Development and Evaluation of A Robust and Efficient Computational Pipeline for Track Density Imaging for Use in a Clinical Research Environment

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Introduction- Track density imaging (TDI) was recently proposed as a diffusion post-processing technique to achieve super-resolution anatomic depiction of gray and white matter structure by using fiber tractography to interpolate data at a spatial resolution that is higher than the nominal voxel size (1). Specifically, by using high angular resolution diffusion imaging (HARDI) with probabilistic streamline tractography that incorporates angular information from neighboring voxels along individual streamlines on a high-resolution grid, TDI results in images with higher resolution than conventional maps of diffusion anisotropy. We have implemented TDI as described in (1), developed a novel combined track density / color orientation display, and have used this method to visualize structures in both normal volunteers at 3T and in patients with various neurological diseases.

Methods- *Acquisition:* Normal volunteers and patients were scanned using a clinical HARDI sequence on a GE 3T scanner equipped with an eight-channel phased array head coil. The acquisition parameters were: matrix 128x128, FOV= 25.6cm, resolution= 2 mm isotropic, number of slices= 38, b-value= 3000 s/mm^2, number of diffusion directions= 36 (derived from electrostatic repulsion), ASSET = 2, TE= 88.7ms, TR= 5s, scan time= 6 min, 30 sec. *Processing:* Fiber tractography was performed using the *MRtrix* package (JD Tournier, Brain Research Institute, Melbourne, Australia, http://www.brain.org.au/software/) for constrained spherical deconvolution (maximum harmonic order= 6) and probabilistic streamline fiber tracking (2). One million tracks were randomly seeded over the entire brain, and tracks <10 mm in length were pruned. Track counts and mean orientations were computed on a 250 μm isotropic grid (1024 x 1024 x 304) using Matlab (MathWorks, Natick, MA). The compiled Matlab code and MRtrix software allowed for efficient computational times of less than 30 minutes per data set. Calculated track densities were modulated by the standard diffusion RGB color map (red = left-right, blue = cranial-caudal, green = anterior-posterior) using the mean orientation of all tracks passing through each voxel. Processing was performed on a 64-bit Linux workstation with eight processing cores to accelerate reconstruction by multi-threading and 12 Gb of RAM to allow for seamless, automated offline processing. *Output and Display:* Both grayscale and RGB color track density maps were ultimately output in DICOM format, allowing for visualization of results on a clinical PACS system. Regarding display, maps of track density had a wide dynamic range, with histograms that were heavily dominated by low track counts (e.g. voxels with 1-5 tracks). For optimal contrast we investigated a novel redistribution of image intensities by applying a logarithmic filter. *Data analysis*- The mean and standard deviation of TDI counts for the following four major white matter tracts were measured for three normal subjects using region of interest (ROI) analysis: inferior longitudinal fasciculus (ILF), anterior region of corona radiata (ACR), body of corpus callosum (BCC), and cingulum bundle (CING). The effects of different contrast adjustment filters were evaluated qualitatively. The contrast-adjusted images from several patients with brain tumors, malformations of cortical development, and neurodegenerative diseases were also evaluated for potential clinical application.

Results- TDI processing required approximately 20 minutes per data set, mostly consumed by tractography and writing the large DICOM files to disk. Representative tract density images are shown in Figure 1, and results of regional analysis of track density are presented in Table 1. Contrast adjustment was beneficial to both the grayscale and color images, but was particularly beneficial for optimal viewing of color maps, which otherwise suffered from a color channel saturation effect that reduced the utility of orientation information (see artifactual whitening in the optic radiations, Fig. 1, middle). To limit this effect, a high window maximum was required (> 90th percentile of any individual RGB color value), thereby limiting low-count contrast unless such a non-linear filter is applied.

	ILF	ACR	BCC	CING
Vol. 1	18.5±8.4	10.3±6.0	10.3±4.6	6.1±3.2
Vol. 2	18.0±6.6	13.3±6.6	9.5±6.7	8.1±4.6
Vol. 3	19.6±10.4	8.0±4.0	10.6±8.2	6.1±3.3
MEAN	18.7±0.8	10.5±2.7	10.1±0.6	6.8±1.2

Table 1. Track density for major white matter tracks in volunteers (units: tracks per voxel)

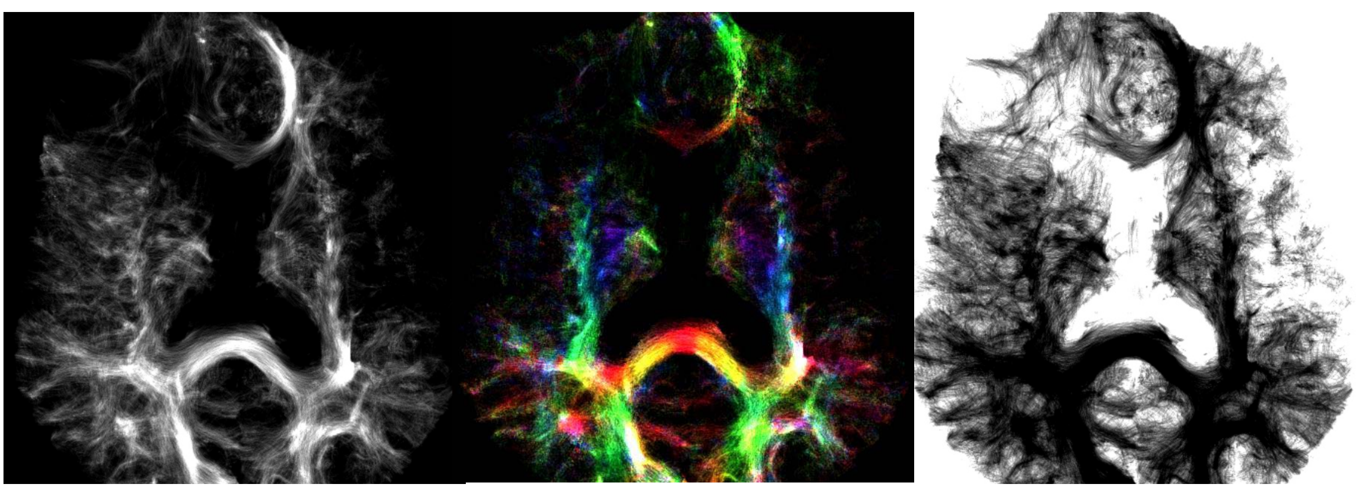

Figure 1. TDI images demonstrating disruption of normal white matter architecture in brain tumor. Left- TDI image. Middle- TDM image. Right- TDI with inverted contrast.

Discussion- We have developed a robust and computationally efficient reconstruction pipeline for super-resolution track density imaging. This framework will be used for future clinical research studies evaluating the potential utility enhanced visualization of gray and white matter structure in a number of different neurological diseases.

References: 1. Calamante et al. *Neuroimage*. 2010. 2. Tournier et al. *Neuroimage*. 2007.