**Dimensional Comparisons of Diffusion Tensor Metrics in Monte Carlo Simulations and Secondary Progressive Multiple Sclerosis**

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**Introduction:** The specificity and characteristics of a series of diffusion tensor (DT) derived parameters and their relative analytical relationships were investigated in numerical simulations and a study of Secondary Progressive Multiple Sclerosis (SPMS), a continued deterioration of multiple sclerosis after the early relapsing-remitting phase, to validate the sensitivity of each DTI index and the evolution of structural and anisotropy change as corresponding diffusion profiles discriminated between anisotropy levels defined as $A = 0.2$ to $0.25$, $A = 0.3$ to $0.35$, $A = 0.4$ to $0.45$, $A = 0.5$ to $0.55$, $A = 0.6$ to $0.65$, $A = 0.7$ to $0.8$, $A = 0.8$ to $0.9$, and $A = 0.9$ to $0.95$. FA was derived as a one-dimensional (1D) function of cylindrical structure with a fixed mean diffusivity, two-dimensional (2D) function of an asymmetric structure, and a 3D function in the diseased stages. We generated a series of diffusion ellipsoids to evaluate the multiple mapping properties of the FA map and computed the exact structures of the corresponding diffusion profiles discriminated between anisotropy levels defined as $A = 0.2$ to $0.25$, $A = 0.3$ to $0.35$, $A = 0.4$ to $0.45$, $A = 0.5$ to $0.55$, $A = 0.6$ to $0.65$, $A = 0.7$ to $0.8$, $A = 0.8$ to $0.9$, and $A = 0.9$ to $0.95$. The Monte Carlo simulation [3] was performed in MATLAB (MathWorks, Natick, MA) to take into account the noise artifacts in the derived tensor parameters as a function of SNR, unique number of direction scheme, fiber orientation, anisotropy level, and compare with the signal acquired from MS in 1.5T scanner.

**Image Processing:** A study of five SPMS patients and five healthy controls were compared to the simulated diffusion tensor parameters. The images were acquired from the GE Signa 1.5T Excite 11.0 scanner with an 8 channel head coil, 21 equal potential unique diffusion gradient schemes, b=1000 s/mm², matrix size = 128x128, voxel size = 1x1x3 mm³, TR/TE = 10800/80ms, and FOV = 24cm. The DW data were registered in the FMRIB Software Library (Oxford Center for Functional Magnetic Resonance, FSL) to the baseline T2 image to correct the motion and eddy current artifacts of the EPI acquisition. Relative diffusion indices, rDI, were defined to evaluate the relative change of FA, axial, and radial diffusivity between control and patient in addition to the volume average of the selected indices. Parametric and nonparametric tests were used to compare the tensor derived parameters in the regions of (I) GCC (genu corpus callosum) (II) SCC (splenium corpus callosum) (III) IC (internal capsule) (IV) CN (caudate nucleus) (V) TH (thalamus) and (VI) CSF (cerebrospinal fluid) within/between group in the same and different ROI. To estimate the specificity of the regional induced variation, Pearson correlation coefficients were calculated across selected ROIs.

**Results and Discussion:** Figure 1 shows the dual structures, prolate and oblate, the positive and negative quantities of the collinear parameter, corresponding to the same FA as a 1D function for $D_1$ evaluated from 0.12 to 0.49. The associated structural complexity differs for FA ranging from 0.2 to 0.9 as a 2D function. More combinations were observed in FA = 0.6 and FA = 0.7 than those observed in FA = 0.8 and FA = 0.9. From the analytical relationship derived, the axial and radial diffusivities are more sensitive to the structural change compared to FA in the high anisotropy level. This framework was implemented in the study of normal and SPMS brains (Fig. 2) that the relative changes in radial diffusivity in GCC, SCC, and IC are greater than rFA whereas the measured variations in radial diffusivity detected in CN and TH are smaller than those of rFA. Reduced FA was found in the selected WM bundles while FA enhancement was observed in GM regions. Figure 3 shows the matrix of Pearson correlation of radial and axial diffusivities that a more global enhancement can be observed in the radial diffusivity of SPMS. Figure 4 are the schemes of contrast-to-noise (CNR) ratios of the radial and axial diffusivities simulated in 21 unique directions for SNR from 0 to 80 as a function of anisotropy level to evaluate the contrast and noise induced variation as a ratio. The strategies to combine the optimized indices to improve the diagnosis accuracy in the secondary progressive multiple sclerosis were demonstrated in this study.