Evolution of quantitative magnetization transfer imaging parameters in acute lesions of multiple sclerosis

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Introduction: Quantitative magnetization transfer imaging (QMTI) [1,2,3] allows mapping of the binary spin bath model parameters such as the restricted-to-liquid proton pool ratio (F), the forward magnetization transfer rate constant (k_f), as well as most of the relaxation parameters of both compartments of the model (R_{1f}, T_{2f}, T_{2r}). The relative size and T2 of the restricted pool have been shown to decrease in chronic multiple sclerosis (MS) lesions [4,5], but have yet to be studied in acute lesions. This study followed the evolution of QMTI parameters in acute lesions, after initial detection via gadolinium enhancement.

Methods: Magnetization transfer and relaxometry data were acquired in a single oblique 7-mm section in five patients with MS (gender/age at entry/number of exams: F/25/5, F/43/5, F/56/6, F/42/7, F/50/4) at monthly intervals up to 5 months post-enhancement, with a follow-up scan at 9 months, for a total of 27 datasets, using the QMTI protocol described in [1]. These patients were selected based on the presence of an active MS lesion as defined by gadolinium (Gd) enhancement. All data were acquired on a 1.5 T Sonata (Siemens Medical Systems, Erlangen, Germany). Slice positions were selected for each subject to intersect the acute lesion and the initial slice position was carefully reproduced for each subsequent exam. Data were analyzed on a voxel-by-voxel basis, including corrections for static and RF transmit field inhomogeneities, to produce parametric maps of the binary spin-bath model. The enhancing regions of the acute lesions were labeled on a high-resolution post-gadolinium T1W scan at the first time point. These labels were automatically propagated to subsequent time points using software developed at the MNI, resampled to the lower resolution of the QMTI scans, and thresholded to 80% purity to limit partial volume contamination by peri-lesional tissue. Control regions of normal-appearing white matter (NAWM) were defined contra-lateral to the lesions in homologous regions free of any visible pathology.

Results: Key model parameter values are plotted as a function of time post-enhancement in Figure 1, and the percent difference relative to NAWM is plotted in Figure 2. Parameter values were compared at each time point using a paired T-test, and significant differences between lesions and NAWM are indicated by an asterisk in Figure 1. All parameters, except T_{2r}, were significantly different in lesions (at a level of $p = 0.05$) at most time points, when compared to contra-lateral NAWM. T_{2r} was the only relatively stable parameter in lesions following enhancement, with a maximum change of -7.5%, and the change was only barely significant in lesions at months 3 and 5 ($p = 0.04$ and 0.047 respectively – data not shown). F, k_f and R_{1f} were substantially reduced in acute lesions and then followed a general recovery pattern after resolution of gadolinium enhancement, peaking around 2 months post-enhancement (3 months for k_f). T_{2f} was dramatically increased in acute lesions, and quickly decreased in the month following enhancement. None of the parameters returned to the NAWM value during the course of this study.

Discussion: This study reports quantitative MT parameters longitudinally in acute MS lesions following gadolinium enhancement. A significant decrease was observed in the ratio of restricted to free protons, along with an increase in the free pool relaxation times. Lesions presented with more heterogeneous parameter estimates compared to NAWM, likely reflecting pathological heterogeneity within lesions. Furthermore, the decrease observed in T_{2r} of acute lesions was barely significant and was smaller than that observed in chronic lesions [4], which may reflect less damage to the macromolecular component. The observed changes were greatest at the time of enhancement, consistent with acute demyelination and edema that resolve over two to three months; however, the degree to which the partial recovery observed here reflects remyelination or simply resolution of edema is uncertain. We suggest that the quick drop in T_{2f} between the first and the second month post-enhancement primarily reflects the resolution of inflammation, while the slower recovery in F and k_f reflects the combination of remyelination and further resolution of inflammation.

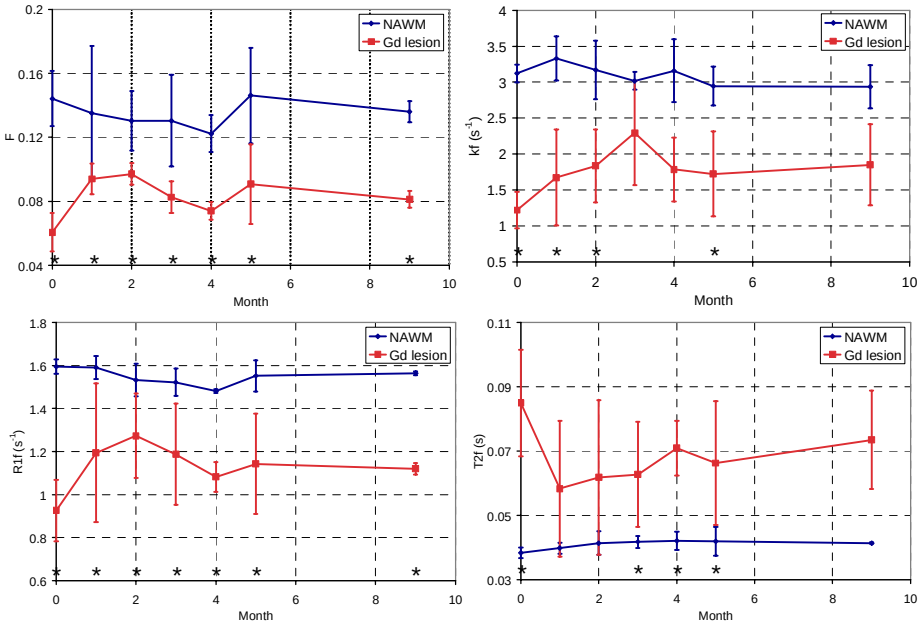

Figure 1. Parameter values (F, k_f, R_{1f}, and T_{2f}) for each month starting at initial Gd enhancement. Asterisks indicate significant differences ($p < 0.05$) at each month.

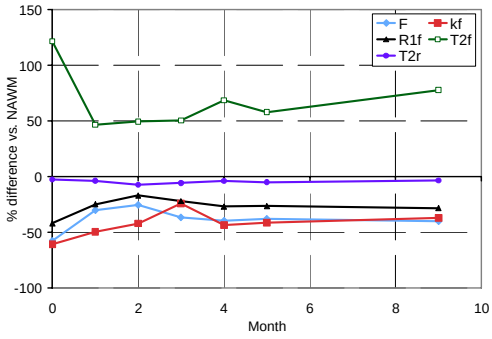

Figure 2. Percent change in each parameter relative to NAWM. Note the relative stability of T_{2r}.

References

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