

# **Voxel-based Morphometric Analysis of Fiber Tract Volume of Corpus Callosum Using Large Deformation Diffeomorphic Metric Mapping and Diffusion Spectrum Tractography**

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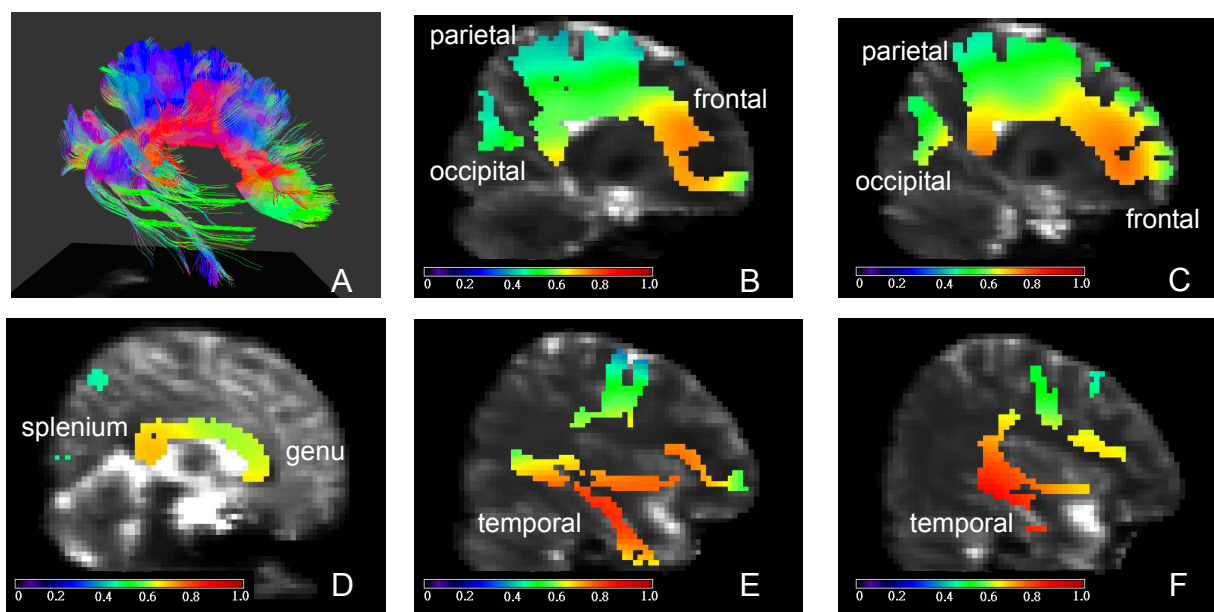
**Introduction** Problems of image registration have been well studied in the field of magnetic resonance imaging. Popular packages addressing this issue include AIR, SPM etc. The general scenario of image registration is to 'normalize' the source images to a template image (or target image) in order to minimize certain cost functions. The success of image registration using these methods has led to great progress in group comparisons of cortical structures and functions. Recent advances in diffusion MRI permit reconstruction of 3D fiber tractography in the brain, and this has opened up the opportunity to study the morphological properties of white matter fiber tracts. However, the registration of the diffusion MRI data, especially when aligning the fiber orientations amongst different brains, is not readily applicable using the current available packages. Recently, we proposed a registration method on a Diffusion spectrum imaging (DSI) dataset by considering the fact that DSI datasets are inherently 6D: 3D in image space and 3D in q-space. Specifically, we generalized the conventional 3D registration to the 6D scenario by implementing a Large Deformation Diffeomorphic Metric Mapping (LDDMM) algorithm [1, 2]. In this study, we applied this algorithm to white matter tracts of the corpus callosum (CC), and computed the gender difference in the tract volumes.

**Materials and Methods** Fourteen healthy subjects were included in this study (7 females/ 7 males; right-handed, aged 19-52 years). Subjects had no self-reported history of neurological or psychiatric disease or brain injury. Images were acquired on a 3T MRI system with a 32-channel head coil (TIM Trio, Siemens, Erlangen, Germany). DSI was performed using a twice-refocused balanced echo diffusion echo planar imaging (EPI) sequence, TR/TE = 9600/130 ms, field of view (FOV) = 200 x 200 cm<sup>2</sup>, image matrix size = 80 x 80, spatial resolution = 2.5 x 2.5 mm<sup>2</sup>, and slice thickness = 2.5 mm without gap. A total of 102 diffusion encoding gradients with the maximum diffusion sensitivity  $b_{\max} = 4000$  s/mm<sup>2</sup> were sampled on the grid points in the 3D q-space with  $|q| \leq 3.6$  units [3]. The 6D LDDMM algorithm was used to normalize all the DSI datasets of individual subjects to a DSI template of a 29-year-old female brain, time steps = 10, smoothing (alpha) = 0.01, smoothing (gamma) = 1.0, and integration of the velocity field to generate deformation maps based on the Euler method. The DSI tractography of the CC of the template was first reconstructed (Fig. A), and the voxels that contained the CC fiber tracts were selected to serve as masks. At each mask voxel, the determinant of the deformation matrix was computed for each normalized DSI dataset. Voxel-based group averaging of the determinants was performed for male and female groups, and from which the spatial mapping of the Z-values was computed for both groups as well. Finally, the mapping of the Z-difference (male - female) was computed to reveal the spatial pattern of the gender difference in CC tract volumes.

**Results** The Z-difference maps showed that the difference in tract volume was larger in the genu and splenium than the middle portion of CC (Fig. D). In both hemispheres, the CC tract volumes were larger in the frontal lobe (Fig. B and C) and temporal lobe (Fig. E and F). In contrast, there was little difference in tract volumes in the parietal and occipital lobes (Fig. B and C).

**Discussions** In this study we have demonstrated the gender difference in the CC tract volume. The results show that the males' CC tract volumes are generally larger than the females'. Using 6D LDDMM, our analysis further shows that there is a spatial variation in this difference between genders. The most prominent difference is found in the frontal and temporal lobes, whereas little difference is found in parietal and occipital lobes. In conclusion, our study demonstrates the feasibility of 6D LDDMM in the analysis of white matter tract volume using a voxel-based morphometric approach.

**References** [1] M.F. Beg et al., Int. J. Comput. Vis. 2005, 61: 139-157. [2] Y-C. Hsu, et al. Proc: ISMRM-ESMRMB, 2010. [3] V.J. Wedeen, et al., Magn Reson Med. 2005; 54:1377-86.



Figures: The color bar indicates the scale of the Z difference. Tractography of the corpus callosum (CC) of the template dataset (A). The Z-difference maps in left para-sagittal CC fibers to left frontal, parietal and occipital lobes (B), right para-sagittal CC to right frontal, parietal and occipital lobes (C), mid-sagittal CC (D), left para-sagittal CC fibers to left temporal lobe (E) and right side para-sagittal CC fibers to the right temporal lobe (F).