Evaluating Tractography in Spatially Normalized DTI Data

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Introduction: Performing tractography in the native space of the acquired diffusion tensor imaging (DTI) data is often considered to be more faithful to the white matter (WM) anatomy than performing it in the normalized space using non-linearly transformed data. However, tractography in the normalized space is playing an increasingly important role in population analyses of white matter. In particular, the emerging tract specific analyses [1, 2] perform tractography in the normalized population specific template data. This approach benefits from the increased SNR in the population average. But, to our knowledge, the effects of normalization with tensor reorientation on the anatomical consistency of tractography results have not been investigated. Objective: This study is to evaluate and compare tractography results obtained in normalized space versus those in native space. The two key hypotheses explored in this study are: 1) Tracts generated in both normalized and native space have a high degree of macrostructural anatomical consistency. 2) Average microstructural measures, such as fractional anisotropy (FA) and mean diffusivity (MD), for tracts obtained in both native and normalized spaces are consistent. Tractography results have been used to measure and influence the quality of spatial normalization approaches [3, 4, 5, 6], but the presented work in this study is addressing a distinct question: whether non-linear spatial transformations preserve even long-range anatomical connections when performing tractography in the normalized space.

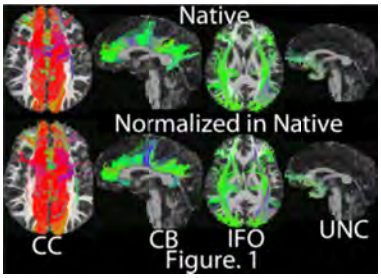

Figure. 1

Methods: Imaging: The diffusion weighted (DW) images for 4 healthy adult subjects were acquired on a GE 3.0 Tesla scanner using 48 non-collinear diffusion encoding directions with diffusion weighting factor of b=1000s/mm^2 in addition to eight b=0 images. The scans were repeated four times to assess reproducibility as well as provide an improved SNR for better tensor estimation. Pre-processing: Eddy current related distortion and head motion of each data set were corrected using FSL software package [7] and distortions from field in-homogeneities were corrected using field maps. Non-linear tensor estimation and tractography was performed using CAMINO [8]. Spatial normalization: The tensors estimated from the individual repeats as well as from the combined scans were spatially normalized to a population average of similarly acquired but a different set of scans from 16 healthy subjects. This was done to reflect a setting of registering a population to a standardized template. We employed DTI-TK [3], which has been shown to be best performing registration method for DTI data [9, 10], for the purpose. Tract extraction: On each of the 16 individual repeats and the 4 combined scans (total of 20), we extracted 4 major white matter pathways using tractography both in native and normalized space. Tractography was performed in 1x1x2mm^3 voxels, which was the dimension generated by the scanner, though the inherent spatial resolution was 2mm isotropic. The structures examined were corpus callosum (CC), cingulum bundle (CB-left & right), inferior fronto-occipital fasciculus (IFO-left & right) and uncinate fasciculus (UNC-left & right). These structures were extracted by systematically following protocols described in [11, 12]. Each structure was extracted by applying waypoint and filter regions of interest (ROI) to whole brain tractography performed in each of the 20 scans. These ROIs were all identified on the population template and were inverse warped onto the native space to extract the pathways in the native space. This reduced manually introduced inconsistencies in identifying the pathways. Evaluations: We performed extensive set of evaluations but report a few representative set of comparisons here, due to space limitations. We report the dice similarity coefficients (DC) between the pairs of masks obtained from warping the normalized space tractography and those from native space tractography. If $M(T_1)$ and $M(T_2)$ denote the binary masks obtained from two tractography sets T_1 and T_2, then $\mathrm{DC}[T_1, T_2] = \frac{2[M(T_1) \cap M(T_2)]}{|M(T_1)| + |M(T_2)|}$. DC reflects the macrostructural consistency between two tractography sets. We also compute DCs between the tractography results of individual repeats and of the combined data to provide a baseline for consistency. To examine the microstructural consistency we compute correlations between the mean FA values obtained using the sets of tractography-masks, for both the individual repeat data and the combined data.

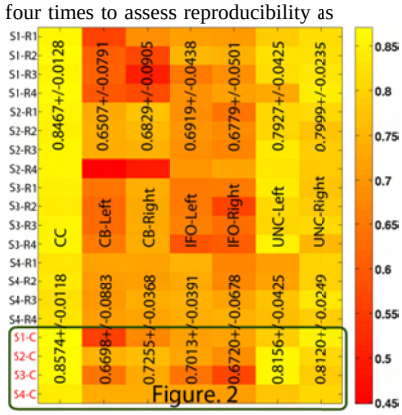

Figure. 2

Results: Visual consistency: The tracts extracted in the native space (Fig. 1, top) show high-level of visual consistency of geometric shapes with those extracted in the normalized space and inverse warped into native space (Fig. 1, bottom). Macrostructural consistency: The DCs (Fig. 2) for most of the structures are high indicating that the normalized space tractography produces macrostructurally consistent results compared to native space tractography. The DC mean and standard deviations for each structure are overlaid in text (individual repeats on the top and combined on the bottom). The DCs using the individual repeats (overall 0.7347±0.0891) are consistent with those using the combined data (overall 0.7505±0.0848) reflecting reproducibility. The DCs between tractography results from individual repeats and those from combined data are 0.7361±0.0910 indicating that the non-linear transformations do not affect the tractography results much worse than the inter-scan variability. Microstructural consistency: Mean FA values obtained using normalized space tractography are highly consistent with those using native space tractography (shown as high Pearson correlations (ρ) in Fig. 3 for both combined and individual repeats). X axis represents mean native FA obtained using inverse-warped normalized space tractography. Y axis represents mean native FA obtained using native space tractography. The bias (intercept difference between the magenta and black lines) is primarily due to smoothing effect of interpolations embedded in normalization, which results in slightly larger tracts in the normalized space resulting in slight reduction of mean FA because of inclusion of neighboring gray matter, particularly for harder structures like cingulum (dark blue circles). However, this bias is not subject specific and hence it is unlikely that the normalized space tractography will introduce any undesirable bias in ROI-based group analyses. We would like to point out that for pathways like cingulum, which are harder to extract the variability both in terms of DC and FA correlations is high compared to other structures.

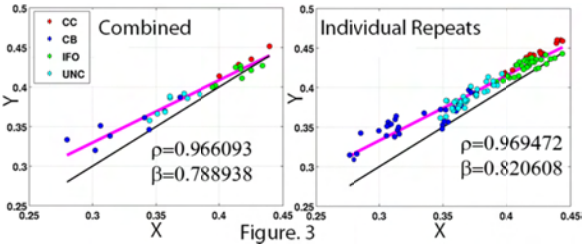

Figure. 3

Discussion: Our results demonstrate that normalized space tractography produces anatomically consistent structures compared to native space tractography. Both macrostructural and microstructural properties of tractography results are preserved during spatial normalization. This has important implications: 1) one can extract quantitative properties from the tractography data in the normalized for performing tract specific analyses, 2) the spatial normalizations preserve individual topological differences and one can build network models using normalized space tractography to study topological differences between individuals and groups. More extensive evaluations using 1) additional pathways, 2) other microstructural properties such as mean MD, mean radial diffusivity, 3) different similarity measures which can take into account the geometric shapes of the tracts and not just treat them as binary volumes, and 4) summary connectivity measures from whole brain tractography will be presented in a forthcoming article. Additionally, to investigate whether tracts from averaged data are adequate for population based studies, we will also report consistencies between tractography results on population averaged DTI template and those on the individual DTI data.

References: [1] Yushkevich et al. NIMG 41(2), 2008; [2] Zhang et al. MIA 14, 2010; [3] Zhang et al. MIA (10)5, 2006; [4] Zollei et al. NIMG 51(1), 2010; [5] Ziyan et al. MICCAI, 2007; [6] Zvitia et al. TMI 29(1), 2010; [7] Smith et al. NIMG 23(S1), 2004; [8] Cook et al. ISMRM, 2006; [9] Wang et al. NIMG 55(4), 2011; [10] Adluru et al. NIMG 59(1), 2012; [11] Mori et al. MRM 47(2), 2002; [12] Catani et al. Cortex 44(8), 2008.