A Pediatric Brain Template for Diffusion Tensor Imaging

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Introduction Diffusion tensor imaging reveals detailed structural information about white matter tracts, and is increasingly used to study the pediatric population. It is highly desirable to construct age appropriate templates so the findings in patients could be reported using coordinates in a standard stereotaxic brain space, and at all brain locations the diffusion measures of an individual patient could be compared with pre-determined normal range. We constructed a DTI template from a group of normal children and adolescents and demonstrated utilities of such a template.

Materials and Methods DTI data used in the template were acquired from 18 normal children (13 males, 6 to 18 years of age, mean age 10). All subjects were right handed monolingual English speakers with normal IQ. DTI was performed at 3T (Philips Achieva Release 2.5) using SS-EPI (56 slices, voxel size 2 mm^3, TR/TE = 8237/74 ms; acquisition matrix 128 x 128, SENSE factor = 2, 30 diffusion encoding directions with a *b*-value of 700 s/mm^2, 3 averages). The DTI raw data was affine registered to the $b = 0$ volume and averaged offline using the Philips research software platform (PRIDE). The data were further processed using FSL 4.1 (FMRIB [The Oxford Centre for Functional Magnetic Resonance Imaging of the Brain] Software Library, http://www.fmrib.ox.ac.uk/fsl) including BET to extract brain tissue and brain mask, FLIRT to conduct inter-subject affine transformation into the MNI152 space, and DTIFit to reconstruct the diffusion tensors with the diffusion encoding vectors rotated by the same affine transformation. Using internally developed software written in IDL, each diffusion tensor element was averaged over all subjects at each voxel location. Maps for FA and unit vector $\mathbf{V}_1$ of the primary eigenvector were generated and used as the template.

The utilities of the template were then explored. The template was tested as a standard for revealing abnormalities of white matter tract morphology and directionality in individual patients. For this purpose, the patient DTI raw data is affine transferred to the MNI152 space. The patient diffusion tensor is spatially smoothed by Gaussian with FWHM of 4x4x4 mm to match the smoothing of brain structure in the template due to averaging. A map of $d\mathbf{V}_1$ (difference in $\mathbf{V}_1$ between a subject and the template) is calculated. To visualize the white matter structural deviations, the product of dV_1 amplitude and FA is displayed, with color encoding by the $d\mathbf{V}_1$ direction. The template was also tested as the target image for nonlinear registration in TBSS[1] analysis for a group of 20 dyslexia subjects in this age range. The skeletonized FA values obtained with this template were compared with that obtained by using one 9 year control data as the target image.

Results Fig. 1A shows the template FA map and Fig. 1B the FA map of a patient with cortical dysplasia. The difference map in Fig. 1C shows marked deviation of the fiber orientation at the right anterior corona radiata. In a case of tuberous sclerosis, no apparent WM abnormality was found on the difference map (Fig. 1D). In two control subjects, the difference map detected apparent variations within subcortical white matter which do not have any clinical significance (not shown).Satisfactory nonlinear warps of the FA maps in TBSS were achieved with the pediatric template. Statistics of the skeletonized FA at various locations obtained with the two different target images are listed in Table 1. In Fig 2, the adult template from FSL and the pediatric template are compared. In a common MNI152 space, there are noticeable differences between the two templates.

Table 1. Comparison of FA (n=20) from TBSS using different targets for non-linear registration (mean+/- s.d)

Region	template as target	most representative subject as target
R-plic	0.758±0.044	0.732±0.049
L-plic	0.760±0.040	0.729±0.042
R-alic	0.602±0.075	0.600±0.075
L-alic	0.592±0.083	0.570±0.080
R-ec	0.384±0.037	0.382±0.041
L-ec	0.386±0.035	0.392±0.043

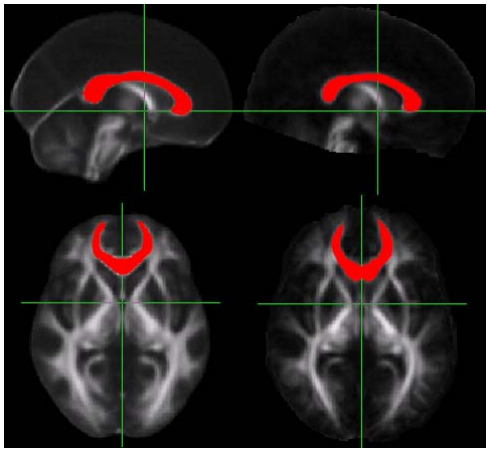

Fig 2. Comparison of FA map: an adult template (FMRIB58_FA from FSL, left) and the pediatric template (right) shows size differences in brain structures.

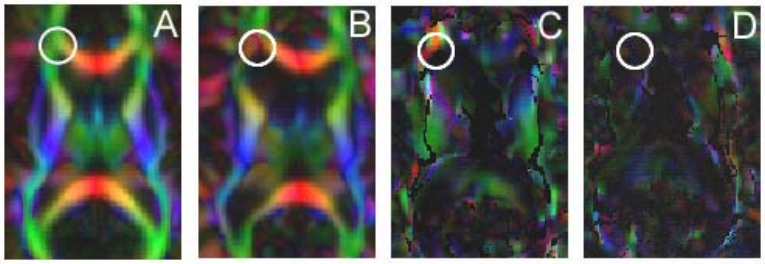

Fig 1. A: template; B: a patient with dysplasia C: difference map (B-A) showing changes in fiber directions for patient in B; D: difference map for a case of tuberous sclerosis without marked deviation of fiber orientations.

Discussion Template constructed with affine transform preserves non-linear spatial variations in the brain structures. This feature is important for construction of stereotaxic atlas in a standard brain space. However, we note, as expected, there are significant decrease in FA values as a result of average over many subjects with substantial normal variation in the brain morphology. This highlights the need to involve non-linear transform for voxel based analysis, such as in TBSS. In TBSS analysis of pediatric data, the use of a template as the target for non-linear registration is preferred over using one typical subject, providing more accurate reporting of results in a standard brain space such as MNI152. DTI templates have been constructed for adults and proven to be valuable [1,2]. For children, the templates need to be constructed for different age ranges. Such age dependent templates would be an important tool to reveal developmental changes in white matter structures. More subjects will be added and templates for more specific and narrower age ranges will be constructed in the future.

References: 1. Smith SM et al. Neuroimage 2006;31:1487-505; 2. Mori S et al. Neuroimage 2008;40:570-82.