Underlying tissue pathologies of focal cerebral ischemia in rat examined using diffusion MRI

Peng Sun[1], Yong Wang[1], Teng-Nan Lin[2], and Sheng-Kwei Song[1]
[1]*Radiology, Washington University in St. Louis, Saint Louis, MO, United States,* [2]2*Institute of Biomedical Sciences, Academia Sinica, Taipei, Taiwan*

Introduction

Brain ischemia causes a loss of organization and structure at the cellular level. DTI had been widely used for precise evaluation of tissue injuries caused by ischemic stroke [1], detecting and characterizing axonal injury and demyelination. However, diffusion properties derived using DTI lose specificity and sensitivity with increasing pathological and anatomical complexity. Herein, diffusion basis spectrum imaging (DBSI) [2] was employed to address DTI limitations by resolving multiple-tensor water diffusion resulting from axon injury, demyelination, and inflammation in a rat model of transient middle cerebral artery occlusion (MCAO).

Material and Method:

Animal Model: Male Long-Evans rats (n = 5) weighing 250 to 300 g were employed. Focal brain ischemia was induced by an intraluminal suture middle cerebral artery occlusion (MCAO) method. Transient focal ischemia was induced for sixty minutes. 7 days after injury, rats were killed and fixed for ex-vivo MRI scan.

MRI: Diffusion MRI of the rat brain was performed using an Agilent DirectDrive console equipped with a 4.7 T magnet and a 15-cm inner diameter gradient coil. Brains were placed in a custom-made birdcage coil for data acquisition. A multi-slice multi-echo sequence incorporating a pair of diffusion sensitizing gradients was used for DWI with the following parameters: TR, 0.75 s; TE, 30 ms; Δ, 16 ms; δ, 7 ms; Image resolution: 150 $\times$ 150 $\times$ 1500 μm^3; total acquisition time: 3 hours.

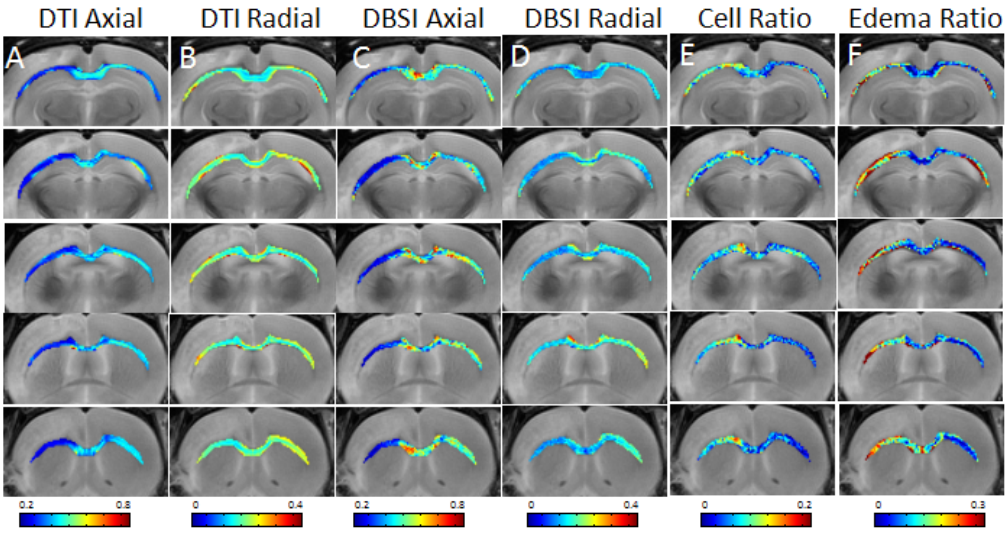

Figure 1 DTI-calculated axial diffusivity (A), radial diffusivity (B), DBSI-calculated axial diffusivity (C), radial diffusivity (D), cell ratio (E) and water ratio (F).

DTI and DBSI Analysis: The diffusion weighted data were analyzed fitting the 100 diffusion weighted signals using a linear combination of diffusion basis set consisting of cylindrically symmetric diffusion tensors with the freedom to vary $\lambda_{||}$ and $\lambda_{\perp}$ to estimate the number of anisotropic diffusion tensor components (N_{aniso}) and the associated principal directions. After N_{Aniso} was computed, the number of isotropic component (N_{iso}) was further determined using nonnegative least-squares (NNLS) analysis[2]. The global nonlinear optimization was conducted employing direct pattern search to solve Eq. [1]. A traditional derivative based optimization method was employed following the global optimization to improve the accuracy of the solution. Indices from DBSI include axial and radial diffusivity of detected fiber, the ratio of cell and water components etc.

$$S_k = \sum_{i=1}^{N_{Aniso}} S_i e^{-\left|\vec{b}_k\right| \cdot \lambda_{\perp}} e^{-\left|\vec{b}_k\right| \cdot (\lambda_{||} - \lambda_{\perp}) \cos^2 \theta_i} + \sum_{j=1}^{N_{iso}} S_j e^{-\left|\vec{b}_k\right| \cdot d_j}, \qquad [1]$$

Both DTI and DBSI maps were calculated from the diffusion weighted images using home-made software by Matlab® (MathWorks, Natick, MA, USA). ROI of corpus callosum was outlined using ImageJ (Wayne Rasband, NIH, USA).

Results and Discussions

Fig. 1 shows the DTI- and DBSI-derived maps from five continuous slices, lesion at the left. The decreased axial diffusivity from DTI (Fig. 1A) and DBSI (Fig. 1C) on the lesion side (left) suggested that axons were injured. There was no evidence suggesting the presence of demyelination based on the DTI (Fig. 1B) or DBSI (Fig. 1D) derived radial diffusivity. Increased cellularity and extent of vasogenic edema were clearly seen at the lesion side of DBSI maps revealing the underlying pathologies (Fig. 1E, 1F). Although it is not clear what kinds of cells were present, the increased cellularity may confound DTI measurements underestimating diffusivity of the injured white matter. In contrast, the presence of vasogenic edema or water content resulting from tissue loss may overestimate diffusivity of the injured white matter. The separation of these components by DBSI allows more accurate diffusivity estimation in stroke than that by DTI. In conclusion, the proposed DBSI provide a new tool to more accurately investigate underlying pathologies in the cerebral ischemia.

References: [1] Sotak CH et al. *NMR Biomed.* 2002. [2] Wang,Y. *et al*. *Brain*. 2011, In Press.