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 in the disease. We simulated the anisotropy dependent fractional anisotropy (FA) [1], which has been used to probe the brain morphology and pathological variations covering the range from low to high anisotropy level at all time points in a newly proposed multiple dimensional framework, and compared with the intrinsic information acquired from the radial and axial diffusivities. As most of the diagnostic and research efforts feature MS as the white matter (WM) disease which mainly damages the myelin due to the response of the immune system, gray matter (GM) involvements [2] were meanwhile probed in this study to verify the presented framework and quantify the water diffusion with the extension to cortical and nuclei regions to better understand the connection between WM and GM related cognitive impairments in MS.

Material and Methods: Analytical and Numerical simulation: The brain structures were simulated as the symmetric cylindrical diffusion ellipsoids and asymmetric diffusion tensors corresponding to two identical diffusivities $\lambda_1 = \lambda_2 \neq \lambda_3$ and three distinct diffusivities $\lambda_1 \neq \lambda_2 \neq \lambda_3$ respectively. 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 $A = (\lambda_1 - \lambda_2)/Trace$. 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/ mm^2, matrix size = 128×128, voxel size = 1×1×3 mm^3, 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.

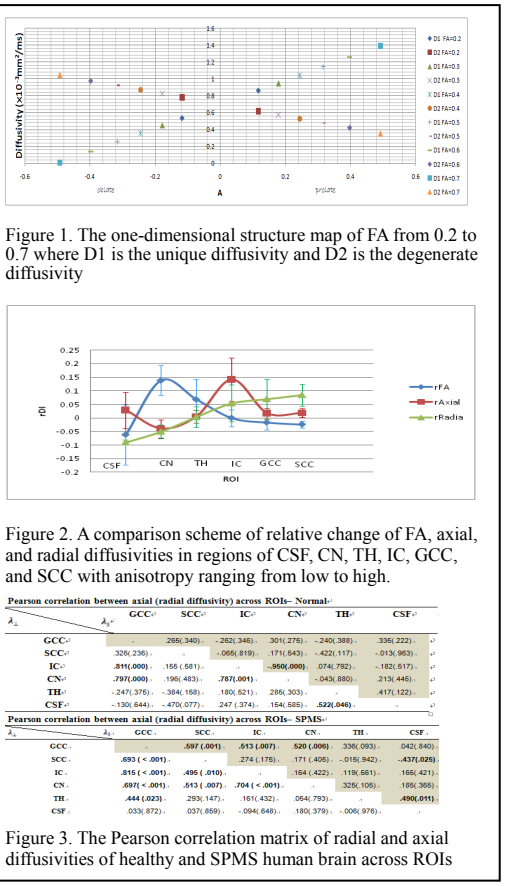

Figure 1. The one-dimensional structure map of FA from 0.2 to 0.7 where D1 is the unique diffusivity and D2 is the degenerate diffusivity

Figure 2. A comparison scheme of relative change of FA, axial, and radial diffusivities in regions of CSF, CN, TH, IC, GCC, and SCC with anisotropy ranging from low to high.

Pearson correlation between axial (radial diffusivity) across ROIs– Normal

$\lambda_\perp$ \ $\lambda_\parallel$	GCC	SCC	IC	CN	TH	CSF
GCC	.	.265(.340)	-.262(.346)	.301(.275)	-.240(.388)	.335(.222)
SCC	.326(.236)	.	-.065(.819)	.171(.643)	-.422(.117)	-.013(.963)
IC	**.811(.000)**	.155(.581)	.	**-.950(.000)**	.074(.792)	-.182(.617)
CN	**.797(.000)**	.196(.483)	**.787(.001)**	.	-.043(.880)	.213(.445)
TH	-.247(.376)	-.384(.168)	.180(.521)	.286(.303)	.	.417(.122)
CSF	-.130(.644)	-.470(.077)	.247(.374)	.154(.585)	**.522(.046)**	.

Pearson correlation between axial (radial diffusivity) across ROIs– SPMS

$\lambda_\perp$ \ $\lambda_\parallel$	GCC	SCC	IC	CN	TH	CSF
GCC	.	**.597(.001)**	**.513(.007)**	**.520(.006)**	.336(.093)	.042(.840)
SCC	**.693(<.001)**	.	.274(.175)	.171(.405)	-.015(.942)	**-.437(.025)**
IC	**.815(<.001)**	**.495(.010)**	.	.164(.422)	.119(.561)	.165(.421)
CN	**.697(<.001)**	**.513(.007)**	**.704(<.001)**	.	.325(.105)	.186(.366)
TH	**.444(.023)**	.293(.147)	.161(.432)	.054(.793)	.	**.490(.011)**
CSF	.033(.872)	.037(.859)	-.094(.648)	.180(.379)	-.006(.976)	.

Figure 3. The Pearson correlation matrix of radial and axial diffusivities of healthy and SPMS human brain across 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 A 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.

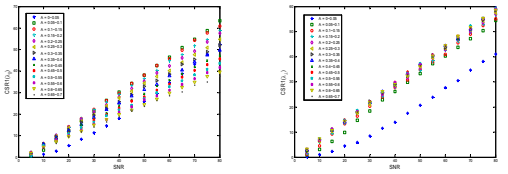

Figure 4 The CNR of radial and axial diffusivity as a function of anisotropy level ranging from SNR = 0 to 80

References: [1] Basser PJ *et al* JMR(B) 1996;111(3):209-219 [2] Pirko I*et al.* Neurlogy 2006;68: 634-42 [3] Pierpaoli, C, Magn Reson Med 1996;36: 893-906