Comparison of DTI Metrics in Neonates Obtained with Manual ROI Analysis vs Modified TBSS

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Introduction Diffusion tensor imaging (DTI) is being used to study brain maturation and disease effects on white matter. Manual region-of-interest (ROI) analysis which is widely used is operator-dependant, tedious, hypothesis driven, and impractical for comparison of groups or large numbers of subjects but does not require potentially confounding spatial normalization. Tract Based Spatial Statistics (TBSS) (1) is an open source operator-independent platform which spatially normalizes tensor data; potentially problematic in neonates as the normalization templates used in adults have not been proven reliable to infants. We performed a direct comparison between manual ROI analysis and TBSS in infants using the modifications proposed by Ball to improve the reliability of TBSS in neonates and then report region-specific tensor metrics in infants 32 -49 weeks post conception age at the time of imaging.

Materials and Methods This investigation was IRB approved and HIPAA compliant. MR DTI was done at 3T (Philips Health Systems, Cleveland, Ohio); SS-EPI; 30 directions; 2^3 mm^3 voxel; 128x128 acquisition matrix; b=700; SENSE factor of 2, 2-3 acquisitions. MR scanner accuracy, transmitter gain, B_0 shifting, spatial resolution and low contrast detection, and SNR were checked weekly. MR imaging was routinely attempted without sedation after bundle and feeding of infants. Infants requiring sedation were sedated with oral chloral hydrate (25–50 mg/kg) prior to scanning and pulse oximetry, and electrocardiography data were monitored and noise was dampened using earmuffs.

All DTI data were co-registered to correct motion and eddy current effects prior to calculation of tensor images; image data was not normalized for purposes of ROI analysis. A single observer manually placed ROIs on the posterior limbs of the internal capsules (PLIC) 2 slices above the anterior commissure and on the callosal genu and splenium. Placement of each ROI was repeated until the standard deviation of the FA for each measurement was ≤10%; the average of 3 FA measures was recorded and exported to a spread sheet. TBSS used the modifications described by Ball et al (2) which includes a 6 degree of freedom (DOF) rigid body linear transformation step followed by the 12 DOF affine transform for alignment to the optimal target FA map selected from among FA maps of all subjects. The final target was the mean of all FA maps co-registered to the initial optimal target; transformation to standard adult space was not done. FA threshold was 0.2. FA values derived from ROI analysis and TBSS were compared using custom software written in IDL. The FA data derived using TBSS was averaged over a 5 mm radius on the FA skeleton within a slice and compared with ROI analysis. Linear regression of FA, axial diffusivity and radial diffusivity vs. post conception age was performed for the PLIC and the callosal genu and splenium. The concordance of FA by TBSS and ROI methods was examined using correlation and Altman-Bland plot.

Results The study subjects (19 females, 20 males) had been referred for MR imaging for seizures, apnea, prematurity, or a known extra-cranial congenital abnormalities and had normal neurologic examinations and conventional MR imaging. The "target" image was from a 40 week old female; the minimum mean warp displacement score was 1.64. The linear relationships between FA, and axial and radial diffusivities vs. age are listed in Table 1.

Table 1 Relationship between DTI measures vs. age and difference between FA obtained by TBSS and ROI analysis.

region	Linear regression against post-conception age (weeks)				FA_{TBSS} vs. FA_{ROI} %difference Mean ± s.d.
	FA_{ROI}	FA_{TBSS}	AD_{TBSS} (10^{-3} mm^2/sec)	RD_{TBSS} (10^{-3} mm^2/sec)	
Left PLIC	0.293+0.0062·y (χ^2 = 0.08)	0.158+0.0082·y (χ^2 = 0.05)	1.590+0.0001·y (χ^2 = 0.21)	1.153-0.0114·y (χ^2 = 0.08)	-9.5% ± 6.9%
Right PLIC	0.274+0.0055·y (χ^2 = 0.17)	0.166+0.0084·y (χ^2 = 0.05)	1.712-0.0017·y (χ^2 = 0.24)	1.192-0.0125·y (χ^2 = 0.10)	2.9% ± 14.8%
Genu	0.084+0.012·y (χ^2 = 0.25)	0.227+0.0102·y (χ^2 = 0.25)	2.134-0.0012·y (χ^2 = 0.77)	1.362-0.017·y (χ^2 = 0.78)	11.4% ± 8.1%
Splenium	0.252+0.0096·y (χ^2 = 0.23)	0.232+0.0111·y (χ^2 = 0.32)	2.134-0.0009·y (χ^2 = 0.89)	1.364-0.0188·y (χ^2 = 0.96)	5.8% ± 10.8%

y is age in weeks; χ^2 (chi-square) is the total variance of linear fit

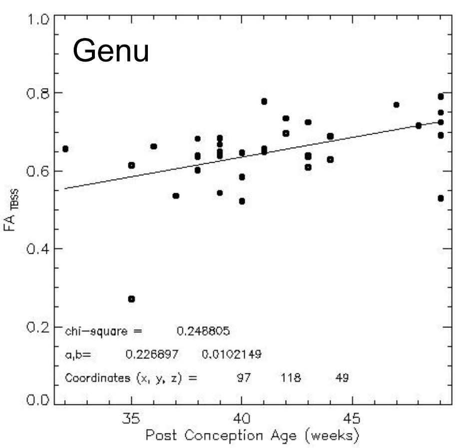

Fig. 1 FA vs. age in the callosal genu

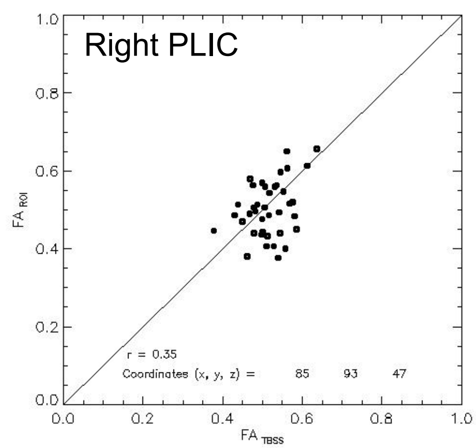

Fig. 2 Correlation of FA in the right PLIC; ROI analysis vs. TBSS

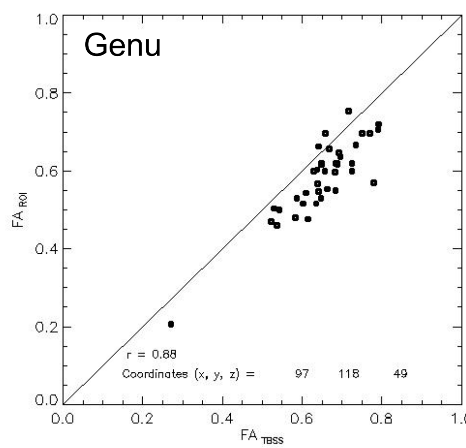

Fig. 3 Correlation of FA in the callosal genu; ROI analysis vs. TBSS

Conclusions Direct comparison between ROI analysis and TBSS modified for use in neonates shows variable concordance in different regions of the brain, which may be due to variability in ROI placement or to the spatial normalization process. FA values were usually higher for TBSS than for ROI for the same region of WM. There are significant age-related differences in tensor metrics in this age group suggesting studies using DTI to study disease and treatment effects on WM should be matched for post-conception age.

References 1 Smith et al., Neuroimage 2006; 31:1487-1505; 2 Ball G, et al, NeuroImage 2010; 53:94-102