Exploring the Information Content of q-Space Diffusion Weighted Imaging: Application to Multiple Sclerosis (MS) Spinal Cord Lesions

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Introduction: In the CNS, axonal and myelin membranes present barriers to water diffusion and diffusion weighted imaging (DWI) has been used to study changes in these tissue microstructures resulting from white matter (WM) disease/damage. Q-space imaging is an emerging analysis technique for DWI data which quantitatively determines the probability density function for molecular diffusion (i.e. the probability that a spin diffuses a particular distance from its initial position). Recently, q-space DWI has been applied to study multiple sclerosis (MS) in the human brain [1] and spinal cord [2]. Using a new, robust analysis method, we describe q-space DWI in a healthy control and two MS patients. The key principle of this new method is an explicit accounting for the noise properties in the diffusion weighted images that constitute a q-space DWI dataset. We present a compact and intuitive visual representation of the information obtained with the PDF, and discuss how robust estimation of the PDF may aid the assessment of diffusion properties in lesions.

Methods: One healthy volunteer and two patients with MS were imaged on a 3T Philips MR scanner with body coil transmission and 2 element phased array surface coil for reception. Thirty axial slices were acquired perpendicular to the long axis of the spinal cord covering C2 to C6 (1.3x1.3x3.0 mm, FOV=62x62x90 mm, matrix=48x48, 32 linearly spaced q-values from 0 to 414 cm^{-1}) with single-shot EPI (SENSE = 1.8, TR/TE = 7000/112 ms). To improve SNR, each DW image was collected with diffusion weighting along two orthogonal directions ($[G_x, G_y, G_z]$ = [1,1,0] and [1,-1,0]) with a total acquisition time of ~10 min. Structural images were acquired for lesion identification (Spin Density/T2*w 3D-GRE with multi-shot EPI (x3), SENSE = 2). Q-space Estimation by Maximizing Rician Likelihood (QEMRL) was used to robustly estimate the diffusion probability density function (PDF) for each voxel, while explicitly accounting for Rician noise [3]. Briefly, PDFs were parameterized by a non-negative mixture of Gaussian distributions spanning a physically realistic range of diffusivities ($3x10^{-5}$ to $3x10^{-3}$ mm^2/s) and estimation was performed with an M-estimator (an estimator of the maximum likelihood type).

Results and Discussion: A structural image, together with images of the several PDF properties (height, P0, full width at half maximum, FWHM, and root mean square displacement, RSMD) are shown at the level of C4. PDF profiles are also shown for voxels along the paths indicated by arrows. Results for a representative slice for the healthy control (**Fig. 1A**) show that PDFs in WM are tall and narrow, whereas PDFs in gray matter (GM) are low and broad. Variability in PDF shape can be appreciated as a function of tissue type in the control (lateral and dorsal columns are indicated). Results are also shown for two MS patients with lesions in the lateral (**Fig. 1B**) and dorsal columns (**Fig 1C**), respectively (hyperintense on the T2*w GRE). MS lesions show abnormal height and shape of PDFs, however, quantitative analysis of the PDFs is complicated by the high dimensionality. To address this complexity, the PDF shape is often summarized by the P0 and FWHM properties, however, this fails to describe the extent to which the observed PDF is truly non-Gaussian. Analysis of the RMSD captures information relating to the heavy tails which, in the case non-Gaussian diffusion, is not equivalent to simply a scaled FWHM.

P0, FWHM, and RMSD may be fused into a multi-spectral image (red corresponds to P0, green to FWHM, and blue to RMSD). The multi-spectral images are not scalar images displayed with a color map; rather, these images contain different information in each color channel much like the color maps used in diffusion tensor imaging. P0 is most sensitive to strongly peaked PDFs which are indicative of highly restricted diffusion environments, such as in WM. FWHM tends to measure the width of the primary lobe, so a high FWHM indicates a weakly restricted diffusion environment. RMSD is also sensitive to weakly restricted environments, but places more emphasis on the tails of the distribution. In the multi-spectral images for the control, WM columns are primarily red/magenta, indicating peaked PDFs with narrow FWHM and RMSD. The central areas of the GM horns are green/teal, indicating a high FWHM, but a low RMSD. The dorso-lateral GM horns demonstrate a purple or light blue color, which indicate both a high FWHM and high RMSD. The purple hue appears to point out the transition between the dorsal and lateral columns in the control. These features may also be used to observe the regional extent of the MS lesions. The large lateral column lesions reduce P0 and increase FWHM (a decrease in the purple color) near the lesion boundaries. The dorsal column lesion reduced the P0 and increased RMSD and leads to an inability to discriminate the surrounding dorsal horn GM as indicated by high FWHM and RMSD.

Conclusions: The PDF for water diffusion can be measured *in vivo* in the spinal cord, and is sensitive to tissue damage caused by MS. These PDFs contain a wealth of information (beyond the typically reported P0 and FWHM) and reveal interesting and subtle properties of the biophysical diffusion restriction environment. There is visual and quantitative heterogeneity in the spinal cord, which may be indicative of substructure within WM and GM. Further histological and theoretical validation will be necessary to determine if it is possible to attribute specific observations of PDFs to intravoxel compartments (i.e., substructural differences) or to partial volume effects (i.e., mixtures of WM and GM within voxels at a macro scale).

References: [1] Cohen Y., Assaf Y., NMR in Biomed, 2002, 15:516 [2] Farrell J. et al ISMRM 2007 #270 [3] Landman et al., submitted to ISMRM 2008

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Fig. 1. Visualization of MS Lesion Involvement in q-Space Diffusion Imaging with Robust PDF Estimation