Susceptibility-Corrected Magnetization Transfer Contrast in a Mouse Model of Glioblastoma Multiforme at 9.4 T

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Introduction: Glioblastoma multiforme (GBM) is the most common primary and malignant brain tumor in humans having median survival times ranging from 12 to 15 months (1). Currently, an important problem in clinical treatment of GBM is the difficulty in delineating tumor boundaries and identifying the extent of tumour infiltration when using conventional T2w, T1w and contrast-enhanced MRI. Magnetization transfer (MT) imaging is a technique that has the potential to distinguish between pathology-confirmed regions of tumour better than existing MRI protocols. In this study, magnetization transfer (MT) imaging was applied to a mouse model (N=4) of GBM at 9.4 T. The goals of this work were: a) to quantify the MT effect in two regions inside the tumour volume (denoted by blue and red ROIs in Fig 1a), as well as in normal appearing white matter (NAWM) and b) to address the technical problems related to B_0 field inhomogeneity affecting MT imaging at high fields.

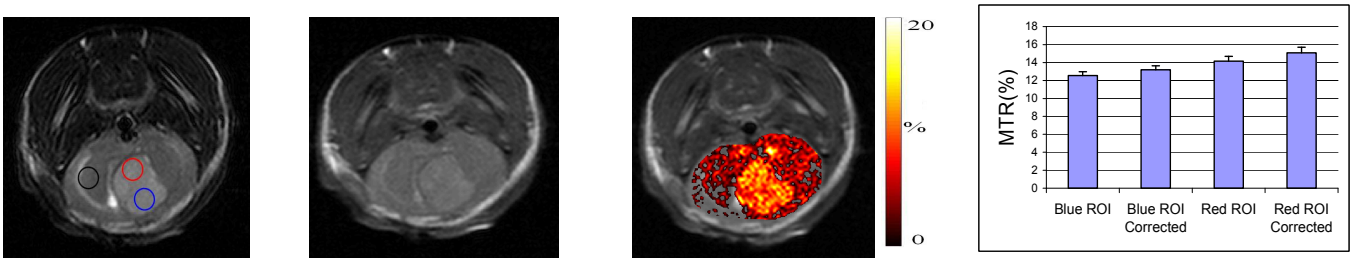

Fig. 1: (a) T2w FSE image (b) T1w FSE image (c) MTR (3.5 ppm) map (d) MTRmax (%) w and w/o Bo correction

Materials and Methods: MT imaging was performed on a Varian, 9.4 T, small animal MRI. Four mice were imaged twelve days after injection of 10000 U87 GBM cells directly into the brain utilizing a Fast Spin Echo (FSE) sequence with a 3 μT, 1 second selective, continuous wave pre-saturation pulse applied before each echo train (ETL =4). Other imaging parameters included: TR/Eff TE = 1000/15 ms, imaging field of view (FOV) = 25.6 mm x 25.6 mm, slice thickness of 2.0 mm, matrix size of 128x128, and total imaging time = 10 minutes. Z-spectra were acquired by varying the frequency of the off-resonance saturation pulse from -10 to 10 ppm in 0.5 ppm increments. The MT signal in brain tumour was quantified using the magnetization transfer ratio ($MTR = 1 - S_{sat}/S_0$). To minimize B_0 field inhomogeneity, a field mapping sequence was used to perform automated higher-order shimming (2). To account for remaining susceptibility differences in the data, a post-processing technique employing calculated B_0 field maps was utilized to correct the z-spectral data. This correction applied the B_0 field frequency shift (Hz) at each voxel to the frequency axis of the z-spectrum. Spectral data was then interpolated using a cubic spline to obtain the z-spectrum at symmetric 0.5 ppm increments.

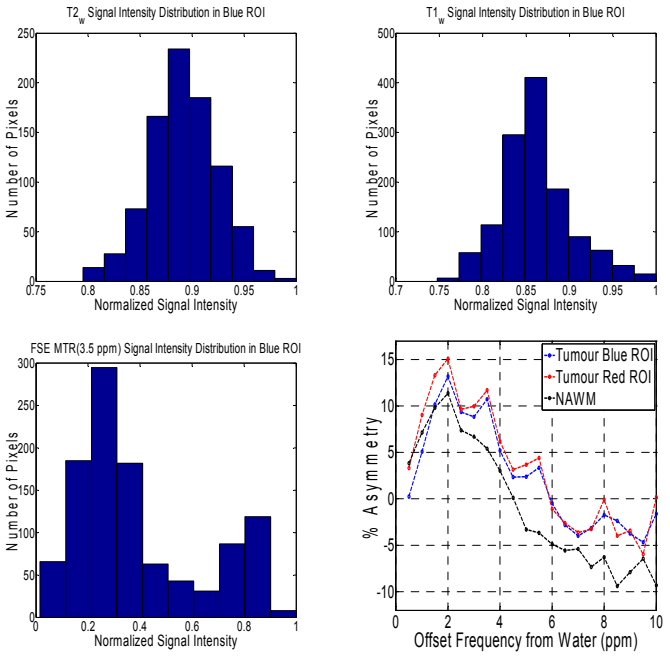

Fig. 2: Histograms of pixel number as a function of normalized signal intensity and asymmetry curves.

Results and Discussion: For the sample data illustrated in Figures 1 and 2, MTR imaging resulted in greater heterogeneity in signal intensity values in the tumour ROIs. This is highlighted in Fig 2 (a-c). A histogram of pixel number as a function of signal intensity in tumour core shows bimodal distribution for MTR images at 3.5 ppm. T1w and T2w histograms, by contrast, displayed normal distributions. Quantitatively, the mean B_0-corrected MTR asymmetry parameter inside the tumour core (blue ROI in Fig. 1a) was 13.2±0.5%, while the maximum of the MTR asymmetry curve in this ROI reached 15.3±0.6% (Fig 2). A secondary maximum was observed in the tumour ROI asymmetry curves at +3.5 ppm, corresponding to the amide proton exchange peak from APT imaging. The magnitude of the B_0-corrected asymmetry curve at this point was 10.7±1.6% in the blue ROI. This finding supports APT imaging as a useful indicator of endogenous protein concentration in tumours. Application of B_0 field maps to correct z-spectra for susceptibility differences on a voxel by voxel basis resulted in an increased MTR signal in all experiments. In tumour core at a frequency offset of 2 ppm, an average increase from 14.6±0.5% to 15.3±0.6% was observed (Fig 1d). Additional work is underway to investigate quantitative magnetization transfer using this data.

References: 1) Hobbs et al. JMRI 2003; 18:530 – 536. 2) Klassen et al. MRM 2004 ; 51: 881 – 887 3) Zhou et al. MRM 2008; 60: 842-849. 4) Jones et al. MRM 2006; 56: 585 – 592.