Correlation of potential myelin measures from quantitative Magnetisation Transfer (qMT) and multi-component Driven Equilibrium Single Pulse Observation of T_1 and T_2 (mcDESPOT)

R. S. Samson[1], S. C. Deoni[2], and C. A. Wheeler-Kingshott[1]

[1]Department of Neuroinflammation, UCL Institute of Neurology, London, United Kingdom, [2]Centre for Neuroimaging Sciences, Institute of Psychiatry, London, United Kingdom

Introduction: The Magnetisation Transfer (MT) effect is based on the exchange of magnetisation between two proton pools; 'free' ('liquid') and 'restricted' (macromolecular). This property allows the MR characteristics of the macromolecular component (usually 'invisible' using conventional MRI due to its very short T_2) to be probed via selective saturation. Analysis is based on a 2-pool quantitative model for MT and several physical quantities associated with both pools can be extracted from the fitting process. The restricted proton fraction (f_b) is thought to be related to myelin content in the brain (since restricted protons are attached to macromolecules such as myelin), and was previously shown to correlate with myelin content in excised MS lesions (2) and to depend on brain location.

The myelin water fraction (f_m) measured using multi-component relaxometry is thought to correspond to water trapped within bilayers of the myelin sheath (3). The mcDESPOT (multi-component Driven Equilibrium Single Pulse Observation of T_1 and T_2) (4) technique provides a new method for investigating tissue relaxation. The SPGR and SSFP-based technique is rapid and exhibits high signal-to-noise ratio (SNR) efficiency. Another major advantage is the large relative contribution of the fast relaxing species to the measured data, as both TE and TR are short (<< 10ms) and constant throughout the experiment, whereas in conventional multi-echo approaches the fast relaxing component contributes measurably over only a few of the (shortest) TE times sampled.

As it is believed that both f_b and f_m are related to myelin in the brain, naively we would expect these measures to show strong correlation. Here we present a preliminary study comparing f_m measured via the mcDESPOT technique with f_b in three healthy subjects.

Methods: 3 female subjects (aged 27-40) were scanned on a 1.5T GE Signa scanner (General Electric, Milwaukee, USA) with an 8-channel head coil. For the qMT data 34 4mm thick slices were acquired, axial field of view (FOV)=22cmx22cm and 256x128 acquisition matrix. A 3D MT-weighted fast SPGR sequence (1) was performed (TR/TE=28.0/1.9 ms, flip angle (FA)=5º, Gaussian MT pulses, duration=14.6 ms) at 10 combinations of MT pulse amplitude (ω_{1CWPE}) and offset frequency (Δf) (given in table 1), optimised for 1.5T (5) but with the additional constraint that all data points be acquired with Δf>1kHz since it has been shown that it is difficult to accurately model the behaviour of the two pools below this cut-off (6). For B_1 correction via the Double Angle Method (7), 2 2D FSE (TR/TE=15s/12.8 ms, ETL=8, FAs=60º, 120º, matrix=256x128) sequences were acquired. For B_0 correction, 2 fast 3D SPGRs (TR/TE1/TE2 = 28.0/3.13/6.0 ms, FA=5º) were acquired and the phase images obtained used to calculate the B_0 map (8). Finally, 3 fast 3D SPGRs (TR/TE=6.2/2.8 ms, FAs=25º, 15º, 5º) were collected for T_1 mapping. Data analysis incorporating B_0 and B_1 correction was performed using the methods described in reference 1.

MT FA (°)	Δf (Hz)
904	1000
905	3025
883	3140
130	48285
903	3075
391	1000
429	1000
904	56445
904	1000
904	13165

Table 1: qMT scheme optimised for 1.5T, with Δf >1kHz for all points

Multi-angle SPGR (DESPOT1) and SSFP (DESPOT2) data were acquired with 86 2mm slices, sagittal FOV=22cmx22cm and 128x128 acquisition matrix. Other acquisition parameters were: (i) SPGR: TE/TR=2.8/6ms, FA={3,4,5,6,7,8,11,13,18}°; SSFP: TE/TR=2/4ms, FA={10,14,19,24,28,34,41,51,67}°. A model for 2 exchanging water pools (4, 9,10) was fitted to combined SPGR and SSFP data to yield maps of component-specific T_1, T_2, volume fraction and exchange characteristics.

Following acquisition and derivation of f_b and f_m maps, data for each volunteer were linearly co-registered and regions of interest (ROIs) were drawn bilaterally in frontal, temporal and parietal WM, cerebellar GM and the thalamus, genu and splenium of the corpus callosum. Mean f_b values were compared with f_m values between and within subjects.

Results: Example f_b (left) and f_m maps are shown in figure 1. Mean f_b and f_m values for each tissue type (averaged right and left for bilateral structures) are given in table 2 as percentages (with standard deviations (SDs) in brackets). In WM f_b was demonstrated to be positively correlated with f_m both within and between subjects. Within-subject Pearson correlation coefficients (r) ranged from 0.66 to 0.89 with p-values of 0.01 for 2 subjects and 0.05 for the last. Between subjects (i.e. mean f_m vs mean f_b) in a positive correlation was also observed in WM (r=0.66, P<0.01). In GM f_b and f_m were positively correlated within subjects (r=0.72-0.99), but only correlated significantly for one subject, whereas between subjects a significant positive correlation was observed (r=0.76, P<0.01).

Discussion: Measured f_b values are consistent with those measured previously at 1.5T (1). Our f_m values are not comparable with those measured using spin echo-based approaches, since the measurement process is weighted more heavily towards the short T_2 component, and we have assumed the presence of only two T_2 components in our modelling. In previous multi-echo experiments assuming 3 tissue proton compartments the myelin water fraction has been found to have a relative size of approximately 15% and a T_2 of 15-20ms in WM (11), whereas here our estimated WM f_m values are 20-25% and fast component T_2 values around 8ms (data not shown). f_b and f_m were shown to correlate positively both in WM and GM, indicating that the two measures are in some way related although the current work cannot provide evidence for whether either are specific for myelin. Tozer *et al* (12) attempted to correlate f_b and f_m measured using a spin echo-based multi-echo technique in a study of 9 normal controls and 19 MS patients. In WM, when patients and controls were grouped together, no significant correlation between f_b and f_m was observed within subjects, but a positive between-subjects correlation was observed (r=0.42, P<0.05). The correlation appeared to originate primarily from the patient group since a positive correlation (r=0.6, P<0.01) was observed in the patientgroup, whereas no significant between-subjects correlation was seen in WM in controls. In GM patients and controls were grouped together since no significant difference in behaviour was observed between the groups. In GM, a negative within-subject correlation (r=-0.3, P<0.01) was observed. In the patient group in MS lesions a positive within-subject correlation coefficient was observed (r=0.18, P<0.05). This variability indicated the presence of other contributing factors in addition to myelin content to at least one of the measures. However, considerable noise was present in the f_m values measured in that study, therefore technical limitations may also have contributed to discrepancies between our results and theirs. The study of normal appearing WM and MS lesions in MS patients using mcDESPOT and qMT would also provide valuable insight into the effect of pathological processes on these two measures, and combined with histology of excised MS lesions may give further understanding as to what each quantity actually measures. It should also be noted that in this study the analysis of data acquired using both methods was limited to two components, however three components may be needed to describe the observed T_2 and MT effects in human brain fully (13,14). We have demonstrated that f_b and f_m are at least partially related and based on this and previous work they are likely to reflect myelin content to some extent, however a larger study and the investigation of other tissue types such as MS lesions is required.

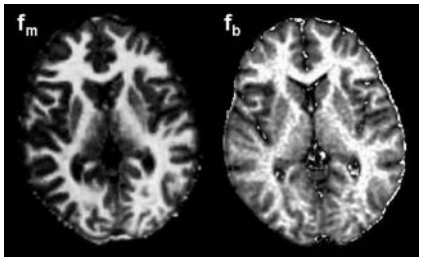

Figure 1: f_m (left) & f_b maps from a single subject

Table 2: Mean ROI f_m and f_b (%) (± SD)

Tissue ROI	f_m (%)	f_b (%)
Temporal WM	22.5 (±0.16)	9.47 (±0.84)
Frontal WM	23.8 (±0.47)	10.0 (±0.56)
Splenium	24.6 (±0.38)	10.9 (±0.84)
Genu	22.9 (±0.66)	9.93 (±0.53)
Parietal WM	23.0 (±0.64)	9.70 (±0.73)
Cerebellar GM	4.65 (±0.31)	4.97 (±0.51)
Thalamus	10.3 (±1.08)	6.13 (±0.44)

References: [1] Cercignani M *et al* NeuroImage 27: 436-41 (2005), [2] Schmierer K *et al* JMRI 26: 41-51 (2007), [3] Whittall KP & Mackay AL JMR 84: 134-52 (1989), [4] Deoni SCL *et al* JRMI 27: 1421-9 (2008), [5] Cercignani M & Alexander DC MRM 56: 2803-10 (2006), [6] Portnoy S & Stanisz GJ MRM 58: 144-55 (2007), [7]Stollberger & Wach MRM 1996; 35:246, [8]Cusack & Papadakis NeuroImage 2002; 16:754 [9] Spencer RGS & Fishbein KW JMR: 142: 120-35 (2000), [10] Deoni et al JMRI 25: 570-8 (2007), [11] Whittall *et al* MRM 37: 34-43 (1997), [12] Tozer DJ *et al* MRM 53:1415-22 (2005), [13] Lancaster JL *et al* JMRI 17:1-10 (2003), [14] Does MD & Gore JC MRM 47: 274-83 (2002)

Acknowledgements: The authors thank Mara Cercignani & Daniel Alexander for providing the optimised qMT acquisition scheme and the MS Society of Great Britain and Northern Ireland & MRC for funding.