Evaluation of the Physiological State of White Matter by High b Value q-Space Analyzed Diffusion Weighted Imaging: Applications to Multiple Sclerosis

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Introduction

The signal decay in diffusion experiments at high b values was shown to be multi-exponential. The slow diffusing component, apparent only at high b values (>4000 s/mm^2) was shown to be sensitive to the physiological state of neuronal tissue (1-2). This sensitivity originates from the higher specifity of the signal at high b value to the axonal compartment. The diagnostic ability of high b value diffusion imaging was demonstrated on animal models of demyelination and neuronal maturation (1-2).

The multi-exponential signal decay can be characterized and analyzed using the q-space approach (1-3). The q-space approach enables the extraction of structural information of the sample. Using the q-space analysis the displacement probability profile of the water molecules can be extracted by Fourier transformation of the signal decay with respect to the q value (defined as $\gamma\delta g/2\pi$). This relation holds under the long time scale limit (long diffusion time relative to the cell dimensions) and the short gradient pulse approximation (3-4).

The application of this method for the human brain is difficult since the gradient system of clinical scanners has much lower amplitude than animal scanners. This implies that long gradient pulses (that violate the short gradient pulse approximation) should be used (4). Here we performed high b value q-space diffusion imaging on the brains of healthy subjects and multiple sclerosis (MS) patients.

Methods

MRI was performed on a 1.5T GE Signa MRI scanner. 13 MS patients and 6 healthy subjects were examined. The q-space images were obtained from a series of 16 diffusion experiments reaching a b value of 14,000 s/mm^2 performed in 6 gradient directions (xy,xz,yz,-xy,-xz and y-z). The q-space diffusion experiment were performed with the following parameters: TR/TE=1500/167ms, Δ/δ=72/65ms, effective maximal gradient strength of 3.1 gauss/cm and matrix of 128x128. The displacement and probability images were analyzed as described before (1-2) for each diffusion direction. Tensor analysis, similar to that used in DTI (5) was used to obtain the smallest displacement images and the largest probability images which should represent the displacement probability profile normal to the long axis of the neuronal fibers. In addition to the q-space data set conventional FLAIR (TR/TE=5000/80ms), T1-IR (TR/TE/TI= 1500/9/700ms) and DTI (TR/TE/Δ/δ=1500/90/31/25ms) images were acquired (b_{max}=1,000 s/mm^2).

Results and Discussion

MS lesions are usually detected by T_2, FLAIR, T_1 and proton density (PD) MR images. It was shown that in the normal appearing white matter (NAWM) of MS patients, MRS detects abnormal metabolite distributions. This implies that the high-resolution MRI methods do not identify key abnormalities in MS brains. Diffusion tensor imaging (DTI) enables the detection of pathologies in the NAWM but only on large statistical data sets (6). We found that the q-space analyzed images provided clear discrimination between healthy and MS diseased brains both in areas of MS lesions and in areas of NAWM. Figure 1 shows q-space displacement and FLAIR images of a control (Figs. 1A and 1B, respectively) and severely diseased MS brains (Figs. 1C and 1D, respectively). The displacement in areas of MS lesions is increased as compared to the control (Figs 1A and 1C). In areas of NAWM in the MS brains (Fig 1D), the displacement in the q-space image is also increased, although this increase is smaller than in the lesion (Fig 1C). Table 1 shows region of interest (ROI) analysis performed on specified areas that include the white matter in these cases. The ROIs were divided into two sub-groups: MS lesion and NAWM areas as detected by the FLAIR images. The data from the MS group was compared to the same regions in the control group and the data is summarized in Table 1. The displacement in the areas of MS lesions was much higher than in the same areas in the control subjects. As expected, the probability showed the opposite trend. In these areas DTI also showed significant reduction in the fractional anisotropy (FA). In areas of NAWM in MS patients, the q-space images showed a significant increase in the displacement and a significant decrease in the probability. The FA value of the NAWM was similar to that of the controls (Table 1).

The increased ability of the q-space imaging to diagnose neuronal degeneration was previously demonstrated on isolated neuronal tissues in which the experimental conditions were adequate for q-space analysis (1-2). Here we show that even when violating the q-space conditions, this analysis of the signal decay at high b values has an increased diagnostic ability towards myelin associated disorders such as MS. This seems to be surprising, however, it was predicted theoretically (4) and we could show experimentally that the use of long gradient pulses emphasize the restricted component thus increasing the sequence sensitivity towards the physiological state of the white matter. Therefore, any disruption of the myelin of the axon which serves as barrier to water diffusion will be reflected as loss of the slow diffusing component.

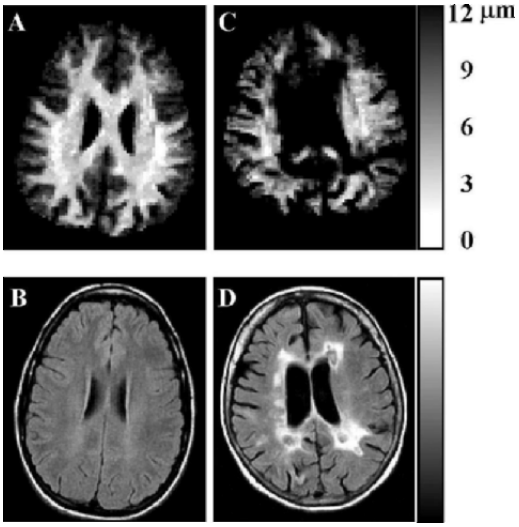

Figure 1

Conclusion

Diffusion at high b values on clinical scanner was shown to be useful for characterization of the diffuse pathologies associated with MS. q-Space analysis of such data enables to quantify the slow diffusing component although without giving the real displacement values. It seems that the combination of long TE, long diffusion time and long diffusion gradient duration produces signal decay that is highly sensitive to the physiological state of neuronal tissue thus enhancing its diagnostic value.

References

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Table 1

	Probability (a.u.)	Displacement (μm)	FA
Control	8.3±0.7	3.3±0.8	0.54±0.15
NAWM	7.5±1.0 p<0.00001	4.0±1.3 p<0.00001	0.54±0.34 n.s.
Lesion	5.0±0.9 p<0.00001	8.1±2.4 p<0.00001	0.39±0.11 p<0.00001