.34 (1.63/7.50)	1.72 (0.83/4.88)	3.51 (1.44/8.67)

DISCUSSION

Minimizing scan time of DTI (4 min 48 s) was of high importance in developing the experimental protocol for the acquisition of DTI data in this study. The protocol is being used in a pediatric group where in the same scan session other acquisitions are performed (routine clinical MRI, 3D–SPGR, and MRSI). The ADC and FA intra-rater and inter-rater reproducibility for this protocol were excellent. We note that a low variability in regional FA and ADC values indicates minimum age-related effects; such variation has been shown in a much younger group (<3 years of age).[12] Lower values for CV in the ADC measurements may be attributed to the lower susceptibility of ADC to SNR and the lower ADC difference between gray and white matter. Slightly higher CVs for FA compared to ADC can be explained both by a more pronounced effect of signal-to-noise ratio (SNR) on FA[13] and by errors in outlining the ROIs, as there is a sharp decrease in FA beyond the borders of the ROIs drawn. The reproducibility estimates showing high precision in ADC and FA determination in our approach may be encouraging for researchers starting a new clinical DTI study. Since determination of anisotropy measures depends on slice position and orientation,[14] keeping the same slice position and orientation in longitudinal measurements is essential.

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REFERENCES

[1]Basser PJ, et al. Biophys J 1994;66(1):259-67.
[2]Wakana S, et al. Radiology 2004;230(1):77-87.
[3]Sun Z, et al. Neuroreport 2003;14(14):1833-6.
[4]Briellmann RS, et al. Epilepsia 2003;44(12):1541-5.
[5]Cassol E, et al. Mult Scler 2004;10(2):188-96.
[6]Ozsunar Y, et al. Eur J Radiol 2004;51(3):195-201.
[7]Steel RM, et al. Psychiatry Res 2001;106(3):161-70.
[8]Foong J, et al. Neuroreport 2002;13(3):333-6.
[9]Burns J, et al. Br J Psychiatry 2003;182:439-43.
[10]Agartz I, et al. Neuroreport 2001;12(10):2251-4.
[11]Buchsbaum MS, et al. Neuroreport 1998;9(3):425-30.
[12]Jones RA, et al. J Magn Reson Imaging 2003;18(6):665-74.
[13]Basser PJ, et al. Magn Reson Med 2000;44(1):41-50.
[14]Virta A, et al. Magn Reson Imaging 1999;17(8):1121-33.