Multi-parametric MR assessment of T1 black holes in multiple sclerosis: Evidence that extracellular water is increased but myelin loss is not greater

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Introduction

Although conventional magnetic resonance imaging (MRI) has become an indispensable tool for visualising lesions and diagnosing multiple sclerosis (MS), it lacks pathological specificity. While lesions are easily identifiable on T_2/proton-density weighted images, the correlation between lesion load and disability is quite low [1]. The correlation between a subset of lesions that appear hypointense on T_1-weighted images with disability however is much better [2,3]. Histopathological studies from biopsy [4] and post-mortem [5,6] have shown these hypointense T_1 lesions or chronic black holes to represent areas of more permanent tissue destruction with severe axonal loss and increased extracellular water. The purpose of this study was to compare the total water content (WC), myelin water content (MWC), magnetization transfer ratio (MTR), T_1 relaxation time (T_1) and T_2 relaxation time (T_2) between MS lesions that are hypointense and those that are isointense on T_1-weighted images.

Methods

MRI procedures: Six clinically definite MS patients (4 female, 2 male, 5 relapsing-remitting/1 primary progressive, median EDSS 3.0 (range 2.0-6.5), mean age 40 years (range 30-50 years), disease duration range 3.5-11 years) were scanned on a GE Signa 1.5 T MR scanner 5 times over one year (month 0, 2, 4, 6, 12). MR studies performed included localizers, 22 slice axial proton density (PD) and T_2 images (TR 2500ms, TE 30/90ms), a single-slice axial 32-echo CPMG T_2 relaxation sequence [3] (TE 10ms, TR 3000ms, 4 averages, matrix 256x128) for the T_2 measurement, a single-slice axial fast gradient echo (GE) with inversion recovery preparation (TE 8ms, 1 average, 15 TIs from 0.05-3s) for the T_1 measurement and a 3D-GE with and without a 2000 Hz off-resonance sinc saturation pulse MT sequence (TR 106ms, TE 5ms, flip 12^{O}) and a post Gadolinium-DTPA enhanced T_1-weighted spin echo scan (TR 550ms, TE 8ms) was collected. All exams used a field of view of 22cm, a 256x192 matrix and slice thickness of 5mm. Water standards were placed within the slice.

Data Analysis: All images were registered to the PD/T_2 scan at month 0. Regions of interest of hypointense and isointense T_1 lesions and contralateral normal appearing white matter (NAWM) were outlined on the PD images and mapped onto the registered T_2, T_1 and MT images. The T_1 relaxation data was fit to a single exponential. T_2 relaxation distributions were extracted from the 32-echo sequence using a regularised least-squares algorithm [8]. The total water content (WC) and myelin water content (MWC) were defined as the total area under the T_2 distribution and area from 0-40ms, respectively, normalised to the water standards and corrected for T_1 relaxation. Geometric mean T_2 (T_2) was calculated on a log scale between 40-200ms [9]. MTR was calculated by MTR = $(M_o - M_t)/M_o \times 100\%$ where M_o and M_t are images without and with the MT pulse, respectively. Statistical analysis was carried out using a two-tailed Student's t test with a p value of <0.05 considered significant.

Results

Mean MR parameters for NAWM, 35 isointense and 17 hypointense T_1 lesions are shown in Table 1. WC, T_1, T_2 and MTR were all significantly different between isointense and hypointense T_1 lesions, isointense T_1 lesions and NAWM, and hypointense T_1 lesions and NAWM; hypointense T_1 lesions had the highest WC, T_1 and T_2 and lowest MTR. While MWC was reduced in both hypointense and isointense T_1 lesions compared to NAWM (did not reach significance), it was not significantly different between them. A proton density image, a T_1-weighted Gd-DTPA image and a myelin map from one patient are shown in Figure 1.

Discussion

Hypointense T_1 lesions have been associated pathologically with areas of tissue destruction and axonal loss. In this study, although an increase in water is evident from the increased WC, T_1 and T_2 of both isointense and hypointense T_1 lesions, the MWC of the two groups was the same. One possible explanation is that demyelination occurs in both the isointense and hypointense lesions but the hypointense lesions are distinguished by greater axonal loss and increased extracellular water, as evident by the greater increase in WC, T_1 and T_2 and decrease in MTR.

Conclusions

Myelin water content is not decreased in hypointense T_1 lesions compared to isointense lesions although both lesion types have lower MWC than NAWM. Water content, T_1 and T_2 are all higher and MTR lower in hypointense lesions compared to isointense lesions.

Table 1: Mean (standard error) MR parameters for hypointense T_1 lesions, isointense T_1 lesions and NAWM

	MR parameters				
Region	WC (%)	MWC (%)	T_1 (s)	T_2 (ms)	MTR (%)
hypointense	86.0 (0.9)	3.6 (0.4)	1.03 (0.03)	122 (5)	24.0 (0.8)
isointense	80.0 (0.6)	3.7 (0.3)	0.87 (0.01)	99 (2)	27.1 (0.4)
cNAWM	75.8 (0.3)	4.5 (0.3)	0.81 (0.01)	86 (1)	30.4 (0.2)

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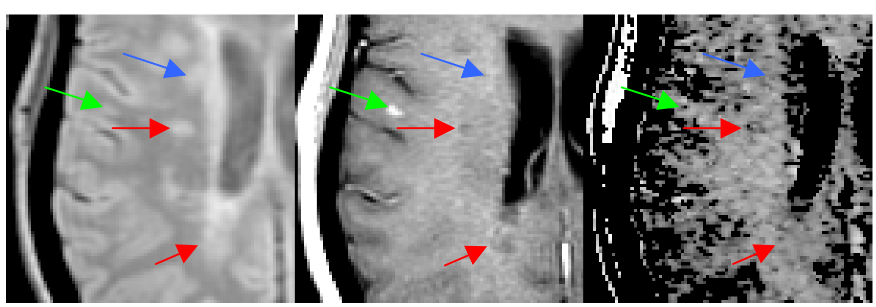

Figure 1: Proton density (left), T_1-weighted Gd-DTPA (centre) and myelin map (right) images of one patient. The red arrows show two hypointense T_1 lesions (black hole) with low myelin water. The blue arrow shows a T_1 isointense lesion with lower myelin water. The green arrow shows an active, gadolinium-enhancing lesion black hole with reduced myelin water.