Visualization of Posterior Fossa High-Resolution Anatomy in the Infant Brain using Tract Density Imaging

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Background: The brainstem and cerebellum can be affected by hypoxic-ischemic injury, malformations, and infection among a number of different disease processes in the developing brain. However, the small size of these structures limits the anatomic localization of these abnormalities in infants. High-resolution T1- and T2-weighted imaging provide a useful overall anatomic assessment, and diffusion tensor imaging (DTI) can depict large white matter tracts with high anisotropy, but these techniques are limited by voxel size. The goal of this work was to determine whether a recently proposed method for using fiber tractography to obtain super-resolution using fiber tractography, tract density imaging (TDI) [1], would allow identification anatomic substructure within the infant cerebellum and brainstem.

Methods: *Data acquisition*: Diffusion data were acquired on ten unsedated pre-term and full-term infants on either 1.5 or 3 T General Electric Healthcare (Waukesha, WI) MRI scanners using whole-body transmit and 8-channel receive head coils using a spin-echo EPI diffusion sequence. Subjects were scanned according to either 55 direction (b=3000 s/mm^2, 47 contiguous slices, voxel size 1.8 x 1.8 x 2 mm^3) or 30 direction (b=700 s/mm^2, 30 contiguous slices, voxel size 2.5 x 2.5 x 3 mm^3) protocols. Additional axial fast spin echo T2 (TR/TE=3000/120 ms) and sagittal 3D spoiled gradient recalled T1 (flip angle 35°, TR/TE=36/min ms) were acquired for anatomical reference. Informed consent was obtained from all subjects as per institution review board guidelines.
Fiber-tracking: Fiber-tracking was performed utilizing probabilistic streamline tractography together with standard diffusion tensor reconstruction (low-b data) or constrained spherical deconvolution [2] (high-b data, harmonic order=8) using in-house software, the Diffusion Toolkit package (Martinos Center for Biomedical Imaging, MGH, Boston, MA, http://www.trackvis.org/) and MRtrix (Brain Research Institute, Melbourne, Australia, http://www.brain.org.au/software/). Tractography was performed by randomly seeding 1,000,000 points throughout the brain for both types of data sets. Fiber-tracking parameters included: 0.1 mm step-size, and maximum angle between steps=20°. Tracts with length <10 mm were discarded and tractography was terminated when streamlines exited the brain.
Track-density imaging: Tract density maps were constructed using the approach proposed by Calamante et al [1] by counting the fraction of the total number of tracts passing through each voxel on grid with subvoxel resolution. For these experiments, an isotropic voxel size of 300 μm was empirically found to be most accurate. Directionally-encoded color maps of tract density were generated using the standard diffusion RGB color-map (red = medial-lateral, blue = cranial-caudal, green = anterior-posterior), with assignment of color based on the mean orientation of all fiber tracts passing through each voxel.
Image analysis: Tract density maps were reviewed by three neuroradiologists for image quality, spatial and contrast resolution and anatomic identification of white and gray matter structures within the brainstem and cerebellum. The images were compared with histologic selections [3], volumetric T1 and axial T2 sequences.

Results: Super-resolution tract density maps reconstructed from the comparatively lower-resolution raw diffusion data yielded a dramatic improvement in both spatial resolution and white matter contrast. In comparison to both traditional anatomic sequences and DTI fractional anisotropy (FA) maps, the technique clearly depicted several white matter tracts and brainstem nuclei (e.g. central tegmental tract, pontocerebellar tracts, decussation of superior and middle cerebellar peduncles, spinal trigeminal nucleus, and others). These midbrain and cerebellar white matter tracks and nuclei were readily visualized on all ten infants scanned. The descending corticospinal tracts within the pons were not depicted well on grayscale maps of tract density (Figure 1). The isotropic grid resolution of 300 μm allowed multiplanar and curved planar reformatting for optimal visualization of structures. Directionally-encoded color tract density maps provided improved contrast relative to grayscale maps, as several tracts with otherwise comparable density in the pons and midbrain could be more readily parcellated based on their orientation.

Conclusion: Color-encoded super-resolution tract density maps allowed unprecedented visualization of brainstem and cerebellar anatomy, approaching the detail afforded by histologic sections. Descending tracts were difficult to visualize using grayscale TDI, a fact which was attributed to increased resolution of crossing fibers with similar tract density. Tract density imaging promises to be a useful tool for studying a number of developmental and acquired disorders in the infant brain.

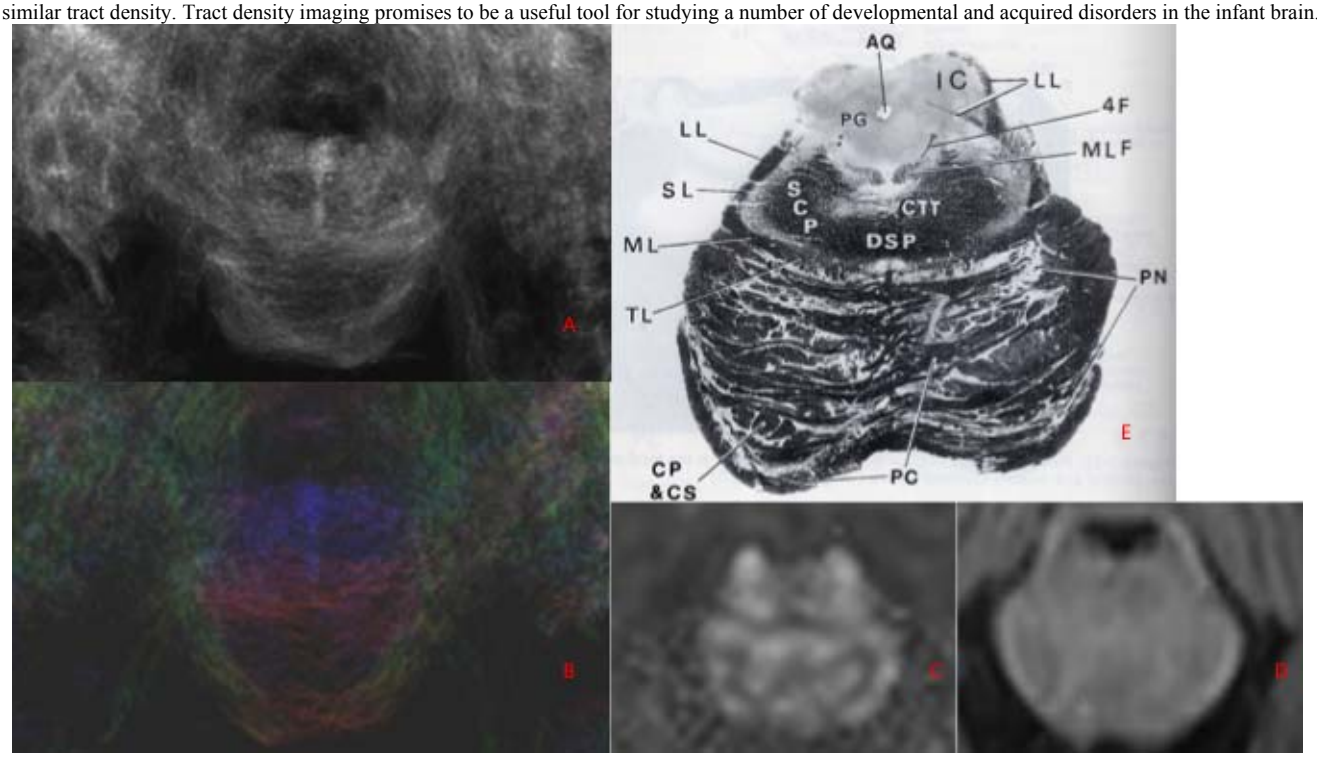

Figure 1. Anatomical axial selections through the mid pons: (A) Tract density map at generated from 1 million tracks with a grid resolution of 300 μm. (B) Matched directionally-encoded color track density map. (C) Conventional DTI fractional anisotropy map. (D) Axial image from a volumetric T1 sequence. For qualitative comparison: (E) Axial histologic selection at the same level [3]. CP-corticopontine fibers, CS-corticosspinal fibers, PT-pontocerebellar fibers, ML-medial lemniscus, LL-lateral lemniscus, DSP-decussation of superior cerebellar peduncles (SCP), CT-central tegmental tract

1. Calamante, F., et al., Track-density imaging (TDI): Super-resolution white matter imaging using whole-brain track-density mapping, NeuroImage 2010; 53:1233.
2. Tournier D., et al. Robust determination of the fiber orientation distribution in diffusion MRI: non-negativity constrained super-resolved spherical deconvolution. Neuroimage 2001; 35: 1459-72.
3. Kiernan, JA: *The Human Nervous System*. Lippincott-Raven 1998.

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