Determining the age of multiple sclerosis lesions using myelin water imaging

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Introduction

Although conventional MRI has become an indispensable tool for visualising lesions and diagnosing multiple sclerosis (MS) [1], it lacks pathological specificity. On proton density (PD) images, lesions appear as bright areas regardless of their age or underlying pathology. Newer techniques show promise in being more specific to pathology, thereby aiding in the characterisation of lesions. T_2 relaxation in human brain can separate the water signal into three components: (1) a long T_2 component (>2s) attributed to CSF, (2) an intermediate T_2 component (~80ms) associated with intra- and extra-cellular water and (3) a short T_2 component (~20ms) assigned to water trapped between myelin bilayers (labelled myelin water) [2]. The purpose of this study was to discriminate between different MS lesion types and ages using water content (WC), myelin water content (MWC), T_1, geometric mean T_2 (GMT_2) and magnetization transfer ratio (MTR).

Methods

MRI procedures: A serial MRI study of seven clinically definite MS patients (4 female, 3 male, 5 relapsing-remitting/1 primary progressive/1 secondary progressive, median EDSS 3.0 (range 1.0-6.5), mean age 42 years (range 30-50 years), disease duration range 2-11 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 PD and T_2-weighted images (TR 2500ms, TE 30/90ms), a single-slice axial 32-echo T_2 relaxation sequence [2] (TR 3000ms, echo spacing 10ms, 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, 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). All exams used a field of view of 22cm and slice thickness of 5mm. Water standards were placed within the slice. Four lesion types were defined: (1) lesions less than 2 months old, (2) lesions between 6 months and 12 months old and stable lesions (which were at least 12 months old) divided into (3) T_1 isointense and (4) T_1 hypointense lesions.

Data Analysis: All images were registered to the PD/T_2 scan at baseline. Lesions and contralateral normal-appearing white matter (NAWM) regions 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 data using a regularised non-negative least-squares algorithm [3]. WC was defined as the total area under the T_2 distribution, and MWC as the area from 0-40ms (normalised to the water standards and corrected for T_1 relaxation). GMT_2 was calculated on a log scale between 40 and 200ms [3]. 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.

Discriminant function analysis: A stepwise discriminant function analysis (DFA) was carried out on the different lesion types using SPSS 12 (Chicago, IL). Wilks's lambda (λ) was used to select MR measurements. An F statistic was used to select the measurements to be entered or removed from the analysis such that only measurements which added significantly to the discriminant function were included. An F-function probability of 0.05 and 0.1 was used for entry and removal, respectively. The predictive value of the discriminant function was also calculated.

Results

The MR measurement range for each lesion type is shown in the figure. There were 20 lesions less than 2 months old, 23 lesions 6-12 months old and 30 stable lesions evenly divided between isointense and hypointense on T_1-weighted scans. No MR measurements were found which separated lesions less than 2 months old and lesions between 6 and 12 months old. Lesions less than 2 months old were separated from stable lesions (>12 months) using 1/WC and MWC. The lesions were successfully categorised 68% of the time with misclassification of 7/20 lesions less than 2 months old and 9/30 stable lesions. Lesions between 6 and 12 months old were separated from stable lesions only using MWC. The lesions were correctly classified 68% of the time with 9/23 6 to 12 month old lesions and 8/30 stable lesions being misclassified. Finally, stable isointense and hypointense T_1 lesions were separated best using MWC and MTR with only 1/14 lesions being misclassified in each category.

Discussion

MWC was the only parameter that was included in all the disciminant functions (except for separation of lesions less than 2 months old and lesions 6 to 12 months old where no function was found). 1/WC and MTR were also included in two of the cases. The interdependence of the four measurements excluding MWC meant that the choice of which measurement was included along with MWC was somewhat arbitrary.

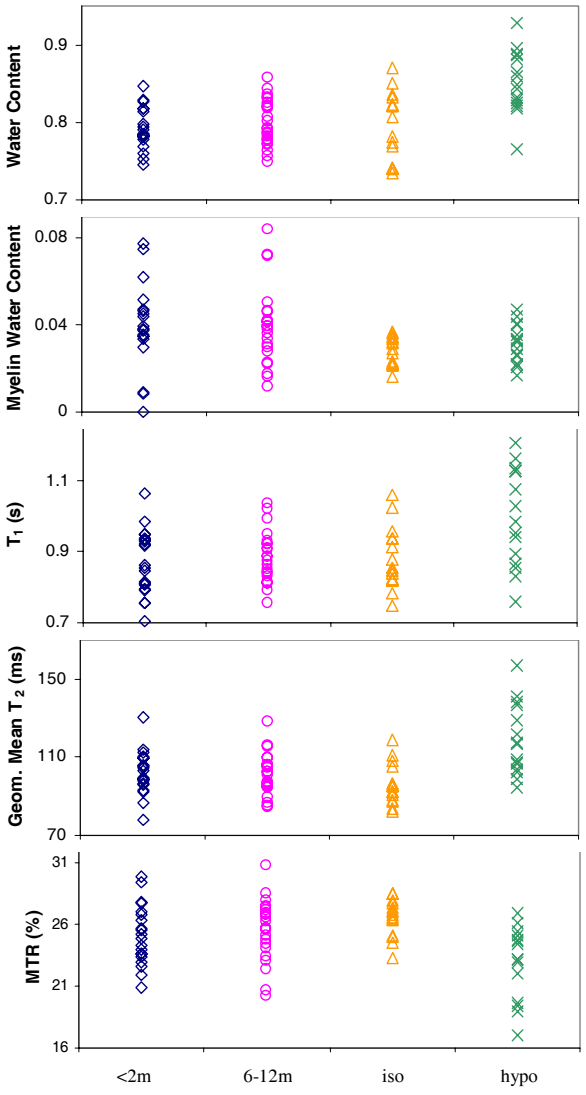
From the results, there appears to be a time dependence to demyelination in new lesions where lesions less than a year old have a wide range of MWC and therefore, on average, have only a slightly reduced MWC whereas stable lesions (which are at least a year old) have a more narrow range of MWC and have a greater average reduction in MWC.

Conclusions

Lesions less than a year old were found to have much greater MWC than lesions at least a year old indicating that MWC may be useful in determining the age of MS lesions.

1. McDonald MI et al. Ann Neurol. 1994;36:14-18.
2. MacKay AL et al. Magn Reson Med. 1994;31:673-677.
3. Whittall KP et al. J Magn Reson. 1989;84:64-71.

Acknowledgements: We would like to thank the MS society of Canada for financial support, the technologists at UBC hospital and the MS patient volunteers.



Plots of each MR measurements for the four lesion types: less than 2 months old (<2m), 6-12 months old (6-12m), stable isointense T_1 (iso) and stable hypointense T_1 (hypo).