Findings of Nonlinear Behaviors of Log-signal Intensities on DTI in Patients with Alzheimer¡¯s Disease

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Introduction: Although diffusion tensor (DT)-MRI is sensitive to the directionality of random motion of water, it may be impossible to verify true diffusion alternations in vivo. Previous findings of DT-MRI in patients with Alzheimer's disease (AD) and mild cognitive impairment (MCI) showed that diffusion isotropy (Trace or mean diffusivity, MD) was increased and diffusion anisotropy (fractional anisotropy, FA) was decreased against cognitive normal (CN) subjects in specific regions of brain. The applied external diffusion-sensitizing magnetic field gradients may be altered by the local susceptibility-related gradient in AD because 1) AD can be characterized pathologically by amyloid plaques and neurofibrillar tangles in the brain, 2) some studies found iron accumulations in plaques in mice with AD(1-3), and 3) patients with AD had more total plaques compared with subjects with mild cognitive impairment(MCI) and cognitive normal (CN) control (3). The findings of DT-MRI in patients with AD and MCI may not support true diffusion alternations caused by tissue degeneration. Therefore, we explore systematically the local background gradient effect in DT-MRI data of human brain, especially under pathological conditions such as AD, which involves iron-contained plaques.

Materials and Methods: Fifteen patients diagnosed with AD (mean age=75 years, 9 males and 6 females, mean MMSE=21.9), eighteen MCI patients (mean age=72 years, 7 males and 11 females, mean MMSE=28.5), and 16 CN controls (mean age=73 years, 9 males and 7 females, mean MMSE=29.3) were studied using a 1.5T clinical MRI system. DT-MRI measurements were performed using a double refocusing single shot spin-echo EPI sequence with inversion-prepared magnetization to suppress cerebrospinal fluid (CSF) (4). Six diffusion encoding directions (5) and five diffusion sensitivities (b-values 0, 160, 360, 640, and 1000 sec/mm^2) were acquired to determine ADC and the diffusion tensor for each voxel. Two DT-MRI data sets were acquired with alternating polarities of the external diffusion-sensitizing gradients (positive $+G_d$ and negative $-G_d$). MD and FA maps were obtained from the positive DT-MRI data or negative DT-MRI data. To define regions-of-interest (ROI), paired T-tests between the positive MD(pMD) or pFA verse the negative MD(nMD) or nFA were performed. Raw DT-MRI signal intensities were obtained from the specific ROIs to investigate a nonlinear behavior of the raw data during fitting ADC maps in certain brain regions.

Results: Representative plots of logarithmic raw DT-MRI data obtained from the ROI 1 (x=-14, y=-20, z=2) shown in the inserted picture of the significant differences between pMD versus nMD for AD patients for the six diffusion encoding directions are shown in Fig 1A and Fig 1B for the negative and positive diffusion-encoding gradients, respectively. LnS in the vertical axis is Log(S/S_0), where S and S_0 are signal intensities with and without diffusion gradients, respectively. In both plots, the logarithmic DT-MRI data of the forth diffusion-encoding direction were different compared to others both with using positive and negative diffusion gradients. We found a nonlinear behavior for the logarithmic raw DT-MRI data in the forth diffusion-encoding directions, but not other diffusion encoding directions.

Fig 1.Plots of logarithmic DT-MRI data among six diffusion-encoding directions (D) obtained from the negative (2A) and positive (2B) diffusion-encoding gradients against five b-values (ROI 1: x=-14, y=-20, z=2).
A. Negative diffusion-encoding gradients
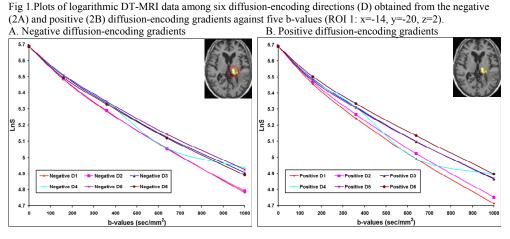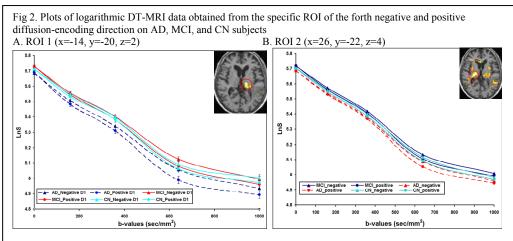B. Positive diffusion-encoding gradients

Figure 2 shows representative plots of logarithmic DT-MRI data obtained from the specific regions-of-interest (ROI) of the forth negative and positive diffusion-encoding direction on AD, MCI, and CN subjects. The corresponding ROI is inserted in the picture. The nonlinear regressions of ROI data sets with using both positive and negative diffusion gradients for all three groups are shown and the degree of nonlinearity for each ROI is different. In addition, degrees of nonlinearity among subject groups are different with the most variation in AD patients and the second most in MCI patients.

Discussions and Conclusion: Nonlinear behaviors of DT-MRI data in some specific areas were demonstrated in this study that may be related to local susceptibility gradients caused by iron-deposits. For accurate DT-MRI measurements, the b-value may be calculated by taking account the local variations in some pathologic brains, especially, in some abnormal brain conditions, such as shown here for AD which is characterized by the accumulation of some substances and any of them contain iron.

Fig 2. Plots of logarithmic DT-MRI data obtained from the specific ROI of the forth negative and positive diffusion-encoding direction on AD, MCI, and CN subjects
A. ROI 1 (x=-14, y=-20, z=2)
B. ROI 2 (x=26, y=-22, z=4)

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