Quantitative Magnetisation Transfer Parameters show Dramatic Changes in Low Grade Gliomas

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Introduction: The purpose of this work is to assess the impact of qMT in low grade gliomas and compare the parameters obtained to those from normal appearing tissues. Gliomas are primary brain tumours that can exist for many years in a low grade state (WHO grade II), before they transform into grade III and IV tumours which cause rapid deterioration and death. Study of gliomas with MRI is of interest with regard to predicting the time course of the tumour and non-invasive histopathological determination of grade and sub-type. Quantitative analysis of magnetisation transfer imaging (qMT) is a recent development of MT techniques, which allows a fuller analysis of the MT phenomenon, including the estimation of more fundamental parameters such as the fraction of protons existing in macromolecules such as myelin (1-3). This parameter has been shown to be altered in multiple sclerosis lesions and white matter (2) and the white matter of Alzheimer's sufferers (4). A single glioma was imaged (5) using a variation of the technique. A lower bound proton fraction and a reduced cross relaxation rate between the free and bound pools of protons compared to white matter were found.

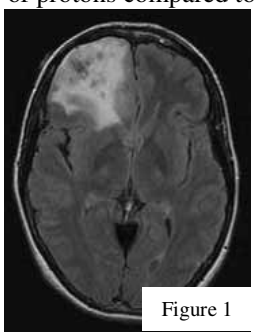

Figure 1

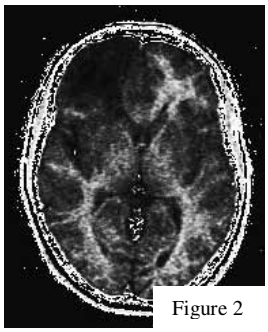

Figure 2

Methods: Six patients (5 female) (mean age(±SD) 44±17 years, range 27-66), were scanned using a 1.5 T scanner (GE, Milwaukee, WI, USA). The patients gave written informed consent and the study was passed by the local ethics committee. Four sequences were then acquired, all were reconstructed to 28 5 mm slices with a field of view of 24x24 cm^2 and a matrix of 256x256 a) qMT images using the 3D sequence described in (6), fast SPGR, TR/TE=30.7/5.3 ms, excitation flip angle=5°, acquisition matrix 256x96x32, acquisition field of view 24x18x16 cm^3. MT saturation was achieved using a Gaussian pulse (standard deviation=2.83 ms, duration=14.6 ms), applied once every TR prior to RF excitation. Ten uniquely MT weighted datasets were collected using two MT pulse amplitudes (described by their equivalent on-resonance flip angles: 212° and 843°). For each amplitude five different frequency offsets, ranging from 400 Hz to 20000 Hz separated by a constant logarithmic step of ~ 0.4 were used. b) Three 3D SPGR volumes, TR/TE=13.1/4.2 ms, excitation flip angles (α = 25°, 15°, 5°), to estimate T_1. c) Fast FLAIR images TR/TI/TE=8774/2192/161ms. d) FSE images TR/TE=5000/81 ms, echo train length=8.

Images were then transferred to a workstation (Sun Microsystems, Mountain View, California, USA) for further processing. Each MT weighted dataset was registered to the first as were the three T_1 weighted, the FLAIR and FSE datasets. Regions were then drawn round the whole tumour on the FLAIR images as they provide the best delineation of the tumour and in contra-lateral normal appearing white matter (NAWM) on the FSE images. In addition pixel-by-pixel maps of the whole brain were generated. The following parameters are obtained from the data: gM_0^A-the arbitrary scanner gain (g) multiplied by the magnetisation of the free pool (M_0^A); RM_0^A-the cross relaxation rate between the pools (R) multiplied by M_0^A; $1/R_AT_{2A}$-the ratio of the relaxation times of the free pool; T_{2B}-the transverse relaxation time of the bound pool (assuming a super-Lorentzian lineshape for this pool) (1, 3); $f/R_A(1-f)$ where f is the bound proton fraction defined as $M_0^B/(M_0^A+M_0^B)$ (7). From these and the estimate of T_1, f, R_A and T_{2A} can be derived. Fitting was performed using the Levenberg–Marquardt algorithm.

Results: Figure 1 shows a FLAIR image with the tumour clearly visible as the area of high signal intensity, figure 2 shows the corresponding f map, indicating the low bound proton fraction seen in the tumour.

Table 1

Tissue	gM_0^A	RM_0^A	T_{2B} (μs)	$1/R_AT_{2A}$	$f/R_A(1-f)$ (s)	R_A (s^{-1})	T_{2A} (ms)	f (pu)	T_1 (ms)
NAWM	559±93	86±17	8.9±0.5	9.7±0.9	0.052±0.003	1.2±0.1	87±8	5.8±0.5	845±64
Tumour	640±120	220±120	6.7±0.8	5.4±0.7	0.027±0.004	0.5±0.1	429±194	1.3±0.4	2207±674
p-value	0.002	0.04	<0.001	0.001	<0.001	<0.001	0.009	<0.001	0.005

Table 1 shows the fitted and derived parameter values (± standard deviation) for NAWM and whole tumour with the p-values for differences between the tissues obtained using the Students paired t-test. As there are only 6 patients at this stage not too much emphasis should be placed on the statistical results, however there are significant changes in most parameters when comparing tumour and NAWM, even after correction for multiple comparisons (not shown). Of particular interest there is a reduction in f and the T_2 of the bound proton pool in tumours.

Conclusions: Although this work is in the early stages it is apparent that qMT may have some utility in imaging low grade gliomas. The reduction in the size of the bound proton pool indicates that macromolecules are being destroyed or displaced by the tumour. An increase in free water as seen by the increase in gM_0^A, which is a measure of PD, and an increase in the free pool T_1 time, often caused by increased water content, would not alone be enough to cause this reduction in f. The reduction in T_{2B} would indicate a change in environment for the bound protons or preferential destruction of some species, however the parameter maps show that the changes in T_{2B} are concentrated in possible cystic/necrotic areas of the tumour and the bulk of the tissue is largely unaffected. Indeed regional variations are seen in many of the parameters and this along with differences between tumour subtypes and possible changes in the parameters as the tumours approach malignant progression are areas for future research.

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