A computational DTI template for aging studies

H. Zhang[1], P. Yushkevich[1], D. Rueckert[2], and J. Gee[1]

[1]University of Pennsylvania, Philadelphia, PA, United States, [2]Imperial College London, London, United Kingdom

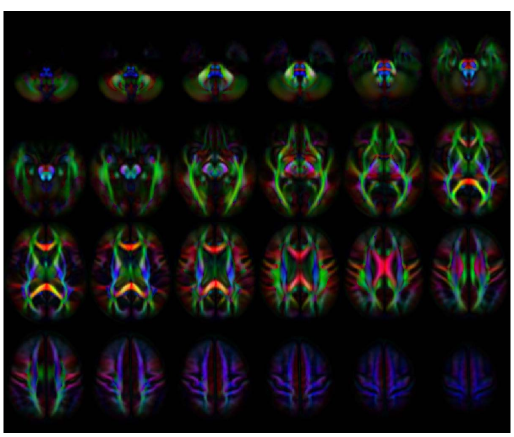
Introduction: Voxel-based analysis, either whole-brain or tract-specific, is a widely used approach for localizing white matter (WM) differences across populations using diffusion tensor imaging (DTI). A prerequisite to this approach is to spatially normalize all subjects to a common template. The accuracy of spatial normalization can be improved by using a population-specific template that is, morphologically, most similar to the subjects in the population of interest. Here, we report the development of a population-specific DTI template for the elderly that supports the tract-specific analysis of WM fasciculi [1]. We hope that this template will be a useful resource for the community studying aging.

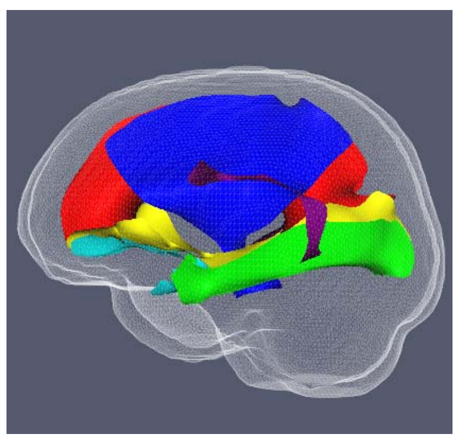
Subjects and data acquisition: The subjects used in this study are extracted from the IXI brain database (http://www.ixi.org.uk) developed jointly by Imperial College of Science Technology & Medicine and University College London. The IXI database consists of brain MR images from 550 normal subjects between the age of 20 and 80 years that are freely available for downloads. The selection criteria for this study include 1) subjects are of age 65 years or older; 2) DT-MR images of sufficient quality (i.e., no significant motion or susceptibility-induced artifacts) are available. A total of 51 subjects, a subset of the ones meeting the selection criteria, have been included in the current paper. The additional qualified subjects will be added in the future. The demographics of the included subjects are age 65-83, mean age and standard deviation 70.4±4.0; 21 male and 30 females. MRI was performed on a Philips 3-Tesla system with maximum gradient strength of 62 mT/m on each independent axis and slew rate of 100 mT/m/ms on each axis using a 6-channel phased array head coil. Diffusion-weighted images were acquired with a single-shot echo-planar diffusion-weighted sequence with 15 non-collinear gradient directions @ b = 1000 s/mm2 with a SENSE factor of 2. The additional imaging parameters are as follows: TR 12000ms, TE 51ms, slice thickness 2mm, field of view 224mm, matrix 128 x 128, resulting in voxel size 1.75 x 1.75 x 2 mm^3.

Construction of the DTI template: The DTI template was constructed using the DT-MR images of all the chosen subjects and with the software package DTI-TK (http://picsl.upenn.edu/resources_dtitk.aspx). DTI-TK implements a template construction approach specifically tailored for handling DT-MR images [2]. Briefly, the initial average image is computed as a log-Euclidean mean [3] of the input DT-MR images. The average is then iteratively refined by repeating the following procedure: register the subject images to the current average, then compute a refined average for the next iteration as the mean of the normalized images. This procedure is repeated until the average image converges. The resulting average is unbiased towards any single subject and captures the average diffusion properties of the population at each voxel with a diffusion tensor. Lastly, the template is computed by "shape-correcting" the average, using the strategy proposed by Guimond et al.[4], to ensure that the template also represents the average shape of the population. Specifically, this is achieved by first computing an average of the deformation fields that warp each subject into alignment with the template, then warping the template with the inverse of the average deformation field. The underlying registration routine implements a novel algorithm that matches DT-MR images directly[5]. By computing image similarity on the basis of full tensor images, rather than scalar features, the algorithm incorporates local fiber orientations as features to drive the alignment of individual WM tracts. By using full tensor information in the similarity metric, the method has been shown to align WM regions better than scalar-based registration methods in a task-driven evaluation study [6].

White matter parcellation of the DTI template: We parcellated the DTI template into individual WM tracts using an established protocol by Wakana et al. [7], which is based on fiber tracking. The FACT fiber tracking algorithm was applied to the DTI template with the FA threshold of 0.15 and an inner product threshold of 0.7, which prevents angles larger than 45^o during tracking. A fiber was tracked from the center of any voxel with a FA > 0.2. Fibers of interest were extracted using a multiple region of interest (ROI) based approach. Two types of ROIs were defined: those through which all fibers in a tract must pass, and those through which none of the fibers may pass. In the current work, we have delineated six major tracts: corpus callosum (CC), corticospinal tracts (CST), inferior fronto-occipital tracts (IFO), inferior longitudinal tracts (ILF), superior longitudinal tracts (SLF), and uncinates (UNC). One common feature of these tracts is that they all have a major portion that is sheet-like and can be modeled using the surface-based representation as described in Sec. 2.4. Binary 3D segmentations of individual tracts were generated by labeling voxels in the DTI template through which at least one fiber passed. The binary segmentations were further edited using ITK-SNAP to remove extraneous connections: the portion of the CST extending to the cerebellum was removed; regions that can not be disambiguated between CC and CST were attributed to both structures.

Surface-based geometric modeling of white matter tracts: Geometrical modeling of the WM tracts involves fitting deformable medial models (cm-reps) to the binary segmentations. The cm-reps proposed by Yushkevich et al. [8] are models that describe the skeleton and the boundary of a geometrical object as parametric digital surfaces with predefined topology. Furthermore, the models describe the geometrical relationship between the skeleton and the boundary, such that deformations applied to the model's skeleton can be propagated to the model's boundary. A key feature of medial models is their ability to parametrize the entire interior of the model using a shape-based coordinate system. This is due to the fact that in medial geometry every point on the skeleton surface is associated with a sphere that is tangent to the boundary surface at a pair of points (which may coincide at edges of the skeleton). The line segments connecting the sphere's center to the points of tangency are called "spokes" and are orthogonal to the boundary. Furthermore, no two spokes intersect inside the model. This allows us to define a coordinate system for interior of the object based entirely on the shape of the object, where two of the coordinate values parametrize the skeleton surface and the third gives the position of a point on the spokes. In the current context of modeling sheet-like white matter tracts, this coordinate system affords us the ability to reduce the dimensionality of the problem by projecting data onto the skeleton along the arguably "less interesting" thickness dimension. Tract-specific analysis described in [1] leverages this feature to improve sensitivity without much loss in spatial specificity.





Results: Figure 1 illustrates the DTI template using the FA-weighted RGB-encoded map of principal direction of diffusion. Observe that the template captures the relative large ventricles common to the brain of the elderly as well as the fine detail in cortical areas. Figure 2 illustrates the medial models of the parcellated WM tracts (visualized with reference to the brain contour): red for CC, blue for CST, yellow for ILF, green for IFO, cyan for UNC and purple for SLF.

Acknowledgement: This work is supported by the NIH under Grants EB006266, NS045839, HD046159, HD042974, and MH068066.

References: [1] Yushkevich et al, NeuroImage, 2008. [2] Zhang et al, MICCAI, 2007. [3] Arsigny et al, MICCAI, 2006. [4] Guimond et al, CVIU, 1999. [5] Zhang et al, Med Img Ana, 2006. [6] Zhang et al, IEEE TMI, 2007. [7] Wakana et al, Radiology, 2004. [8] Yushkevich et al, IEEE TMI, 2006.