

Early Detection and Assessment of White Matter Abnormalities in Preterm Infants using 3-D DTI Tractography

S-S. Yoo^{1,2}, J. S. Soul³, H-J. Park⁴, H. Park⁵, C-F. Westin¹, S. E. Maier¹, H. Mamata¹, A. J. Du Plessis³, R. L. Robertson Jr.⁶, S. A. Ringer⁷, J. J. Volpe³, G. P. Zientara¹

¹Radiology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, United States, ²BioSystems, KAIST, Daejeon, Korea, Republic of, ³Neurology, Children's Hospital Boston, Harvard Medical School, Boston, MA, United States, ⁴Nuclear Medicine, Yonsei Medical Center, Seoul, Seoul, Korea, Republic of, ⁵Electrical Engineering, KAIST, Daejeon, Korea, Republic of, ⁶Radiology, Children's Hospital Boston, Boston, MA, United States, ⁷Newborn Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, United States

Introduction: Brain injury in preterm newborns is a major problem. Up to 50% of very low birth weight (VLBW) infants (<1500 g) exhibit school difficulties and about 10% will develop cerebral palsy [1]. It is likely that injury to the cerebral white matter (WM) tracts underlie later functional disabilities. We report preliminary data for the detection and assessment of the WM abnormalities in preterm infants using 3D WM tractography based on the analysis of diffusion tensor magnetic resonance imaging (DTI) data. 3D tractography computed from volumetric DTI data provides a compelling, explicit rendering of WM fiber tracts in the brain *in vivo*, previously unobtainable from preterm infants. We have developed a computational environment for DTI tractography, designed to establish inter-regional connectivity between major WM fibers in healthy preterm infants [2]. Using this environment, we aimed to visualize the abnormalities in WM structure to enable the early detection and characterization of WM injury and its effect on subsequent WM development.

Method: The study was conducted according to the ethical and safety standards set forth by the Institutional Review Board. Images for this study were acquired from a 1.5 Tesla MR scanner (GE Medical Systems, Milwaukee, WI). All infants were asleep during the MRI examination without use of sedation. Data from 6 preterm infants (2 female, scanned at 35-41 weeks post conceptional age - PCA) with confirmed radiological abnormality were analyzed. After the acquisition of a T1-weighted sagittal localizer, a line scan diffusion imaging (LSDI) sequence was used to acquire the diffusion tensor images. Imaging parameters were as follows: TR/TE=2592/64 msec; slice thickness=4 mm; in-plane resolution=1.4x1.4 mm² using 128x96 scan matrix; reconstructed in-plane resolution=0.7x0.7 mm²; Field-of-view=180x135 mm²; Receiver bandwidth=4KHz. Depending on the size of the brain, 10 to 17 slices of axial images were obtained, covering most of the brain volume. For each slice location, six images with high diffusion weighting ($b_{high}=1000s/mm^2$) were acquired along the six non-collinear directions.

Since low anisotropy is present in neonatal WM due to immature WM microstructure and high water content, *manual* selection of the seeding areas was necessary for initiation of the tracking routine. Based on the subject's anatomy, the posterior limbs of the internal capsules (bilaterally) were manually segmented to visualize the corticospinal tracts [2]. Once seeding areas were defined, fiber bundles were traced by following the primary eigenvectors (*i.e.*, the first eigenvector - the largest of three principal eigenvectors) in 3D space until the FA of the tensor in a given pixel fell below a predetermined threshold level of FA=0.2 or until a rapid change of tensor direction (30° per 1mm) was detected. In order to calculate the pixelated trajectories of the vector field in 3D, the 4th-order adaptive Runge-Kutta method for the integration solver was used [3]. Traced fiber bundles were visualized with a stream tube rendering method [2]. Several display options were implemented, whereby the traced WM tracts were pseudo-colored according to the regional FA values (from 0 to 1) and were overlaid on FA images or T2-weighted anatomical images for anatomical reference.

Following the establishment of guidelines for normal neurodevelopment [2], abnormal features (such as asymmetry of tract formation or early termination near the lesion sites) of WM morphology were examined. Any signs of damaged WM anatomy (e.g. abnormal ADC or FA) were also noted.

Results: The figure shows the example of visualization of the traced corticospinal tracts obtained from a male infant (35 wk PCA) with a large left periventricular hemorrhagic infarction (PVHI) (Panel A) and a female infant (38 wk PCA) with posthemorrhagic hydrocephalus (PHH) and a left PVHI (Panel B). The corticospinal tracts traversing through the internal capsule were easily identified. Color-coded FA values overlaid on the visualized WM tracts showed that the seeding areas in the internal capsule contained elevated FA values compared to the peripheral areas (in green). The fiber tracking for the corticospinal tracts was abruptly terminated just inferior to the large lesions (PVHI) in both cases, compared with the similar tracts in the contralateral healthier hemisphere. This indicates the abnormal WM structure and development in this region as a consequence of the severe lesion affecting the cerebral WM tracts superior to the posterior limb of the internal capsule.

Discussion: DTI for the infant population poses a unique set of technical challenges, especially for preterm infants. For example, complicated scan logistics, ill-advised sedation for a routine MRI exam, reduction in the SNR, along with the inherently low anisotropy of an immature brain makes tracking problematic. In spite of these challenges, we have shown that it is possible to detect abnormal WM fiber tracts from a premature neonatal brain. We employed a rule-based regularization scheme and human intervention (manual definition of seeding areas), which could introduce user-bias in tractography results. Further study is necessary to provide tracking criteria/parameters for neonatal DTI studies that would eventually become operator-independent. Correlation of visualization results with anatomical MRI and other clinical parameters (such as functional outcomes and associated functional plasticity/recovery) will be the focus of our future investigation.

References: [1] Volpe JJ. *Pediatrics*. 2003; 112: 176-180; [2] Yoo *et al.* *In Vivo* Visualization of White Matter Fiber Tracts of Preterm- and Term- Infant Brain with Diffusion Tensor MRI, *Investigative Radiology*, in press; 2005; [3] Catani *et al.* *Neuroimage*. 2002;17:77-94.

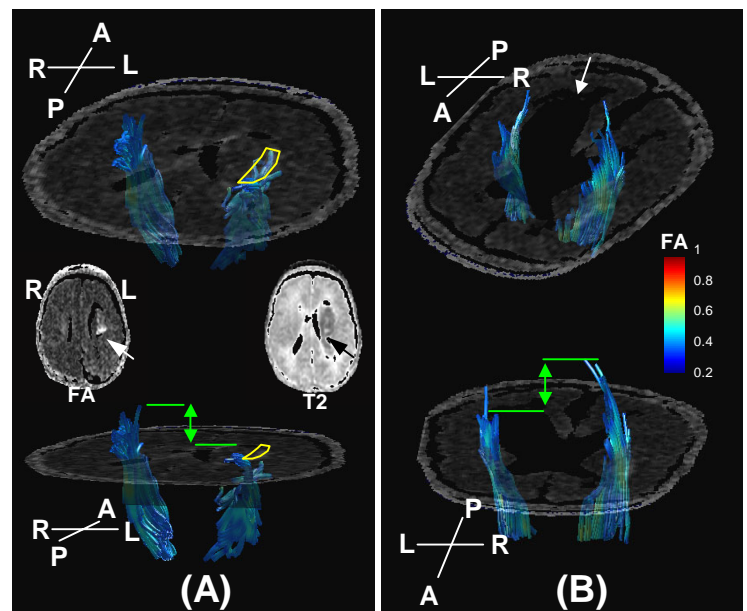


Figure. (A) Tractography from a male infant (35 wk PCA) with a left periventricular hemorrhagic infarction (PVHI) (in yellow; also shown in the FA and T2-weighted images with arrows), and (B) tractography from a female infant (38 wk PCA) with post hemorrhagic hydrocephalus (note the enlarged ventricular shape from the FA map, arrow) and PVHI.