Q-Space Diffusion Weighted Imaging (DWI) in the Spinal Cord: Comparison with Conventional DWI and Magnetization Transfer Imaging in Multiple Sclerosis

J. A. Farrell[1,2], S. A. Smith[1,2], E. M. Gordon-Lipkin[3], D. S. Reich[1,3], P. A. Calabresi[3], and P. C. van Zijl[1,2]

[1]Neuroscience Section, Division of MR Research, Department of Radiology, Johns Hopkins University School of Medicine, Baltimore, Maryland, United States, [2]F.M. Kirby Research Center for Functional Brain Imaging, Kennedy Krieger Institute, Baltimore, Maryland, United States, [3]Department of Neurology, Johns Hopkins University School of Medicine, Baltimore, Maryland, United States

Introduction: The spinal cord, with densely packed, myelinated axons, is an ideal system to investigate the effects of restricted diffusion. Diffusion measured perpendicular to the white matter (WM) fiber bundle should be sensitive to WM damage, as in multiple sclerosis (MS). Q-space analysis is an alternative method for analyzing diffusion weighted imaging (DWI) data in which the probability density function (PDF) for molecular diffusion is estimated without the need to assume a Gaussian shape [1]. Although used for human brain imaging [2], q-space DWI has only recently been applied to the human cervical spinal cord *in vivo* [3]. Here we demonstrate the feasibility of the technique in patients and, with respect to the ability to detect lesions, compare q-space contrasts to the apparent diffusion constant perpendicular to the WM fiber orientation ($ADC_\perp$) and magnetization transfer (MT) measurements. We also characterize which contrasts show the most significant deviation between patients with MS and controls.

Subjects and Methods: Eight healthy volunteers and four MS patients were studied after IRB approval and written informed consent. Three patients were scanned twice in a follow-up study. A 3T Philips MR unit was used with body-coil excitation and a 2 element surface coil for reception. Diffusion weighted images were acquired using multi-slice, single-shot spin echo EPI, (SENSE = 1.8, TR/TE = 7000/112 ms) with second order shimming. Thirty axial slices were acquired covering C1 to C6 (nominal resolution = 1.3x1.3x3.0 mm^3) with diffusion weighting applied perpendicular to the axis of the spinal cord. The gradient strength (G) was linearly increased to achieve 31 q-values from 0 to 414 cm^{-1} ($q = \gamma\delta G/2\pi$, δ = 16ms, Δ = 74.5ms, b_{max}= 4685 s/mm^2). To improve SNR, data were collected with diffusion weighting along [x,y,0] and [x,-y,0] and averaged after motion correction. Scan time = 10 min. Following methods in [3], the PDF for each voxel was computed by taking the Fourier transform of the signal decay with respect to q. Root mean square displacement (RMSD) and probability (P_0) maps were computed from the full width at half height and height of the PDF, respectively. For conventional DWI analysis, $ADC_\perp$ was computed by fitting the Stejskal-Tanner equation to the signal decay at b-values $\leq$ 1020 s/mm^2. For each slice, ROIs were delineated in dorsal column WM (dcWM) on the RMSD maps and applied to P_0 and $ADC_\perp$ maps. MT data were acquired with and without a 24ms sinc-shaped RF prepulse (8.5μT, 1.5kHz off-resonance from water, nominal resolution = 0.69x0.69x2.25 mm^3) and are denoted as MT weighted (MTw) and MT_{ref}, respectively. MT data were coregistered and resliced to match the number and thickness of slices of the DWI data. MT ratio (MTR) maps were computed. To prevent anatomical mismatch from confounding the comparison of results, separate ROIs were delineated in dcWM on the MTw images and applied to the MTR images. The MTw signal was normalized by the mean CSF signal on the same slice in the MT_{ref} image to provide so-called MTCSF values [4]. The mean and standard deviation of RMSD, P_0, $ADC_\perp$, MTCSF and MTR over all voxels within the ROIs were computed and normalized to a consistent anatomical coordinate system based on cervical vertebral levels. **Statistics:** At each slice level a distribution of ≈ 600 values was obtained by pooling the voxels within each ROI from all controls. Corresponding distributions were obtained for each patient. Two-tailed and one-tailed Student's t-tests, assuming unequal variance, were performed to test if the control and MS patient distributions had equal means (α = 0.01). Tests were performed for each contrast, at each slice level. An approximate measure of sensitivity to WM damage was defined as the number of slice levels (expressed as %) identified as significantly different from controls. For one-tailed t-tests, it was expected that RMSD, $ADC_\perp$, and MTCSF increase, while P_0 and MTR decrease in lesions.

Results and Discussion: Fig 1: MTw, RMSD, P_0, and $ADC_\perp$ maps in a healthy control and two MS patients. Lesions in dcWM are hyperintense in MTw, RMSD and $ADC_\perp$, and hypointense in P_0 images. The RMSD of the PDF reflects the amount of diffusion perpendicular to the cord's long axis while P_0 is the probability of no net molecular displacement. Diffusion in healthy WM is restricted, resulting in a tall, narrow PDF. **Fig 2:** ROI analysis of diffusion and MT measurements in dcWM, as a function of cervical level, for two patients, compared to the mean ± SD over 8 controls. Areas of lesion involvement are indicated by increased RMSD, $ADC_\perp$, and MTCSF and decreased P_0 relative to controls. Changes in MTR were generally small. The change in the shape of the PDF, and increase of $ADC_\perp$ in MS lesions can probably be explained by the loss of axonal and/or myelin barriers to diffusion. **Table 1:** Compared to $ADC_\perp$, RMSD and P_0 exhibited improved detection of abnormal diffusion for all 4 patients. The mono-exponential fit, which assumes a Gaussian PDF, describes the signal decay at low b-values and $ADC_\perp$ is sensitive to the fast diffusion component. However, a slow diffusion component (non-monoexponential signal decay) was observed at b ≥ 1500 s/mm^2. Q-space analysis may therefore permit evaluation of WM damage through its effects on both the fast and slow diffusion components, which may correlate with different pathological changes. Direct comparison of the sensitivity of diffusion and MT measures to WM damage is not straightforward given the differences in resolution, SNR, and scan time. However, it is encouraging that the location and extent of WM damage compares favorably in both the images and the ROI analysis as a function of cervical level.

Fig 1: Diffusion and MT Images

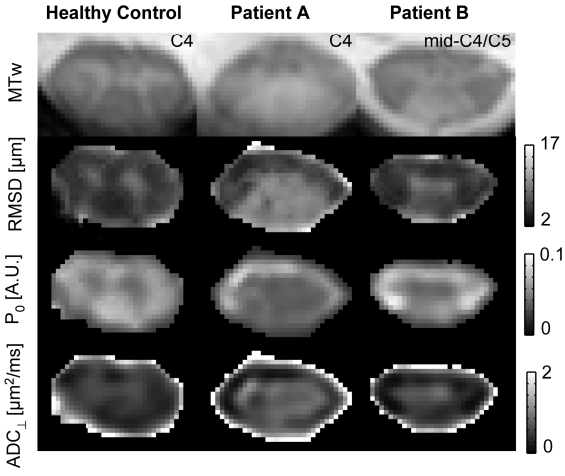
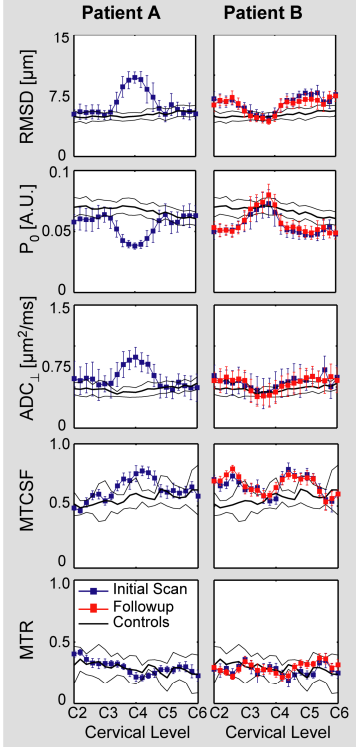


Table 1: Percent of slices significantly different from controls

Patient	A		B		C		D	
T-test sides	**two**	**one**	**two**	**one**	**two**	**one**	**two**	**one**
RMSD	76	67	86	79	93	93	86	86
P_0	71	71	83	79	95	95	86	86
$ADC_\perp$	67	62	55	50	86	86	79	76
MTCSF	86	76	95	81	90	43	95	93
MTR	86	52	79	57	88	43	88	57

Fig 2: ROI Analysis in Dorsal Column



Conclusion: q-space DWI can be used to study diffusion in the human spinal cord *in vivo* and compared to conventional DWI analysis, exhibited improved detection of abnormal diffusion. This method should be particularly sensitive to the loss of axonal and myelin barriers, and combined with MT, may be useful in quantitatively assessing WM damage in MS lesions.

References: [1] Cory D., Garroway A., MRM, 1990, 14:435; [2] Cohen Y., Assaf Y., NMR Biomed, 2002, 15:516; [3] Farrell J. et al ISMRM 2007 #270 [4] Smith S. et al, MRM, 2005, 54:201. **Funding:** NIH/NCRR-P41RR15241; NMSS CA1029A2, TR-3760-A-3; NIH AG20012; Nancy Davis Center without Walls.