Probabilistic Atlas of Human Brainstem and Application to Quantitative Analysis of Anatomical Abnormalities in stroke patients

W. Zhang[1,2], X. Li[2], A. Luft[3,4], D. F. Hanley[3], J. Zhang[1,2], P. C. van Zijl[1,2], and S. Mori[1,2]

[1]Department of Radiology, Johns Hopkins University School of Medicine, Baltimore, Maryland, United States, [2]F.M.Kirby Center for Functional Brain Imaging, Kennedy Krieger Institute, Baltimore, Maryland, United States, [3]Division of Brain Injury Outcomes, Dept. of Neurology, Johns Hopkins University, Baltimore, Maryland, United States, [4]Dept of General Neurology & Hertie Institute for Clinical Brain Research, University of Tuebingen, Tuebingen, Germany

Introduction:

DTI can delineate white matter anatomy based on fiber orientation information, from which we may detect injuries to specific white matter tracts caused by diseases in the brain. However, quantification of the altered white matter anatomy is not straightforward. One of the widely used approaches for such quantification is brain normalization and mapping. Currently, normalization and mapping of tensor data is not straightforward and tools are not widely available. We have developed a landmark based software that allows users to perform group analyses using DTI data. The software first performs automated linear transformation, followed by landmark-based non-linear transformation. It contains a standard landmark set in template spaces (JHU-DTI template (lbam.med.jhmi.edu) or ICBM-152). By mapping these landmarks to individual subject data, the tensor fields are normalized to selected templates, and statistical maps can be calculated. We used this tool to quantitatively characterize Wallerian degeneration in the brainstem consequential to stroke in the MCA region. This analysis allowed us to identify white matter tracts connected to the primary stroke areas. Thus, important information for anatomy – function correlation studies can be obtained. The results are compared to manual-ROI-based quantification of the size of the corticospinal tracts.

Methods:

For the DTI acquisitions, using a 1.5T Philips MRI scanner, SS-EPI with SENSE (r = 2.5) was used, with diffusion gradients applied in 30 non-collinear directions. Imaging parameters: FOV=240mm, slice thickness/gap=2.5 mm/0.0 mm, acquisition matrix=96*96, reconstruction matrix=256*256, TR>4s, TE=80 ms, b-value =700s/mm^2. DTI was processed using DtiStudio[1] . For the anatomical template, ICBM-152 was used. Because this widely-used statistical template doesn't have DTI-based white matter information, we first normalized our 30-subject normal DTI data into this template using the 12-mode affine transformation (called ICBM-152/DTI). For tensor transformation, we used a method proposed by Xu et al[2]. In the brainstem of this template, 53 landmarks were defined, which served as the "standard landmark set". We first normalized subject data into this template using 12-mode affine transformation, and then superimposed the 53 landmarks on the subject data, followed by manual adjustment of individual landmarks to subject anatomy. After the landmark adjustment, the subject image was non-linearly transformed to the template using a method proposed by Miller et al [3]. Images of 8 normal adult subjects, which were not used for the template creation, were normalized and served as the control probabilistic map. Images of 6 stroke patients with infarct in the territory of middle cerebral artery (MCA) were also normalized and the patient probabilistic map was obtained. Between these two maps, voxel by voxel statistic of FA and ADC were performed using Student's T-statistic. For visualization of the results, ratio maps were calculated using the following equation: Ratio Map = $|(\text{patient} - \text{mean}_{\text{control}}) / (\text{std}_{\text{control}})|$. ROI-based measurements were also performed by manually defining the corticospinal tracts at an axial slice of the pons using color-coded maps and superimposing the coordinates on FA and ADC.

Results and Discussion:

Fig.1 compares averaged FA maps of normal subjects after affine registration and after the landmark-based non-linear registration. White matter structures in the averaged map after nonlinear registration appears sharper than after affine registration. The standard deviation among the 8 subjects is noticeably smaller after non-linear registration than after affine registration. The smaller standard deviation is most likely due to higher registration quality and it may lead to higher sensitivity in detecting abnormality in white matter structures in the brainstem.

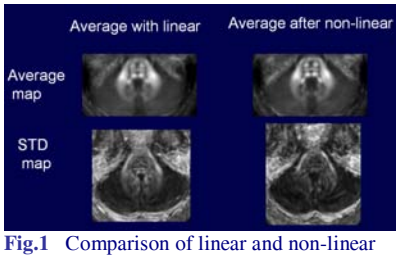

Fig.1 Comparison of linear and non-linear based average and standard deviation maps.

Fig.2, a FA map of a stroke patient is statistically analyzed after linear and non-linear transformation. Abnormality of the corticospinal tract is clearly detected when using the non-linear registration (P <0.005)

Fig.3 shows group analysis results of 6 MCA stroke patients in the left hemisphere. Clear FA abnormality in the left corticospinal tract and the right cerebellar peduncles are detected. These abnormalities of the contralateral cerebellar peduncles are expected because these tracts have decussation in the brainstem. Manual ROI-based approach agrees with the results (left FA: 0.30±0.07, right FA: 0.44±0.02).

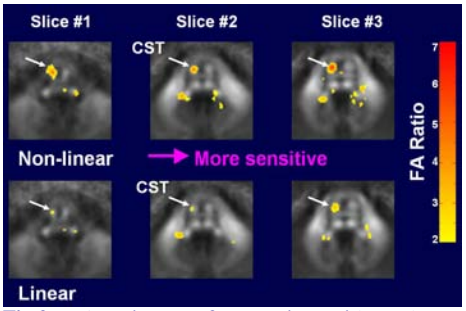

Fig.2 FA Ratio map of one patient with stroke in the territory of right MCA.

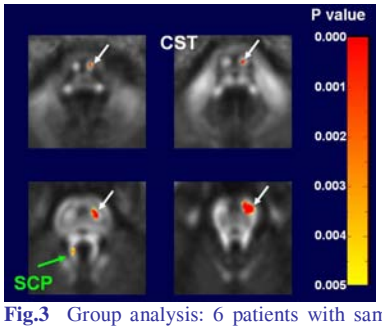

Fig.3 Group analysis: 6 patients with same size primary lesions in left MCA are pooled.

In the past, this type of analyses has been performed mostly using manually delineated ROIs. While it is a valid approach, it depends on prior knowledge on the region of interest, in which reproducible ROI protocols have to be developed for pre-determined brain regions. The normalization-based approach on the other hand allows us to examine the entire brainstem. In this study, we developed a software that is capable of registering DTI data by aligning corresponding white matter tracts non-linearly. One drawback of the proposed method is the involvement of manual landmark placement, which is time-consuming and subject to placement error. The computational time is, however, is much shorter than typical automated nonlinear algorithms (15 min vs ~10 hours). The placement error can also be characterized for each landmark based on reproducibility measurements and incorporated to the normalization process, which is currently being implemented to the software tool.

References:

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