q-space Diffusion Weighted MRI of the Human Spinal Cord *in vivo*: Application to Multiple Sclerosis

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Introduction:

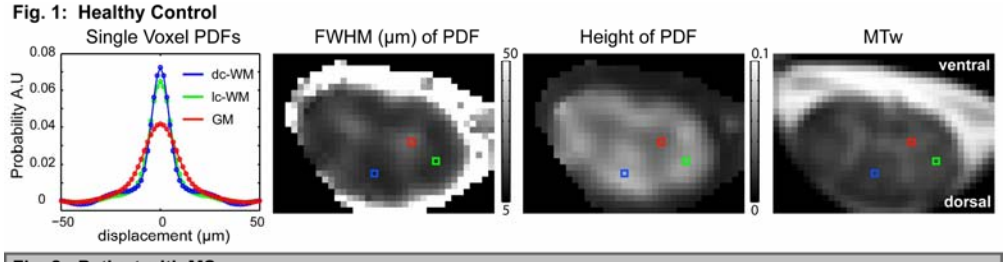
Diffusion weighted magnetic resonance imaging (DW-MRI) is sensitive to the molecular displacements of water and can be used to study tissue microstructure. In the central nervous system, axonal membranes and the myelin sheath present barriers to water diffusion and DW-MRI has been used to study white matter (WM) degeneration (e.g. in multiple sclerosis, MS). DW-MRI data is often analyzed with a diffusion tensor model, which assumes underlying Gaussian diffusion. However, DW-MRI can be performed and analyzed with the q-space technique which relies on the Fourier relationship between the measured signal attenuation and the loss of phase coherence due to spin displacement [1,2]. The key principle is that a Fourier transform (FT) provides a probability density function (PDF) for molecular diffusion, which may be non-Gaussian. Previously, q-space DW-MRI has been used to study myelin development and WM damage in the murine spinal cord [3] and MS in the human brain [3]. Here we show that q-space DW-MRI can be successfully applied to study diffusion in the human spinal cord *in vivo*. We investigate diffusion perpendicular to the spinal cord axis, which should be particularly sensitive to the breakdown of axonal and myelin barriers due to WM damage, and show preliminary results from a healthy male volunteer and a male patient diagnosed with relapsing-remitting MS.

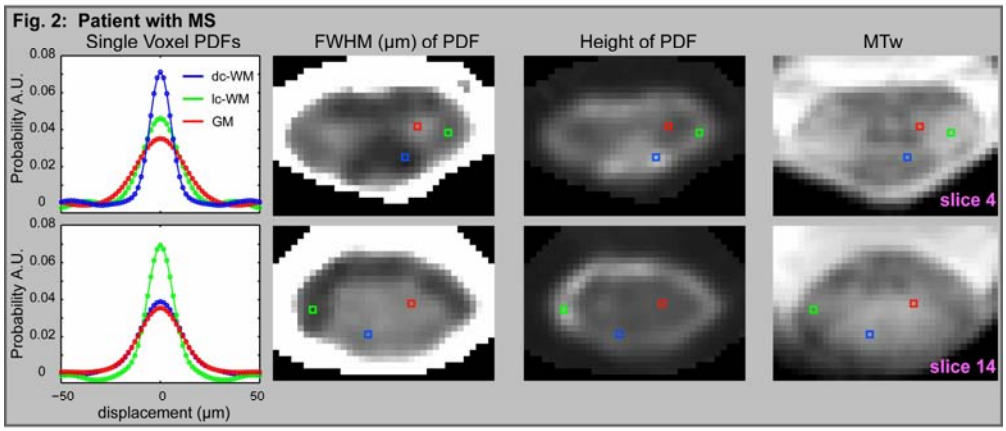
Subjects and Methods:

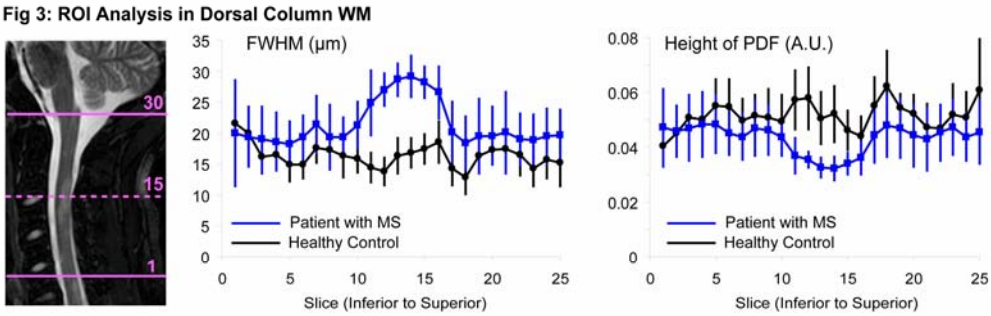
Subjects participated in this study after written informed consent. A 3T Philips MR scanner was used with body-coil excitation and a 2 element surface coil placed bi-laterally around the neck for reception. DW-MRI data was acquired using multi-slice, single-shot spin echo EPI, (SENSE = 1.8, TR/TE = 7000/112 ms) with second order shimming. Thirty axial slices were acquired perpendicular to the axis of the spinal cord covering C1 to C6 (nominal resolution = 1.3 x 1.3 x 3.0 mm). Diffusion weighting was applied perpendicular to the axis of the spinal cord. The length (δ = 16ms) and leading edge spacing (Δ = 74.5ms) of the gradients were kept constant (diffusion time = $\Delta - \delta/3 \approx$ 69ms), while the strength (G) was linearly increased to achieve 31 q-values from 0 to 410 cm^{-1} ($q = \gamma\delta G/2\pi$, maximum b-value = 4685 s/mm^2, G_{max} = 62 mT/m). To improve SNR and mitigate the effect of background gradients, separate data series were collected with diffusion weighting along [x,y,0] and [x,-y,0] and averaged after motion correction. Total acquisition time = 10 min. To reduce truncation and ringing artifacts in the calculated FT, a bi-exponential was fit to the acquired signal decay to extrapolate the signal attenuation to 2% which was then zero-padded to q = 6150 cm^{-1}. A FT of the concatenated data series (acquired, extrapolated and zero padded data) gave the PDF for each voxel. A magnetization transfer weighted (MTw) gradient-echo dataset [4] was also acquired for anatomical reference. The MTw images are sensitive to macromolecular content.

Results and Discussion:

PDFs for voxels in dorsal and lateral column white matter (dc-WM, lc-WM), and gray matter (GM) are shown and the location given on adjacent images. The FWHM of the PDF reflects the amount of diffusion perpendicular to the cord's long axis while the PDF height is the probability of no net molecular displacement. **Fig.1** In the healthy control, PDFs in dc-WM and lc-WM are similar, and distinct from the GM PDF. This agrees with expectations as WM contains myelinated axons which confine diffusion perpendicular to the cord (resulting in narrow and tall PDFs), whereas diffusion in GM is less restricted (resulting in broad and short PDFs). The GM horns and surrounding WM can be visualized in the FWHM and PDF height maps, and agrees favorably with the anatomy shown in the MTw image. **Fig.2** Results for the patient with MS are shown at two slice levels (slices 4 and 14 show lc-WM and dc-WM involvement, respectively). The shapes of the PDFs in diseased and normal appearing WM are different, with the diseased WM PDF resembling the GM PDF. This result might be explained by the loss of axonal and/or myelin barriers to diffusion in the MS lesion. Good agreement is seen between an increase of the FWHM, decrease of the PDF height and the location of the hyper-intense MS lesion shown on the MTw image. **Fig.3** The mean value and the standard deviation (error bars) over the voxels in the selected ROI in the dc-WM were computed and plotted as a function of the slice level for the control and patient. Slices 10 through 18 show a marked increase of the FWHM and decrease of the height of the PDF relative to the control. The sagittal short tau inversion recovery (STIR) image (left) is a guide to locate the hyper-intensities indicative of MS lesions.







Conclusion:

We show that q-space DW-MRI can be used to study diffusion in the human spinal cord *in vivo*. This method, which does not rely on a Gaussian assumption, can investigate diffusion perpendicular to the cord axis which should be particularly sensitive to the breakdown of axonal and myelin barriers. Preliminary results suggest that q-space DW-MRI could potentially differentiate the microstructural changes due to WM damage in the human spinal cord.

References: [1] Cory, D.G., Garroway, A.N., MRM, 1990, 14: p435; [2] Le Bihan D., NMR Biomed, 1995, 8(7-8) p375. [3] Cohen, Y., Assaf Y, NMR Biomed, 2002, 15:516 [4] Smith, S.A. et al, MRM, 2005, 54:201.

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