Quantification of the magnetization transfer phenomenon in the human head at 7T

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Introduction: Magnetization Transfer (MT) and technically related effects such as Chemical Exchange Saturation Transfer (CEST) are important sources of contrast in MRI. We are particularly interested in investigating the relationship between these parameters and known variations in myelination and axonal structure [1]. Endogenous CEST contrast becomes sufficiently sensitive to be practically feasible at ultrahigh field (7T) due to the relative decrease in exchange rate compared to frequency offset. However the measurement of CEST and MT at 7T are challenging because of increased T1 and RF power deposition [2]. Previously we used EPI to measure the CEST spectrum at 7T, since standard MT imaging sequences (interleaving single MT pulses and imaging pulses in a TFE readout) are limited by SAR considerations at 7T [3]. However EPI suffers from artefacts that limit effective spatial specificity. To overcome this, we have now used pulsed saturation at a range of offset frequencies, followed by a Turbo Field Echo readout (MT-TFE, recently developed for high resolution MTR mapping at 7T), to acquire the z-spectrum at high spatial resolution in a reasonable imaging time. We have measured the z-spectrum at different power depositions (bandwidth of the pulses), and used the data to quantify regional differences in the parameters describing the CEST spectrum of the human brain in vivo.

Method: Healthy subjects (N=4) were scanned in accordance with approval from the local ethics committee. Scanning was carried out on Philips Achieva scanners at 7T. The sequences consisted of a train of 20 off-resonance pulses (13.5 μT Gaussian-windowed, sinc pulses with a bandwidth from 150 Hz to 250 Hz, 50 ms between each pulse), followed by a Turbo Field Echo readout (TFE: shot-to-shot interval: 10s, TR/TE=11/5.6ms, 1.25x1.25x1.25mm^3). Pulsed saturation is less efficient and broader bandwidth than CW saturation but is readily implemented on standard scanner hardware. For the MT-TFE sequence [2], the frequency offset of the saturation pulses was varied from -10 to +10 kHz in logarithmic steps, allowing the MT spectrum to be measured in < 5 min at 16 points (24 measurement on one subject in < 8min). This was repeated for three different pulse bandwidths. MT ratio (MTR) maps were calculated and MT asymmetry (MT_{asym}) maps were calculated by taking the different between MTR maps acquired with positive and negative off-resonance pulse trains, divided by the positive off resonance train image. Z spectra and asymmetry spectra were also computed for white matter regions of interest. The data were corrected for the effects of B_0 inhomogeneities and eddy currents by shifting the spectra on a pixel-by-pixel basis according to an acquired Bo map, and then correcting for the average offset of the B_0 map, as well as for B1 inhomogeneities by reducing the amount of saturation according to the B_1 map before the fitting process.

Results: Figure 1 shows regional variations in the z-spectrum at 7T in the human brain showing a peak due to amide protons at 3.5ppm, present with the different saturation pulse bandwidths. The CEST peak was lower than previously observed with EPI. As the bandwidth of the MT pulses decreased, the MT effect decreased, but the spectral resolution is increased as expected. Figure 2 shows the MT images acquired at for two different offset of saturation pulses. The endogeneous Amide Proton Transfer effect [5] was larger in the white matter (0.11±0.02), but still present in the grey matter at a lesser extent (0.06±0.02). Figure 3 shows the results of the quantification with a modified 3-pool model [4] applied at region of interest level (~8000 voxels per region). The quantification of the pools (M_0^b and M_0^c) shows that the amount of bound protons inside the Corpus Callosum (CC) is increased, while the amount of exchangeable protons is the same as the frontal white matter, in contrast to previous EPI results.

Discussion: The z-spectrum and approach to saturation has been measured in a reasonable imaging time at high spatial resolution at 7T using MT-TFE, allowing MT parameters to be quantified in vivo with anatomical image quality. This will allow detailed analysis of the variation in the CEST parameters across the white matter and cortex. The results do not quite agree with previous EPI results [3], but this is likely to be due to the effect of the additional pulses in the MT-TFE sequence and the different sensitivities to different water components of the EPI and TFE readouts (because of their different echo times). These effects will be investigated by including them in the 3 compartment model used to fit the data.

[1]: Yarnykh et al, Neuroimage; 23:409-424. **[2]:** Tyler, Gowland. Magn. Reson. Med. 2005; 53:103-109. **[3]:** Mougin et al, NeuroImage 2010; 49:272-281. **[4]:** Woessner et al, Magn. Reson. Med, 2005; 53:790-799. **[5]:** Blakeley et al, 2007; Neurology 2007; 68(A) 288. *Supported by the Medical Research Council (UK) and Fp6 Marie Curie Action Programme (MEST-CT-2005-021170).*

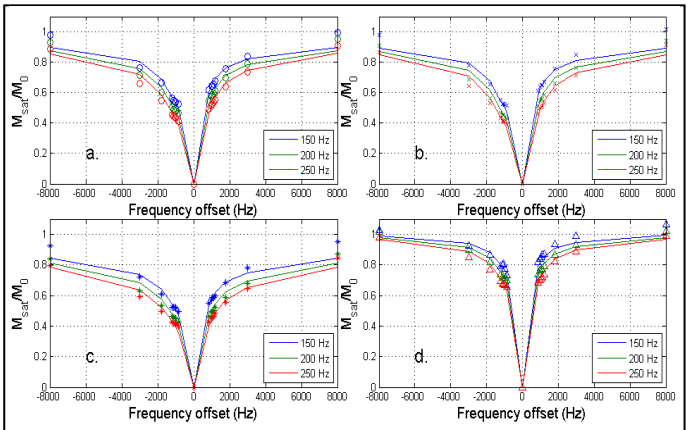

Fig. 1: Z-spectrum at 7T in an healthy brain in vivo (symbols) with quantification (lines), showing a large asymmetry around the amide peak at 3ppm for the white matter (a,b), the Corpus Callosum (c) and at a much lesser extent in the cortex (d).

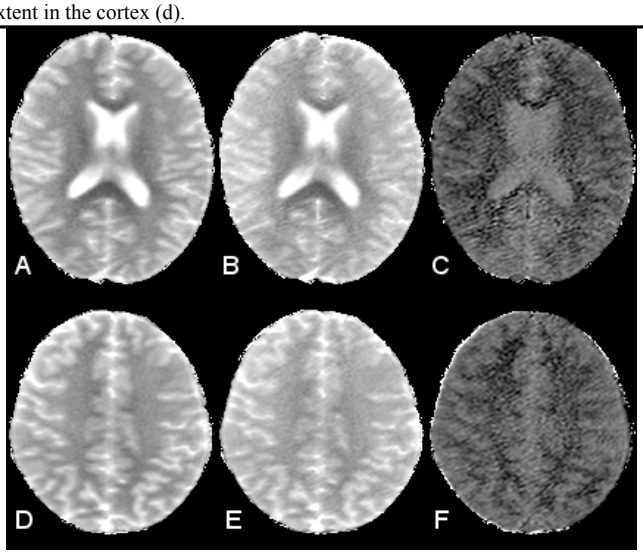

Fig. 2: MT images at 7T showing more MT effect on negative offset (A, D: -1050Hz) compared to positive offset (B, E: +1050Hz), with the corresponding MT_{asym} map (C, F) calculated for +/-1050 Hz using $MT_{asym}= (MT^+-MT^-)/MT^+$.

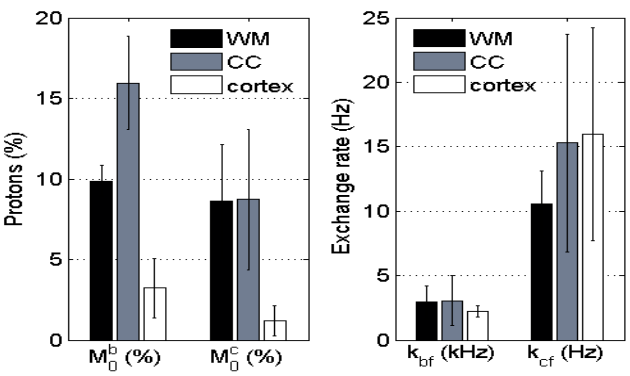

Fig. 3: Results of the quantification of the exchange pool and the bound pool averaged over the four healthy subjects. Results are for white matter regions and cortex.