Investigating the role of ICBM-space human brain diffusion tensor templates in inter-subject spatial normalization

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Introduction: Diffusion tensor (DT) templates of the human brain are commonly used as a reference for inter-subject spatial normalization, which is a critical step in voxelwise comparisons of neuronal microstructural integrity and brain connectivity across populations. The recently published IIT2 DT template [1] is shown to be more representative of single-subject human brain DT data, is characterized by higher image sharpness, contains minimal image artifacts and lower noise levels, and better matches the ICBM152 space than other DT templates. However, the effect of the choice of DT template on the accuracy of inter-subject spatial normalization is unknown. Therefore, the purpose of this study was to investigate the role of two ICBM-space DT templates (ICBM81 [2] and IIT2) in inter-subject spatial normalization of DT data with a) minimal and b) visible artifacts, using three different DT registration approaches.

Methods: *Data and Pre-Processing*: Two groups of DT data were used in this study. Group 1 consisted of DT data from 22 healthy subjects collected with Turboprop on a 3T MRI scanner, containing minimal artifacts. Group 2 consisted of DT data from 22 healthy subjects included in the IXI brain database (http://www.brain-development.org) and collected with SE-EPI-DTI (with an acceleration factor of 2) on a 3T MRI scanner, containing visible artifacts. The sex and age in the two groups was matched. Data from Group 1 were corrected for motion only, while data from Group 2 were corrected for motion and eddy current distortions (eddy current distortions are minimal in Turboprop). *Subject-to-Template Registration*: Two ICBM-space DT templates, the ICBM81 and the $IIT2_{mean}$, were used as reference for spatial normalization, and three different techniques were used for registration to the template: DTIGUI (SBIA, UPenn, PA, USA) [3], MedINRIA (Asclepios Research Project, France) [4], and DTITK (UPenn, PA, USA) [5]. Both groups of DT data were registered to each template using all registration methods, which yielded 12 sets of normalized data from 22 subjects. *Assessment of Registration Accuracy*: For each set of normalized data, the mean FA, the coherence of coregistered primary eigenvectors (COH) [1], the 95% cone of uncertainty (COU) [1], and the overlap of eigenvalue-eigenvector pairs (OVL) [1] were calculated for each voxel in the brain. K-means clustering was applied on mean FA maps of each of the 12 sets of normalized DT data to identify the FA value that best segmented white matter (WM). Histograms of COH, COU and OVL in WM were produced for each of the 12 sets of normalized data. Histograms were compared first among different registration techniques for registration to the same template, and then between templates using the best registration technique for each template. These comparisons were performed for both Group 1 (minimal artifacts) and Group 2 (visible artifacts) data. The Kolmogorov-Smirnov (KS) statistical test was used to compare histograms. Differences with $p<0.05$ were considered significant.

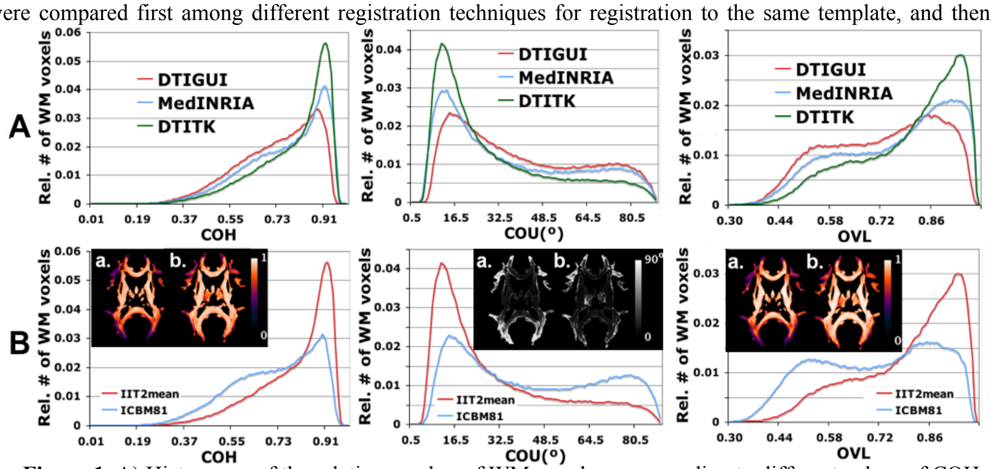

Figure 1. A) Histograms of the relative number of WM voxels corresponding to different values of COH, COU and OVL, for registration of Group 1 data to the $IIT2_{mean}$ template using 3 registration methods. B) Histograms of the relative number of WM voxels vs. COH, COU, OVL, for registration of Group 1 data to two templates (inset image a. ICBM81, b. $IIT2_{mean}$), using the most effective registration method for each template.

Results: For Group 1 data and registration to the $IIT2_{mean}$ template, DTITK resulted in a significantly higher percentage of WM voxels with high COH, low COU, and high OVL values than the other two registration techniques (Fig.1A). For Group 1 data and registration to the ICBM81 template, MedINRIA resulted in more accurate WM DT normalization (results not shown here). Using the preferred registration method for each template, normalization of Group 1 data to the $IIT2_{mean}$ template resulted in a significantly higher percentage of WM voxels with high COH, low COU, and high OVL values, than registration to the ICBM81 template (Fig.1B) (p-values for KS tests in Fig.1B were $<10^{-6}$). For Group 2 data and registration to ICBM81 or $IIT2_{mean}$, MedINRIA was shown to be consistently the preferred registration method (results not shown here). Using MedINRIA for registration of Group 2 data to both templates, normalization to the $IIT2_{mean}$ template again resulted in a significantly higher percentage of WM voxels with high COH, low COU, and high OVL values, than registration to the ICBM81 template. Although significant, the differences for registration of Group 2 data to the two templates were less evident than those shown in Fig.1B for Group 1 data (p-values for KS tests were again $<10^{-6}$). Finally, using the most preferable registration method for each case, registration of Group 1 data to the $IIT2_{mean}$ template was more accurate than registration of Group 2 data to any of the two templates (Fig.2).

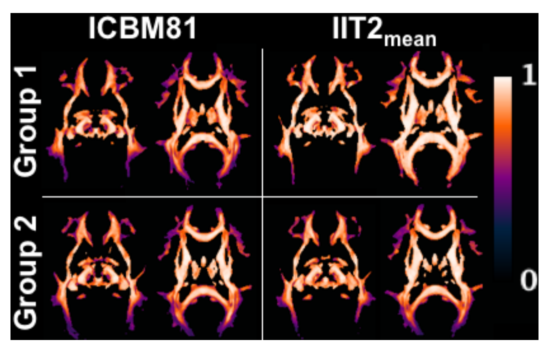

Figure 2. OVL from 2 slices for registration of Group 1 (top row) and Group 2 data (bottom row) to ICBM81 (left column) and $IIT2_{mean}$ template (right column).

Discussion: In summary, this study first demonstrated which of three publicly available registration techniques results in more accurate DT spatial normalization when using the ICBM81 or IIT2 templates for data with different levels of artifacts. This investigation then showed that, regardless of the artifact levels of the DT data, when using the IIT2 template as a reference, inter-subject normalization was significantly more accurate than with the ICBM81 template. Also, this difference between templates was more substantial when normalizing data with fewer artifacts, such as those produced with Turboprop, than data with more visible artifacts, such as those obtained with SE-EPI-DTI with parallel imaging, but significant for both data types. Consequently, using the more accurate template (IIT2) as a reference for inter-subject spatial normalization results in higher registration accuracy. In conclusion, this research determined a) registration techniques and b) templates that increase the accuracy of inter-subject spatial normalization of DT data. This is critical information for a large number of clinical studies performing voxelwise comparisons of neuronal microstructural integrity across populations.

References: [1] Zhang S, et al., Neuroimage 2010; in print. [2] Mori S, et al., Neuroimage 2008;40:570-582. [3] Yang J, et al., Proc. SPIE Med.Imaging 2008. [4] Yeo B, et al., Proc. IEEE ISBI 2008; p.700-703. [5] Zhang H, et al., Medical Image Analysis 2006;10:764-785.