The Effect of Tissue Erosions and Segmentation Probability Thresholds on Magnetisation Transfer Ratio Histograms

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Introduction: The magnetisation transfer ratio (MTR) has become one of the most widely used quantitative MRI parameters in multiple sclerosis (MS) (1, 2). This is because the pathologies seen in MS such as inflammation and demyelination are those which can be demonstrated by changes in the MTR (3). In addition to abnormalities in focal white matter lesions much work has used histogram analysis of the normal appearing tissue to investigate the effect of the disease on the MTR (4). However, histogram generation involves arbitrary decisions such as the choice of a lower probability threshold for tissue classification in segmentation and whether to erode the final tissue segments to reduce partial volume effects. These can have a major effect on the histogram parameters extracted and may affect control and patient groups differently. This work investigates how the two issues mentioned effect MTR histogram parameters extracted from a group of multiple sclerosis patients and controls.

Methods: Fifteen subjects with relapsing remitting MS (RRMS) (13 female, average(±SD) age 31±8, average disease duration 15 months, average EDSS 2) and 15 healthy controls (7 female, average(±SD) 34±8) were scanned as part of a longitudinal study investigating MS disease progression. The subjects were scanned on a 1.5 T GE Signa scanner (GEMS, Milwaukee, WI, USA) with 28 contiguous 5 mm axial slices, a field of view of 24 cm and a matrix size of 256x256. Of interest a dual echo spin echo sequence was acquired with TR: 1720ms; TE: 30ms and 80ms. These were acquired with and without a sinc MT weighting pulse 2 kHz off resonance. The short echo data was used to calculate the MTR map. The T_2 weighted image (Long TE) was then used to mark the T_2 lesion load which was used to mask the lesions out of the MTR map.

The T_2 weighted images were then segmented into white matter (WM), grey matter (GM) and CSF using spm5 (www.fil.ion.ucl.ac.uk/spm/). The resulting probability maps were then converted into tissue segments using a variety of lower probability thresholds for tissue inclusion, these are: The most likely tissue regardless of the actual probability (NT), 50%, 70% and 90%. The WM and GM tissue segments for the various probability thresholds were eroded by 0, 1, 2, 3, and 4 pixels. The final tissue segments were applied to the MTR map and MTR histograms calculated with a bin width of 0.1 pu, they were normalised for total volume and smoothed with a moving average window of 0.7 pu.

The peak location (PL), peak height (PH) and histogram mean were extracted from each histogram and were plotted as a function of probability threshold and number of erosions. An initial statistical analysis was performed comparing the MTR parameters within the patient and control groups for each combination of probability threshold and number of erosions. This was done using the ANOVA to test for variation with number of erosions for a given probability threshold and vice versa.

Results: Tables 1 and 2 show the p-values for the ANOVA for the various comparisons.

	Cont WM	Pat WM	Cont GM	Pat GM
NTPH	**9.3×10^{-05}**	**0.004**	**2.2×10^{-05}**	**1.8×10^{-10}**
NTPL	0.054	0.636	**3.4×10^{-10}**	**0.003**
NT Mean	**2.1×10^{-11}**	**0.004**	0.078	**0.049**
50%PH	**0.0003**	**0.012**	**2.4×10^{-05}**	**8.4×10^{-11}**
50%PL	0.094	0.597	**2.2×10^{-09}**	**0.002**
50% Mean	**2.4×10^{-08}**	**0.035**	0.124	0.066
70%PH	**1.1×10^{-05}**	**0.007**	**4.0×10^{-06}**	**7.4×10^{-12}**
70%PL	0.413	0.504	**1.1×10^{-06}**	**0.0005**
70% Mean	**5.9×10^{-05}**	0.181	0.183	0.092
90%PH	**0.0001**	**7.4×10^{-09}**	**3.4×10^{-08}**	**0.010**
90%PL	**0.0006**	0.971	**4.9×10^{-07}**	**0.025**
90% Mean	**1.7×10^{-05}**	0.620	0.586	0.420

Table 1: The p-values associated with the ANOVA test. The number of erosions varies for the given probability threshold

	Cont WM	Pat WM	Cont GM	Pat GM
E0 PH	0.116	**0.007**	**0.021**	**1.4×10^{-06}**
E0 PL	0.052	0.143	**0.006**	0.078
E0 Mean	**1.9×10^{-08}**	**0.015**	0.103	0.534
E1 PH	0.506	0.164	**0.020**	**1.6×10^{-06}**
E1 PL	0.116	0.219	0.096	0.423
E1 Mean	**0.014**	0.368	0.470	0.861
E2 PH	0.213	0.076	**0.006**	**1.0×10^{-06}**
E2 PL	0.149	0.834	**0.036**	0.155
E2 Mean	0.071	0.515	0.837	0.991
E3 PH	**0.013**	**0.010**	**0.0008**	**1.1×10^{-09}**
E3 PL	0.163	0.540	0.097	0.097
E3 Mean	0.100	0.647	0.950	0.992
E4 PH	**0.001**	**8.3×10^{-08}**	**8.0×10^{-06}**	**0.017**
E4 PL	**0.0007**	0.284	0.453	0.080
E4 Mean	**0.003**	0.936	0.977	0.336

Table 2: The p-values associated with the ANOVA test. The probability threshold varies for a given number of erosions (Ex)

Inspection of the graphs of these parameters for individual subjects show a variety of patterns, however for the majority of both patients and controls the biggest change in any of the histogram parameters is between 0 and 1 erosions regardless of probability threshold. The PL and mean tend to be maximised after 2-3 erosions and then often drop with 4 erosions. The PH tends to increase with the number of erosions as would be expected. As far as changing the probability threshold is concerned the changes in the parameters are less consistent (as indicated by the reduced number of significant p-values seen in table 2), in particular this applies to the PL and mean. Once again the PH changes with the probability threshold regardless of the number of erosions. Despite the differences between the behaviour in the control and patients seen in the tables, this does not translate to any systematic difference in the behaviour of the individual subjects.

Conclusions: In general tables 1 and 2 show that the PL and mean are largely independent of the probability threshold used in the segmentation, whereas the PH is altered. This is understandable as the reduction in tissue with an increased threshold will change the normalised PH, however the PL is less likely to be altered as the outer partial volume voxels are unlikely to be those that are at the PL. However when the number of erosions is changed, for a given threshold, the effects on the PL and mean seem more widespread. There is some difference in the behaviour of patients and controls, but on the whole these differences do not appear to be systematic. These results indicate that the number of erosions performed on the tissue is more important than the probability threshold used for determining the MTR histogram parameters. Whether this is due to the removal of partial volume effects or inherent differences in the MTR in different areas of the brain is not clear.

Acknowledgements: This work and the NMR Research Unit was funded by the MS society of GB and NI

References: [1] Hiehle et al. MRM 1994;32:285-293 [2] van Buchem et al. MRM 1996:36;632-636 [3] Schmierer et al. MRM 2008;59:268-277 [4] Hayton et al. J. Neurol 2009;256:427-435