Correlation of the Bound Proton and Myelin Water Fractions from Quantitative Magnetisation Transfer and Multi-Exponential T2 Analysis in Normal and Multiple Sclerosis Brain

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Introduction: Demyelination is an important element of white matter diseases such as multiple sclerosis (MS). Along with axonal loss it is thought to have a bearing on the disability status of a patient. Quantitative Magnetisation transfer (qMT) (1) and analysis of the various T_2 components in a tissue (2) are relatively new techniques for analysing the structure of brain tissue. qMT has been shown (3) to give estimates of the fundamental parameters involved in the MT phenomenon such as the T_2 and fraction, f_b, of the protons bound to macromolecules in brain tissues, including those attached to the myelin. In contrast the short T_2 component measured from multi-exponential analysis of T_2 decay curves and its corresponding fraction is believed to give a measure of the myelin content of a tissue by measuring the water trapped between the myelin bilayers. Histopathological evidence of demyelination has been shown to correlate with the myelin water fraction, f_m, seen in the T_2 analysis (4) and f_b has shown to be reduced in MS lesions where demyelination is known to occur (3). The aim of this work is to investigate any correlation of these parameters to determine whether the two fractions are differing methods of measuring demyelination or whether other processes such as the presence of bound protons in axons or glial cells mean that they give complementary information.

Methods: The qMT image sequence was a 2D spoiled gradient echo sequence was MT prepared using a Gaussian pulse of variable power and offset frequency. 28 5mm thick slices acquired in ~ 1.5 minutes per MT weighting, 10 MT weightings, TR/TE = 1140/12 ms, FA = 25°, reconstructed matrix size = 256x256, number of excitations = 0.75, FOV = 24x24 cm (3). T_1 maps were also acquired. Fitting was carried out to produce estimates of the qMT parameters, RM_0^A where R is the exchange rate between the two pools and M_0^A is the magnetisation of the free pool, gM_0^A where g is a scanner dependent scaling factor, T_{2B} the relaxation time of the bound pool $1/R_AT_{2A}$ the ratio of the relaxation times of the free pool and through $f_b/R_A(1-f_b)$ and the T_1 of the tissue f_b the bound proton fraction. In addition a single slice was chosen to be imaged using a 32 echo T_2 measurement sequence as described in (2). (TE_1=ΔTE=10 ms, TR=3 s, FOV=24x24 cm, slice thickness=5 mm, image matrix=256x128, NEX=4.) Fitting was carried out using the NNLS algorithm developed by Lawson and Hanson (5) to give T_2 values and tissue fractions for the myelin (T_{2m} and f_m), intra- and extra-cellular (T_{2e} and f_e) water components and CSF (T_{2c} and f_c). On 3 patients no T_1 maps were acquired so f_b could not be calculated. Parameter values were calculated from regions corresponding to the same tissue on both data sets in regions drawn in white matter and MS lesions (where seen) in 3 controls and 8 MS patients. For this preliminary study only lesions visible and identifiable on both the qMT and T_2 images were used, 12 regions were drawn in control WM, 28 in NAWM and 32 in lesions. The qMT and T_2 analysis parameters were then correlated, using the Pearson correlation coefficient, within the three tissue types and with all the regions pooled.

Results: The parameter values seen from both imaging techniques were in line with previously published results (2, 3). Selected p-values for correlations between the qMT parameters and f_m are shown in table 1. As can be seen f_b and f_m do not correlate for the three tissue types, but the p-value for the lesion group is only 0.29 (r=0.24) indicating a possible trend. When all the regions were pooled there were some significant correlations (table 1), f_b and f_m did correlate (r=0.58) indicating that the two parameters may be linked. There were also significant correlations seen between T_{2B} and f_m both for lesions (r=0.4) and for all regions pooled (r=0.45) and between $1/R_AT_{2A}$ and f_m for all regions pooled (r=0.38). Figures 1 and 2 show the scatter plots for f_m against f_b and T_{2B} respectively.

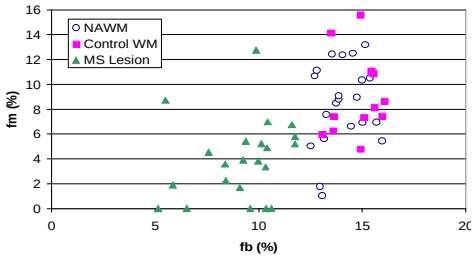

Figure 1: (left) The scatter plot showing the values for f_m against f_b for the three tissue types.
Figure 2: (right) Again a scatter plot, this time for f_m against T_{2B}.

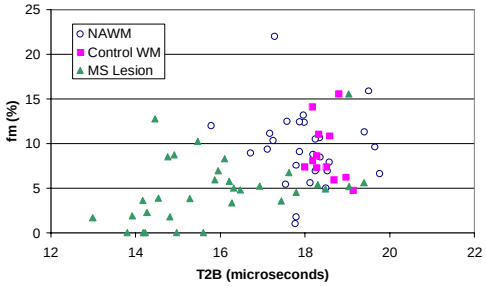

Table 1: Selected p-values for the correlation of qMT parameters with the myelin water fraction, f_m. Figures in bold represent correlation at the 0.05 significance level.

Parameter	Control WM	NAWM	MS Lesions	All regions
f_b	0.8	0.32	0.29	**<0.001**
$f_b/R_A(1-f_b)$	0.34	0.25	0.41	0.52
T_{2B}	0.47	0.62	**0.02**	**<0.001**
$1/R_AT_{2A}$	0.81	0.14	0.42	**0.001**

Conclusions: The wide range of f_m values seen is probably due to the variation seen in different WM structures, the WM regions were not all from the same location and analysis of this is one area of future work, despite this the correlation of f_b and f_m when all the regions are pooled indicates that both techniques, to some extent, measure the same process. In many ways this is not surprising as both T_2 and qMT analysis have shown a reduction in parameter values in MS lesions and so when compared with WM should show some correlation, however it does support the idea that both techniques measure, most likely, demyelination and therefore give, at least partially the same information, although as they do not measure the same fractions they may give some complimentary data. That the same result is not seen in the individual tissues could be a result of the small group sizes or that the measurements are not sensitive enough to pick up within tissue differences which would be smaller than those between tissues or the variations in WM mentioned above. The correlation between T_{2B} and f_m is also interesting; correlations have been seen between f_b and T_{2B} in WM in a qMT study (6) indicating that these parameters are linked and this result suggests a triangular relationship also exists. This work is in the preliminary stages and it must be noted that the group sizes are small. Other correlations seen in the work are much harder to explain than the relationship between f_b and f_m and may well be spurious; analysis of a larger sample size would be needed to confirm or refute them.

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