Magnetic Resonance Imaging 32 (2014) 625–629

Contents lists available at ScienceDirect

Magnetic Resonance Imaging

journal homepage: www.mrijournal.com

Multiple sclerosis: Benefits of q-space imaging in evaluation of normal-appearing and periplaque white matter

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ARTICLE INFO

Article history:
Received 6 July 2013
Revised 12 February 2014
Accepted 14 February 2014

Keywords:
Multiple sclerosis
Diffusion tensor imaging
q-space imaging
Root mean square displacement
Periplaque white matter
Normal-appearing white matter

ABSTRACT

Introduction: Diffusion tensor imaging (DTI) reveals white matter pathology in patients with multiple sclerosis (MS). A recent non-Gaussian diffusion imaging technique, q-space imaging (QSI), may provide several advantages over conventional MRI techniques in regard to in vivo evaluation of the disease process in patients with MS. The purpose of this study is to investigate the use of root mean square displacement (RMSD) derived from QSI data to characterize plaques, periplaque white matter (PWM), and normal-appearing white matter (NAWM) in patients with MS.

Methods: We generated apparent diffusion coefficient (ADC) and fractional anisotropy (FA) maps by using conventional DTI data from 21 MS patients; we generated RMSD maps by using QSI data from these patients. We used the Steel–Dwass test to compare the diffusion metrics of regions of interest in plaques, PWM, and NAWM.

Results: ADC differed ($P < 0.05$) between plaques and PWM and between plaques and NAWM. FA differed ($P < 0.05$) between plaques and NAWM. RMSD differed ($P < 0.05$) between plaques and PWM, plaques and NAWM, and PWM and NAWM.

Conclusion: RMSD values from QSI may reflect microstructural changes and white-matter damage in patients with MS with higher sensitivity than do conventional ADC and FA values.

1. Introduction

Several imaging techniques are potentially useful for elucidating the disease process in patients with multiple sclerosis (MS). In addition to conventional MRI techniques (including T2-weighted imaging), quantitative brain MRI techniques such as diffusion-weighted imaging (DWI) and its derivative technique, diffusion tensor imaging (DTI), enable MS lesions to be characterized in vivo according to quantitative values, such as fractional anisotropy (FA) and the apparent diffusion coefficient (ADC). In addition, DWI and DTI offer advantages over conventional techniques in their ability to detect otherwise hidden abnormalities in normal-appearing white matter (NAWM) [1–5]. Moreover, DTI has been reported to reveal differences in white matter abnormality between the white matter at the periphery of plaques and distant NAWM [1].

Non-Gaussian diffusion MRI techniques, including q-space imaging (QSI) analysis [6–8] and diffusional kurtosis imaging (DKI) [9], have emerged recently. Unlike DWI and DTI, QSI and DKI do not require the assumption of a Gaussian shape when modeling the distribution of free water molecules. QSI and DKI have yielded promising results in the evaluation of brain [10–13] and spinal cord [14–18] disorders in vivo because they provide diffusion metrics, such as the root mean square displacement (RMSD), that are additional to, and different from, those of Gaussian techniques. In addition, DKI has demonstrated its usefulness in characterizing the disease process in patients with MS [6,19,20]. In particular, RMSD values obtained from QSI data reflect the full extent of water molecule movement and provide more accurate

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http://dx.doi.org/10.1016/j.mri.2014.02.024

microstructural information than do ADC and FA values [8,21]. We therefore hypothesized that RMSD values derived from QSI analysis would provide more information on in vivo structural and pathologic changes in the brains of patients with MS, and at higher sensitivity, than do conventional DTI metrics.

Our aim here was to investigate the use of RMSD derived from QSI data to characterize plaques, periplaque white matter (PWM), and NAWM in patients with MS.

2. Materials and methods

2.1. Patients

Between December 2011 and August 2012, we evaluated a total of 21 consecutive patients with relapsing–remitting ($n = 20$) or secondary progressive ($n = 1$) MS (6 male; 15 female; age [mean ± 1 SD], 44.3 ± 10.06 years; median [range] Expanded Disability Status Scale score [22], 2.0 [0.0–6.0]) who had a previously established diagnosis of MS according to 2005 revisions to the McDonald Criteria [23] without acute plaques. Informed consent was obtained from each patient. We obtained ethics approval from the institutional review board before the study.

2.2. Image acquisition

All images were acquired on a 3-T scanner (Achieva, Philips Medical Systems, Best, The Netherlands). After routine MRI comprising turbo spin-echo T2-weighted and fluid-attenuated inversion-recovery axial imaging, we acquired T1-weighted, sagittal 3D magnetization-prepared rapid-acquisition gradient-echo and QSI data. Imaging parameters for conventional axial images were: repetition time (ms)/echo time (ms): 4000/100 for T2-weighted imaging, 10000/100 for fluid-attenuated inversion-recovery axial imaging; number of signals acquired, two; section thickness/gap, 5/1 mm; 22 sections; and pixel size, 0.45 × 0.45 mm. Imaging parameters for magnetization-prepared rapid-acquisition gradient-echo imaging were: repetition time (ms)/echo time (ms), 15/3.5; number of signals acquired, one; section thickness/gap, 0.86/0 mm; 170 sections; and pixel size, 0.81 × 0.81 mm. Parameters used for QSI were: repetition time (ms)/echo time (ms), 4000/96; number of signals acquired, one; section thickness/gap, 4/0 mm; 10 sections; field of view, 256 × 256 mm; matrix, 64 × 64; imaging time, 4 min 36 s; and 12 *b*-values (0, 124, 496, 1116, 1983, 3099, 4463, 6074, 7934, 10041, 12397 and 15000 s/mm^2), with diffusion encoding in 6 directions for every *b*-value. The q-value was linearly incremented from 0 to 104.64 cm^{-1} [16,19,24]. The gradient length (δ) and time between the two leading edges of the diffusion gradient (Δ) were 37.8 and 47.3 ms, respectively. QSI was limited to large, semioval areas of white matter to minimize the scanning time to that appropriate for clinical use.

2.3. Analysis of DTI and QSI data

After we corrected for distortions due to eddy currents using an affine registration on the magnetic resonance imager, diffusion tensor and q-space analyses were performed with dTV II FZR and Volume-One 1.81 software (Image Computing and Analysis Laboratory, Department of Radiology, The University of Tokyo Hospital, Tokyo, Japan) [8] on a stand-alone personal computer running Windows (Microsoft, Redmond, WA, USA).

ADC and FA were calculated pixel-by-pixel according to the conventional mono-exponential model from part of the q-space data, *b*-values of 0 and 1116 s/mm^2, because these data included multiple *b*-value data. Next, the full width at half maximum (FWHM) of the probability density function (PDF) was calculated as previously described [8,24]. Briefly, the key principle in q-space analysis is that a Fourier transform of the signal attenuation with regard to q provides the PDF for diffusion by using multiple q-values [17]. The shape of the computed PDF can be characterized by the FWHM and the maximum height of the curve. In the condition of unrestricted Gaussian diffusion, the diffusion constant D and the RMSD for one-dimensional diffusion can be computed from the FWHM. Mean RMSD was calculated from the FWHM values (RMSD = 0.425 × FWHM) [16,17].

By referring to conventional MR images, two experienced neuroradiologists (M.Y. and M.H.) manually placed ovoid region of interests (ROIs) on b = 0 QSI data by using dTV II FZR and Volume-One 1.81 software (Image Computing and Analysis Laboratory, Department of Radiology, The University of Tokyo Hospital). ROIs were drawn in plaques (defined as areas of abnormally high signal intensity on the b = 0 q-space image), periplaque white matter (PWM; defined as a white-matter area that had normal signal intensity and was closest to a plaque), and NAWM (defined as an area of WM with normal signal intensity that was contralateral to a plaque; Fig. 1) [1]. The dTV II FZR software allowed for copying of the ROIs and guaranteed the evaluation of the same region with diffusion metric maps. The average FA, ADC, and FWHM values in each ROI were measured; areas with severe signal loss or calculation errors were excluded from analysis.

2.4. Statistical analysis

The three areas (plaques, PWM, and NAWM) were compared according to the Steel–Dwass test for multiple comparisons by using the statistical software package R (Version 2.8.1). A *P* value of less than 0.05 was considered to indicate a statistically significant difference. Interrater reliability was assessed by using Pearson's correlation coefficient.

3. Results

Data from all 22 patients were included in the evaluation, without fatal image degeneration or artifacts. Fig. 2 shows representative b = 0 DTI image (echo-planar T2-weighted image), FA, and ADC maps generated by using conventional DTI data, and an RMSD map created from QSI data. All plaques yielded low values on FA maps and high values on both RMSD and ADC maps.

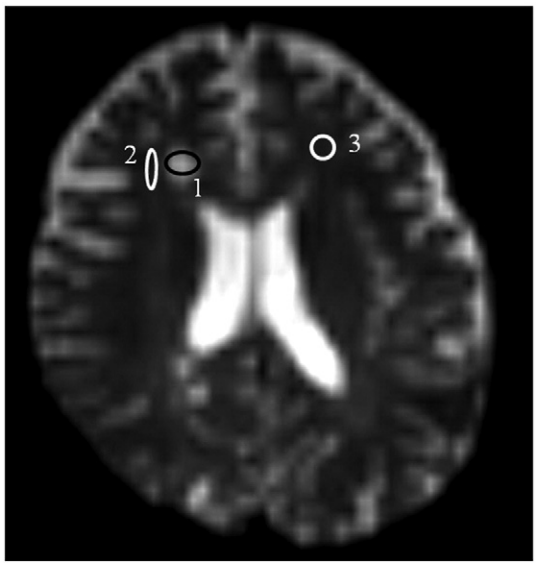

Fig. 1. ROIs manually placed in the plaque (region 1), PWM (region 2), and NAWM (region 3) on a b = 0 diffusion-weighted image of a patient with MS.