Skeletonized white matter atlas and atlas-based segmentation

Shengwei Zhang[1], and Konstantinos Arfanakis[1]
[1]*Department of Biomedical Engineering, Illinois Institute of Technology, Chicago, IL, United States*

Introduction: Atlas-based white matter (WM) segmentation is often used to automatically define WM regions of interest (ROIs) in individual diffusion imaging datasets for the purpose of ROI analysis. This requires warping a digital WM atlas to the space of an individual subject, and transferring the labels from atlas-space to subject-space. The spatial transformation parameters are typically obtained by registering the diffusion tensor or diffusion anisotropy template included in the atlas to the corresponding information of the individual subject. However, misregistration leads to partial volume effects in the segmented ROIs, thereby reducing the accuracy and sensitivity of ROI analyses. In diffusion imaging studies involving voxel-wise analysis, the issue of misregistration has been addressed to a great extent by skeletonizing WM and studying exclusively voxels of the skeleton [1]. In this work, we propose a similar approach for ROI analysis. More specifically, we propose to use a skeletonized WM atlas to automatically project information from the central voxels of WM structures of individual subjects onto the atlas, minimizing the effects of misregistration. The purpose of this work was to a) demonstrate the differences in diffusion characteristics of structures selected with conventional and skeletonized atlas-based WM segmentation, and b) develop a skeletonized WM atlas based on the high-quality IIT2 diffusion tensor template [2].

Methods: Differences in diffusion characteristics extracted using conventional and skeletonized atlas-based segmentation. Diffusion tensor imaging (DTI) data was collected on 20 adult subjects using a 3 Tesla GE MRI scanner (General Electric, Waukesha, WI) and a Turboprop-DTI sequence. Brain extraction, motion correction, and tensor estimation were performed for all datasets. Fractional anisotropy (FA) and trace maps were produced for all subjects.

The diffusion tensor template of the Eve atlas [3] was registered to the DTI data of all subjects using DTI-TK (UPenn, PA, USA) [4]. The resulting spatial transformations were applied to the 118 WM labels of the Eve atlas, transforming the labels to each subject's space. The mean FA and trace values were calculated for each label in each subject. The mean and standard deviation of mean FA and trace values over all subjects were calculated for each label.

The diffusion tensor Eve template was skeletonized using TBSS [1]. The skeletonized version of the Eve atlas was then generated by applying the WM skeleton mask on the labels of the original Eve atlas. The FA and trace information of each subject was projected onto the skeleton of the Eve atlas using TBSS. The skeletonized atlas was used to estimate mean FA and trace values for each label in each subject. The mean and standard deviation of mean FA and trace values over all subjects were calculated for each label. A paired t-test was used for each label to test for significant differences in FA and trace values obtained with conventional vs. skeletonized atlas-based segmentation (significance at $p<0.01$).

Development of a skeletonized WM atlas corresponding to the IIT2 diffusion tensor template.

The IIT2 DTI template was recently published [2]. In brief, IIT2 was constructed based on Turboprop-DTI data from 67 subjects, is characterized by high image sharpness, provides the ability to distinguish small WM structures, has minimal image artifacts, contains diffusion tensor information representative of single-subject brain data, and is located in ICBM152 space [2]. A skeletonized atlas was developed for the IIT2 template based on the labeling of the Eve atlas and the skeletonization approach described above. Appropriate adjustments were made to account for differences in positioning of WM structures between the two templates. The final atlas contains 118 WM labels.

Results and Discussion: For 99 of the 118 WM labels, the mean FA over all subjects was significantly higher when using skeletonized compared to conventional atlas-based segmentation ($p<0.01$). Figure 1A shows the mean and standard deviation of FA over all subjects for six WM labels with significant differences across approaches (scp: superior cerebellar peduncle; cp: cerebral peduncle; fx/st: fornix/stria terminalis; gcc: genu of corpus callosum; bcc: body of corpus callosum; scc: splenium of corpus callosum). Similarly, for 81 of 118 WM labels considered, the mean trace over all subjects was significantly lower when using skeletonized compared to conventional atlas-based segmentation ($p<0.01$) (Fig.1B). Similar results were observed in both hemispheres.

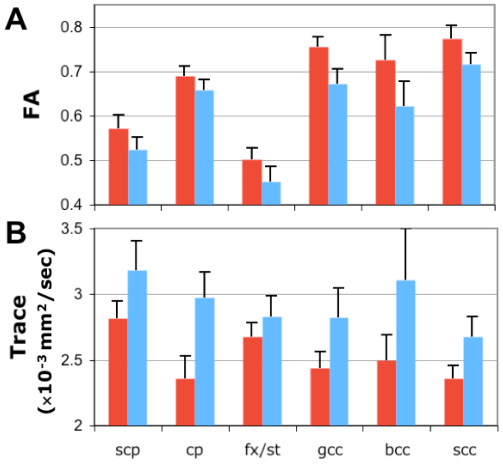

Figure 1. Mean and standard deviation of A) FA and B) trace over all subjects for 6 WM labels, obtained using skeletonized (red) and conventional (blue) atlas-based segmentation.

The above results demonstrate the significant differences in diffusion characteristics obtained with conventional and skeletonized atlas-based segmentation. For FA, these differences are caused by two reasons. First, a skeletonized label includes mainly the high FA values of a conventional label's ROI. Second, due to misregistration of a traditional atlas with an individual dataset, the combination of partial volume effects with the fact that FA values change dramatically from WM to gray matter and cerebrospinal fluid, significantly reduce the mean FA value in a conventional label, while the value for the corresponding skeletonized label remains largely unaffected (for reasonable amounts of misregistration). For trace, the significant differences observed between conventional and skeletonized atlas-based segmentation are primarily due to misregistration.

Examples of the new IIT2 skeletonized WM atlas, and a demonstration of the level of spatial matching between the new atlas and the T2-weighted map of the ICBM152 template are shown in Figure 2. The IIT2 skeletonized atlas contains 118 carefully defined WM labels, in addition to the whole brain DTI template (which was previously published [2]).

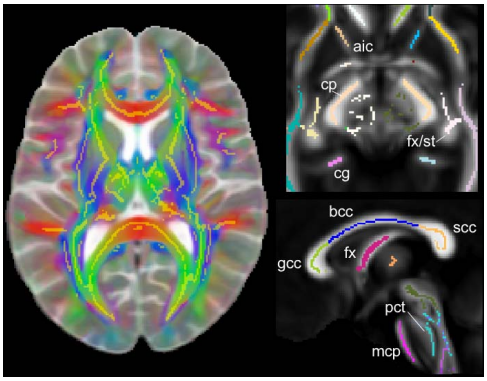

Figure 2. (Left) The IIT2 skeleton (in yellow), overlaid on the IIT2 FA-weighted color map, as well as the T2-weighted map of the ICBM152 template. (Right) Slices through the IIT2 skeletonized atlas.

In conclusion, this work demonstrated that diffusion imaging studies employing automated ROI selection by means of conventional atlas-based segmentation suffer from the effects of misregistration. We adopted the main principles of TBSS [1] and proposed an alternative automated approach, termed here "skeletonized atlas-based segmentation", which is relatively immune to misregistration. Furthermore, a new skeletonized atlas was developed in ICBM152 space based on the IIT2 DTI template. The combination of the whole brain DTI template and skeletonized WM atlas has the potential to increase the accuracy and sensitivity of both voxel-wise and ROI analyses in DTI, as well as high-angular resolution diffusion studies.

References: [1] Smith SM, et al., Neuroimage 2006;31:1487-1505. [2] Zhang S, et al., Neuroimage 2011;54:974-984. [3] Oishi K, et al., Neuroimage 2009; 46:486-499. [4] Zhang H, et al., Medical Image Analysis 2006;10:764-785.

Acknowledgements: Supported by NIBIB grant R21EB006525.