Towards Accurate In Vivo Diffusion Measurement in Human Optic Nerve

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Introduction

Pathologic heterogeneity is postulated as a key contributor to the 'MRI paradox' in multiple sclerosis (MS). Diffusion tensor imaging (DTI) can potentially discern axonal loss in clearly defined white-matter tracts and serve as a marker for demyelination and remyelination. To evaluate if DTI parameters correlate with the neurological disability in MS, the optic nerve was chosen as a tissue model to study because it is often affected in MS patients. And the optic nerve provides a white matter tract with relatively simple architecture (no gray matter or neurons).

Methods

Volunteers: Twelve normal subjects with no symptoms or signs of neurologic or ocular pathology were recruited (6 men and 6 women, age 21 - 48 with mean 37). In addition, 2 individuals were imaged three times, and 2 individuals were imaged two times to determine coefficient of variation.

Image Acquisition: MR images were acquired using a 4-element phased array custom-fabricated "optic nerve" coil on a 3 tesla scanner (Allegra, Siemens AG, Erlangen, Germany). A fat-suppression single shot spin-echo echo planar imaging (ss-SE-EPI) diffusion sequence was employed with reduced field of view (rFOV) [1] and gradient reversal technique [2]. Diffusion weighted images were acquired trans-axially (FOV 168×84 mm, matrix 128×64, partial Fourier 6/8, and TE 65 ms) with two collated groups of 1.3 mm thick slices. Each slice group is comprised of five interleaved slices and was cardiac gated (one slice acquisition per heartbeat, starting with 150 ms delay after the rise of the sphygmic wave as measured with a peripheral pulse oxymeter), yielding a TR of 4 - 6 sec. Eight to twelve image data sets, each consisting of one image with b value of 0 (b0) and twelve diffusion sensitized images on twelve diffusion encoding directions with b value of 600 s/mm^2, were acquired for each slice group.

Data Analysis: After image acquisition, DTI data sets were motion-corrected and averaged [3]. A resampling step outputs images with resolution of 0.65×0.65×0.65 mm^3 before DTI calculation. The region of interest was selected manually on the b0 image to include 15-20 voxels longitudinally, only including the center of the nerve, and starting 10-12 voxels posterior from the retina.

Statistics: The mean, standard deviation (SD) and 95% confidence interval (CI) of apparent diffusion coefficient (ADC), scaled relative anisotropy (sRA), axial diffusivity and radial diffusivity were estimated from 1000 bootstrap samples of 1 measurement from each of 10 different subjects (Tab. 1). There are a total of 32 measurements (left and right eyes) from 16 scans of 10 individuals.

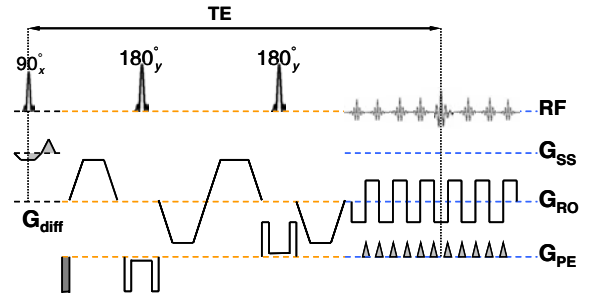

Figure 1. rFOV diffusion sequence scheme.

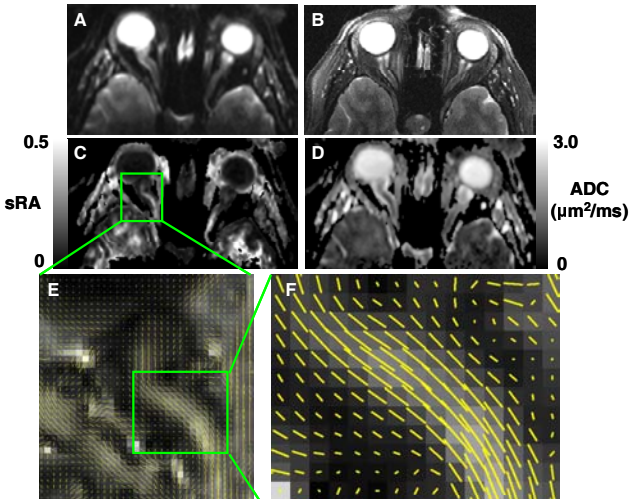

Figure 2. Representative transverse images illustrating high quality of the optic nerve diffusion images. A) b0, B) T2W, C) sRA, D) ADC, E) whisker plot, and F) magnified whisker plot. Little susceptibility artifacts and blurring were observed comparing to the T2W image. Clear delineation can be seen between the nerve and the surrounding CSF. Whisker plots, showing the projection of the principal eigenvector in each voxel overlaying the sRA map, demonstrate the fiber coherence despite the curvature of the subject's optic nerve.

Results and Discussions

The high quality diffusion images (Fig. 2) reveals the exquisite details of the fiber coherence in the optic nerve. The minimum amount of distortion and blurring benefited from the short EPI echo train length (ETL=48) enabled by the rFOV technique. Although parallel imaging can be used with the phase array coil in our study, the reconstruction artifacts and amplified noise level introduced unnecessary errors. Our implementation of the rFOV sequence further combines the technique with twice refocused spin echo (TWSE) [4] and gradient reversal [2] techniques to provide better Eddy current compensation and fat suppression, respectively (Fig. 1).

The signal-to-noise ratio (SNR) is a big concern in high resolution optic nerve diffusion imaging. Low SNR can underestimate ADC and overestimate sRA. A plot of voxel signal intensity *vs.* axial diffusion demonstrates that at low levels of signal intensity, axial diffusion was dependent upon the signal. Also, as the signal intensity reached a critical threshold, the signal intensity no longer predicted axial diffusion. The voxel signal intensity equivalent to an SNR of 32 was chosen as the cut-off to ensure informative voxels. Below the cut-off, the correlation coefficient (r^2) of voxel signal intensity vs. axial diffusion was 0.43; at or above the cut-off, the r^2 was 0.03 (both p values were <0.05). Utilizing this cut-off, voxel signal intensity had little dependency upon the other diffusion parameters (ADC r^2=0.05, sRA r^2=0.05, radial diffusivity r^2=0.05). After the cut-off was applied, the diffusion parameters displayed a Gaussian distribution.

DTI Parameters	Mean	95% CI	SD	95% CI
ADC	1.09	(1.02, 1.12)	0.21	(0.15, 0.24)
sRA	0.29	(0.27, 0.31)	0.09	(0.07, 0.10)
Axial diffusivity	1.66	(1.58, 1.69)	0.18	(0.16, 0.21)
Radial diffusivity	0.81	(0.73, 0.84)	0.26	(0.17, 0.28)

Table 1. DTI parameters in normal health volunteers

Reference [1] Jeong, et al. *Megn. Reson. Med.* **54**, 1575-1579, 2005. [2] Gomori, et al. *Radiology* **169**, 493-495, 1988. [3] Shimony, et al. *Cereb. Cortex*, **16**, 1653-1661, 2006. [4] Reese, et al. *Megn. Reson. Med.* **49**, 177-182, 2003.