# Toward a highly valid quantitative study of diffusion tensor fields

D. Xu<sup>1</sup>, H. Huang<sup>2</sup>, D. Shen<sup>3</sup>, S. Wakana<sup>4</sup>, L. Poetscher<sup>4</sup>, C. Davatzikos<sup>3</sup>, P. C. van Zijl<sup>4</sup>, S. Mori<sup>4</sup>

<sup>1</sup>Psychiatry Department, Columbia University & New York State Psychiatric Institute, New York, NY, United States, <sup>2</sup>Biomedical Engineering Department, Johns Hopkins University School of Medicine, Baltimore, MD, United States, <sup>3</sup>Department of Radiology, University of Pennsylvania, Philadelphia, PA, United States, <sup>4</sup>Department of Radiology and Radiological Science, Johns Hopkins University School of Medicine, Baltimore, MD, United States

## Introduction

In order to perform group analysis, spatial normalization is a powerful quantitative technique. However, with local biological microstructure information encoded, diffusion tensor (DT) fields contain much higher dimensional signals than intensity-based images. Therefore, warping DT fields is more complicated. Several DTI warping algorithms were postulated [1, 2], which can properly reorient tensors through a statistical analysis of local displacement in a small neighborhood. In this study, HAMMER [3], a very high dimensional elastic transformation procedure in 3D volume space was employed for this purpose, which can effectively determine correspondence between a pair of intensity images co-registered with the DT images. In previous studies, we performed spatial normalization of diffusion tensor fields using co-registered  $T_1$ -weighted images. However, validity of the results was affected by the EPI distortion and errors from the mismatches of co-registered  $T_1$ -weighted image and DT image. It would be highly preferable if inter-subject normalization is based solely on DT images. Instead of using the transformation determined from co-registered  $T_1$ - weighted images, we adopted that directly from the averaged DTI map. Then it becomes crucial to minimize EPI-related image distortion and to know the extent of residual space distortion. In this study, SENSitivity Encoding (SENSE) parallel imaging was used to reduce diffusion weighted image (DWI) distortion. We measured residual discrepancy between  $T_1$ -weighted image and DTI and assessed the quality of the averaged DTI map using data from 13 healthy volunteers.

### Methods

**Data acquisition:** *In vivo* human data of 13 subjects were acquired using a 1.5 T Philips Gyroscan NT system. A single-shot EPI sequence with SENSE parallel imaging scheme (SENSitivity Encoding, reduction factor R = 2.5) was used for DTI data acquisition, with an imaging matrix of 96× 96 and a field of view of 240 × 240 mm (nominal resolution 2.5 mm), which was then zero-filled to  $256 \times 256$ . Axial slices thickness was 2.5 mm parallel to the anterior–posterior commissure line. A total of 50 to 55 slices covered the entire brain and brainstem leaving no gap. The diffusion weighting was encoded along 30 independent directions and the b-value was 700 mm<sup>2</sup>/sec. Five additional images with minimal diffusion weighting (b= 33 mm<sup>2</sup>/sec) were also acquired. Co-registered magnetization–prepared rapid gradient echo (MPRAGE) images of the same resolution were also recorded for anatomical guidance. **Image warping:** We randomly selected one of the 13 subjects as a template, and subsequently normalized the other 12, using the algorithm presented in [1]. Instead of taking the co-registered T<sub>1</sub>-weighted images for HAMMER [3] to derive a displacement field between a pair of DT images, we used their averaged DWIs, which guaranteed perfect co-registration inherently. By averaging all 13 normalized DT images, we obtained an average DT image, displaying the common aspects of this small population of 13 subjects. In order to demonstrate the difference of using co-registered T<sub>1</sub>-weighted images and using average DWIs, we calculated and normalized their difference images, with the same batch of displacement fields. In a similar averaging process, we obtained the average difference.

#### Results

Figure 1 is one slice of the color map of one individual's principal direction (PD), and Figure 2 is the same slice of the average result. We showed the colormap by assigning PD's x-component (horizontal) to red, y (vertical) to green and z (perpendicular to screen) to blue. Figure 3 is the average difference between  $T_1$ -weighted images and DWIs with gray matter and white matter assigned value 255 and all others 0. Although the brain shapes before and after normalization are very different, the tensors are properly reoriented and thus fiber pathways are preserved.

#### Discussion

By using SENSE imaging, mismatches between  $T_1$ -weighted images and DTI images have been largely ameliorated. Small disagreement is shown in the front and temporal regions, while most of the brain volumes match well. This implies the white matter anatomy and volume information is kept well in normalized maps. From a comparison between the individual subject in Fig 1 and the average map in Fig. 2, it can be seen that the high order elastic warping could preserve many details of white matter anatomy after normalization. This technique will allow us to quantitatively compare white matter anatomy between subject groups for these structures visible in the averaged maps.

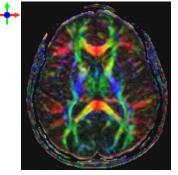


Fig. 1 A slice of one individual's DT colormap

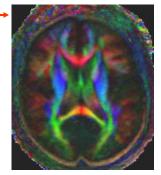


Fig. 2 A slice of the average DT colormap of 13 normalized healthy subjects.



Fig. 3 . Average difference between 13 subjects' DWIs and  $T_1$ -weighted images

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