Summary Statistics for Diffusion Tensor Imaging Brain Templates: Mean vs. Median Tensors

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Introduction: Human brain diffusion tensor imaging (DTI) templates developed to date use the mean tensor to summarize the DTI information from a group of subjects[1]. However, spatial normalization of DTI data between subjects contains inaccuracies, and the mean of imperfectly matched tensors may have significantly different characteristics than the individual tensors. It is well known that, in distributions with statistical outliers, the median may be a more accurate summary statistic than the mean[2]. The purpose of this work was to investigate the role of the mean and median tensors in summarizing the DTI information from a group of subjects.

Methods: ***Experiments:*** Sixty-seven healthy human subjects (20-40 years of age) were scanned on a 3T GE MRI scanner (Waukesha, WI) with Turboprop-DTI (voxel volume 10.5mm^3, b=900s/mm^2, 12 diffusion directions, 2 b=0sec/mm^2 images for each slice, 21'57" scan time). Motion was corrected in each subject using 3D rigid-body mutual information registration (FSL, Oxford, UK). The DTI data from one subject functioned as a temporary template. The DTI data from all 67 subjects were normalized to the temporary template, using non-linear registration based on 3D discrete cosine transform (DCT) basis functions (SPM5). The diffusion tensors were reoriented using PPD. In each voxel, the mean tensor was obtained by averaging the tensors from all 67 subjects on an element-by-element basis. The median tensor was selected to be the tensor with the minimum average distance from the tensors of all other subjects[2]. The resulting mean and median DTI templates were compared on a voxel-by-voxel basis by subtracting maps of different quantities derived from the diffusion tensors. ***Simulations:*** Simulations were conducted in order to explain the differences between the two templates. First, a cylindrical diffusion tensor (λ_1=1.7x10^{-3} mm^2/sec, λ_2=λ_3=0.2x10^{-3} mm^2/sec) was simulated so that its primary, secondary, and tertiary eigenvectors were parallel to the x, y, and z axes, respectively. One thousand tensors were then simulated by first rotating the original tensor around the y axis, and subsequently around the x axis. The angle of rotation around the y axis was selected from a Gaussian distribution with a mean of zero and a FWHM of 10°, and the angle of rotation around the x axis was selected randomly. The mean and median of the 1000 tensors were estimated, and their shape was compared using quantities such as the linearity, planar and spherical indices, and the FA. The simulation was repeated for angles of rotation around the y axis selected from Gaussian distributions with FWHM between 10° and 180°, in increments of 10°. Plots of quantities describing the shape of the mean and median tensors were produced. In a separate simulation, cylindrical tensors were mixed with spherical tensors (λ_1=λ_2=λ_3= 0.7x10^{-3} mm^2/sec). The percentage of spherical tensors included in the mixture was varied between 0% and 100%, and the primary, secondary, and tertiary eigenvectors of all tensors were parallel to the x, y, and z axes, respectively. The mean and median tensors were estimated and plots of quantities describing the shape of the mean and median tensors were produced.

Results and Discussion: Images derived from the median DTI template appeared more noisy than the corresponding images from the mean template, especially in regions near the surface of the brain (Fig.1). In these regions, the accuracy in registration of different structures is lower than in the rest of the brain. In the same regions where the median template appears noisy, the mean template is characterized by low anisotropy due to averaging of tensors with different shape and orientation. Subtracting FA maps corresponding to the mean and median templates demonstrated that, in white matter, FA of mean tensors was lower on average than FA of median tensors (Fig.2A,B). This was due to misalignment of white matter tensors from different subjects and was explained in the simulations. When averaging simulated cylindrical tensors that were not aligned with each other, the linearity and FA of the mean tensor decreased, and the spherical index increased with increasing angles between the simulated tensors (Fig.3A). In contrast, the values of all quantities derived from the median tensor remained constant and equal to those of each individual simulated tensor (Fig.3A). Furthermore, in the experiments, near the interface of brain tissue and CSF-filled spaces, the eigenvalues and trace were increased, and the FA was in some cases decreased for mean compared to median tensors (Fig.2). These effects were due to mixing of highly anisotropic and isotropic tensors caused by registration errors, and were explained in the simulations. When simulated cylindrical tensors were mixed with spherical tensors, the linearity and FA of the mean tensor decreased, and the spherical index increased with increasing percentage of spherical tensors included in the mixture (Fig.3B). In contrast, the values of all quantities derived from the median tensor remained constant and equal to those of the simulated cylindrical tensors, as long as the percentage of spherical tensors was lower than 50% (Fig.3B). When the percentage of spherical tensors was higher than 50% the values of all quantities derived from the median tensor were equal to those of the simulated spherical tensors.

Based on the results of this investigation, one may conclude that the median tensor better represents the characteristics of tensors grouped during registration, compared to the mean tensor. However, the decision of using the median instead of the mean DTI template, ultimately depends on the task that one wishes to accomplish. For example, when a template that accurately represents the shape of the grouped tensors is of highest importance, then the median template would be most appropriate. The apparent SNR in different regions of the brain in the median template may be used as a measure of confidence for the information presented by both templates in these regions. For spatial normalization purposes, the mean template may be most appropriate since the noise in the median template may lead to registration errors, especially when combined with non-linear normalization techniques. These differences in the two templates will be reduced as the accuracy in the spatial normalization used for the construction of the templates is improved. Further research is required to evaluate the utility of the mean and median DTI templates.

References: 1) Mori S. et al., Neuroimage 2008;40:572-582. 2) Jones D.K. et al., Neuroimage 2002;17:592-617.

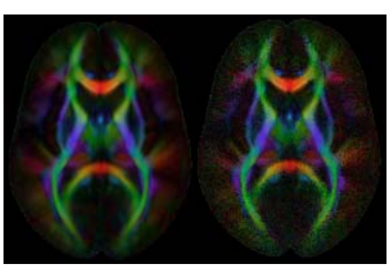

Figure 1. Diffusion anisotropy color maps derived from the mean (left) and median (right) DTI templates.

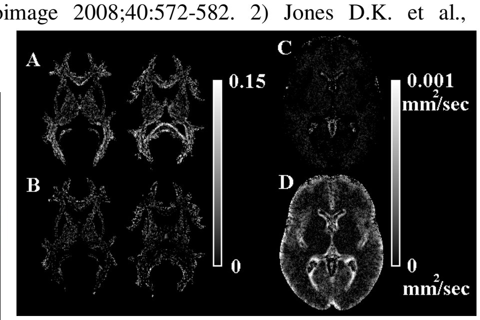

Figure 2. Maps of the voxels in which the FA$_{median}$> FA$_{mean}$ (A), FA$_{mean}$>FA$_{median}$ (B), trace$_{median}$>trace$_{mean}$ (C), and trace$_{mean}$> trace$_{median}$ (D).

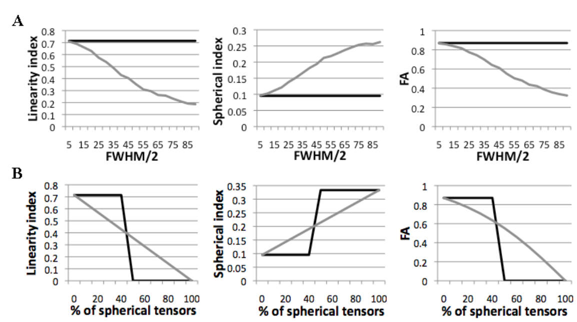

Figure 3. A) Simulation of averaging misaligned cylindrical tensors: Plots of the linearity, spherical index and FA of mean (grey line) and median (black line) tensors as a function of half of the FWHM of the Gaussian distribution used to select the rotation of simulated cylindrical tensors around the y axis. B) Simulation of averaging cylindrical and spherical tensors: Plots of the linearity, spherical index and FA of mean (grey line) and median (black line) tensors as a function of the percentage of spherical tensors included in the mixture.