# Enhanced ICBM diffusion tensor template of the human brain

**S. Zhang[1], H. Peng[1], R. Dawe[1], and K. Arfanakis[1]**
[1]Biomedical Engineering, Illinois Institute of Technology, Chicago, IL, United States

**Introduction:** Development of a diffusion tensor (DT) template that is representative of the micro-architecture of the human brain is crucial for comparisons of neuronal structural integrity and brain connectivity across populations. Furthermore, a DT template in ICBM space may simplify the combination of information from DT, anatomical and functional MRI studies. Recently, the IIT DT brain template was developed in ICBM space, and a) was characterized by higher image sharpness, b) provided the ability to distinguish smaller white matter structures, and c) contained fewer image artifacts, than several previously published DT templates[1]. However, low-dimensional non-linear registration was used in the development of that template, which reduced the accuracy of inter-subject matching, and led to a loss of local diffusion information and errors in the final tensors. Also, low-dimensional registration led to a mismatch of the anatomy in the IIT and ICBM templates. The purpose of this study was to use the high-quality DT data with minimal artifacts collected for the purposes of the previously published IIT template, and high-dimensional non-linear registration, in order to develop a template that is more representative of single-subject brain DT data, and more accurately matches the ICBM space.

**Methods:** *Data & pre-processing*: Turboprop-DT data from 67 healthy subjects, acquired on a 3T GE scanner, were used in this study[1]. Brain extraction, motion correction, and tensor estimation were performed. The b=0 s/mm$^2$ volume from each subject was first registered to the ICBM-152 template with rigid-body registration, and then with high-dimensional non-linear registration using the Automatic Registration Toolbox[2] (ART). The subject with the lowest total deformation was identified. The spatial transformation applied to the b=0sec/mm$^2$ images of that subject was also applied on the corresponding DW data. Tensors were estimated in ICBM-152 space, and the resulting DT dataset functioned as a temporary template. *Spatial normalization*: All 67 datasets were registered to the temporary template using DTIGUI[3] (SBIA, UPenn, PA, USA). This process involved segmentation of white matter, grey matter and cerebrospinal fluid in each dataset based on fractional anisotropy (FA) and trace maps, followed by registration of the three components to those of the temporary template using a high-dimensional elastic registration method (HAMMER, SBIA, UPenn, PA, USA), and appropriate tensor reorientation[3]. *Evaluation of inter-subject matching*: The normalization accuracy achieved for the 67 DT datasets using the high-dimensional non-linear registration method described above, was compared to that achieved with the registration method used in the development of the previously published IIT DT template. The average cross-correlation of FA and trace maps over all pairs of subjects was compared between methods. The average Euclidean distance of diffusion tensors, Euclidean distance of deviatoric tensors[4], overlap of eigenvalues-eigenvectors, over all pairs of subjects, as well as the coherence of primary eigenvectors[5], were also compared between registration techniques. Two-tailed Student's t-tests were used to assess the significance of any differences. Only differences with $p<0.01$, corrected for multiple comparisons with the Bonferroni approach, were considered significant. *Template development and evaluation*: Both mean and median[1] tensors were used to generate DT templates. The new templates were compared to the previously published IIT templates in terms of level of artifacts, template-derived FA values, sharpness of template-derived FA maps, and accuracy in matching the anatomy of the ICBM-152 template.

**Results and Discussion:** The use of high-dimensional non-linear registration resulted in significantly higher average cross-correlation of FA (0.901±0.006) and trace (0.946±0.006) over all pairs of subjects, compared to the registration method used for the development of the previously published IIT template (0.874±0.009 for FA & 0.928±0.01 for trace). Furthermore, in the selected white matter ROIs, the high-dimensional registration method resulted in significantly lower average Euclidean distance of diffusion tensors and deviatoric tensors, significantly higher average overlap of eigenvalues-eigenvectors, over all pairs of subjects, as well as significantly higher coherence of primary eigenvectors (Fig.1). Therefore, it was concluded that the normalization accuracy achieved for the 67 DT datasets in this study was significantly increased compared to that achieved for the development of the previously published IIT DT template. As a result, local diffusion information was preserved in the new templates (Fig.2A). The template-derived FA values were significantly higher than those of the existing IIT DT templates, and more similar to single-subject values (Fig.2A) (FA values not presented here). The template-derived FA maps were significantly sharper in the new compared to the existing IIT DT templates, as shown by simple visual inspection (Fig.2A), and manifested in the power spectrum (Fig.3). These enhancements were particularly significant in white matter near the surface of the brain (Fig.2A). Furthermore, similar to the existing IIT templates, the new templates did not contain any visible artifacts due to the use of Turboprop-DT data, in contrast to several published templates that are contaminated by susceptibility and eddy-current artifacts[1]. Finally, the cross-correlation between the $T_2$-weighted ICBM-152 maps and mean b=0sec/mm$^2$ images of the DT templates was significantly higher for the new DT templates than the existing IIT templates (Fig.2B). Thus, the information in the new DT templates more accurately matched the ICBM-152 space, than the existing IIT DT templates. This enhancement was particularly significant in the corpus callosum (Fig.2B). In conclusion, the use of high-dimensional non-linear registration significantly increased the accuracy of inter-subject spatial normalization of the available 67 DT datasets with minimal artifacts. Consequently, a new template that is more representative of single-subject human brain diffusion properties, and more accurately matches ICBM-152 space than the previously published IIT template, was produced. It is anticipated that the new template will significantly increase the accuracy of subject-to-template registration, and will play an important role in facilitating accurate comparisons of neuronal structural integrity and brain connectivity across populations.

**References:** [1] Peng H et al., Neuroimage 2009;46:967-980. [2] Ardekani BA et al., J Neurosci Methods 2005;142:67-76. [3] Yang J et al., Proc. SPIE Med. Imaging 2008. [4] Alexander DC et al., Comp Vis Im Und 2000;77:233-250. [5] Basser PJ et al., MRM 2000;44:41-50.

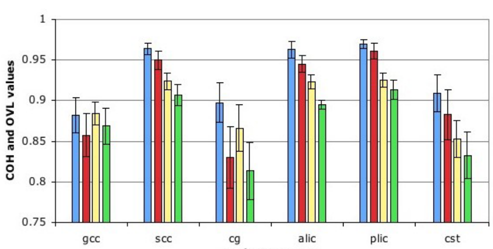


**Figure 1.** Coherence of primary eigenvectors (COH) and average overlap of eigenvalue-eigenvector pairs (OVL) over all pairs of subjects, in selected ROIs of two DT templates. Blue: COH for new template. Red: COH for previously published IIT template. Yellow: OVL for new template. Green: OVL for IIT template.

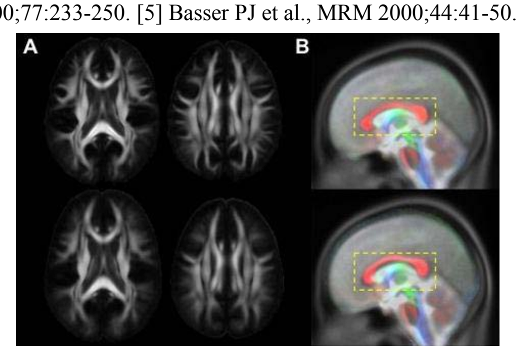


**Figure 2.** A) FA maps from the new DT template (top row) and IIT template (bottom row). B) Anisotropy color maps of the new (top) and existing IIT (bottom) templates overlaid on the ICBM-152 template.

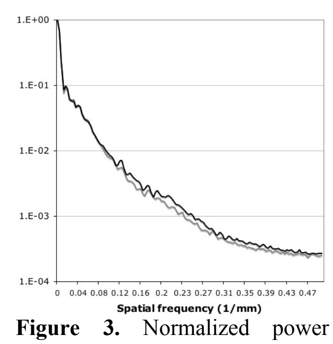


**Figure 3.** Normalized power spectra from FA maps derived from the new (black) and existing IIT (grey) templates.