CEST analysis via MR fingerprinting

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AIM: To develop a new method to fit z-spectra for proton pool concentrations taking into account variations in B1 and the longitudinal relaxation time, by using a physically realistic look-up table.

INTRODUCTION: Magnetization Transfer (MT), Nuclear Overhauser Effect (NOE) and Chemical Exchange Saturation Transfer (CEST) are processes which modulate the 1H MR signal and which can be studied by analysing the z-spectrum. A major challenge is to quantify NOE and CEST effects and separate them from other signal contributions such as Direct Water Saturation (DS) and MT[2,3]. Full fitting of the spectra to numerical models based on the Bloch-McConnell equations would be ideal but is too time consuming to be practical. Here we propose a new method of measuring MT, NOE and CEST effects in vivo: measured z-spectra are compared to a large pre-existing database of spectra obtained by numerical simulation of the Bloch-McConnell equations for MT, NOE, CEST and DS pools of various relative concentrations, taking account of variations in RF power and longitudinal relaxation times.

METHODS: Bloch simulation: z-spectra were simulated for the pulse sequence used experimentally using Bloch equations modified to account for exchange between the pools[7] for a range of relative amplitudes of the NOE, APT and MT pools, a range of B1 values (0.3– 3μT), and a range of T1 values (1 – 3s). These spectra provided a library against the experimentally measured spectra were compared (similar to the approach used in MR Fingerprinting[5]) taking account of T1 and the B1 at which the spectra were acquired, whilst fitting for an absolute B1 scaling factor. Monte Carlo simulation was used to determine the SNR of the fit and showed the resulting error in the size of pools to be CEST: 10%, NOE:<1% and MT:34% for typical in vivo parameters. Experimental According to ethics approval, 2 control subjects and 2MS patients were scanned using a 7T Philips Achieva system with a 32 channel receiver coil. Z-spectra were acquired at 1.5mm^3 isotropic spatial resolution using a MT-TFE sequence[7]. A whole head z-spectrum at 16 offset frequencies was acquired in ~7min, repeated for nominal B_{1rms} powers of 1 and 1.5 μT. Fitting Z-spectra were fitted pixel-wise for the amplitude of the 4 pools (water, MT, NOE and APT) calculating the sum of squares difference between the measured spectra to the spectra in the data base with interpolation between simulated spectra where required. T1 maps were used to constrain the fit to the spectra for the correct T1. B1 maps were used as starting points in the fit.

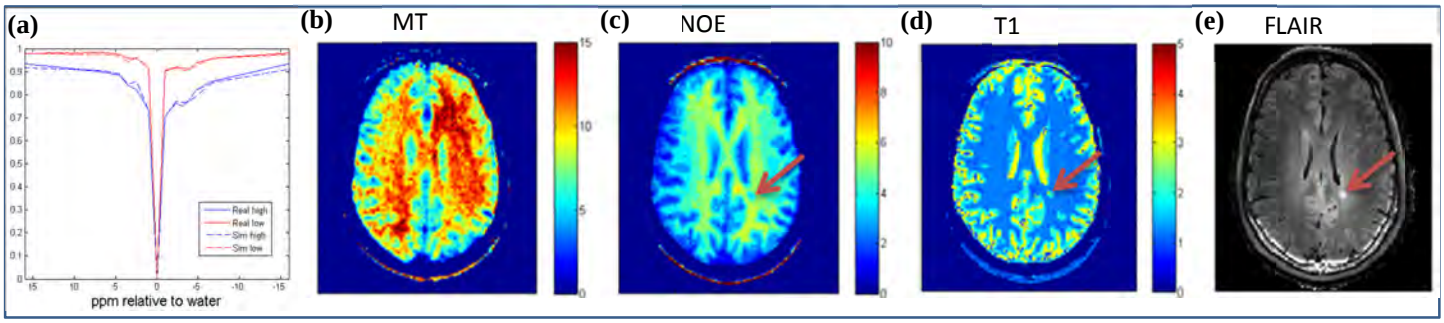

Figure 1 (a) Real vs. fitted spectra and fitted maps of (b) MT and (c) NOE % pool size, (d) T1 map and (e) FLAIR. Arrow indicates MS lesion.

RESULTS: Figure 1 (a) shows an example of the difference between real and the fitted simulated spectra, figure 1b and c show resulting MT and NOE maps figure 1d and e show the corresponding T1 map and FLAIR image. Figure 2a shows mean with standard deviations for fitted pool sizes in a whole brain grey and white matter mask, averaged across subjects. It also shows a significant drop in MT and NOE between normal appearing white matter and a white matter MS lesion. Spectra from neighbouring healthy WM and GM regions are also plotted in Figure 2(b).

DISCUSSION: Even with the current limitations of a small database, the fit works well and gives good contrast between WM, GM and MS lesions, with small residual errors. Simulations have shown that would be possible to fit the z-spectra for T1 and B1 (instead of collecting separate maps) and it is likely that this database fitting approach could be expanded to include other parameters such as exchange rates and T2 provided that data are acquired to give sensitivity to these measures. Monte Carlo simulations will be used to determine the optimal data sets to acquire (in terms of B1 and T1 maps and different RF powers and frequency offset etc.) to maximize signal to noise ratio in the fitted parameters.

CONCLUSION: The study presents a new method for fitting z-spectra to physically meaningful models, taking account of B1 inhomogeneities in a reasonable computational time.

References: [1] Van Zijl. et al., MRM 50 (6), 1120-1126 (2003). [2] Sun, P. Z. & Sorensen, A. G. MRM (2008). [3] Zaiss, M. et al., NMR Biomed. (2013) [4] Zaiss et al., JMR, 211 (2), 149-155 (2011). [5] Dan Ma, et al., 10.1038/nature11971 (2013). [6] Jin T et al., MRM 2013 [7] Mougin et al. NMR Biomed. 2013.

ACKNOWLEDGEMENTS: Supported by the Initial Training Network, HiMR, funded by the FP7 Marie Curie Actions of the European Commission (FP7-PEOPLE-2012-ITN-316716) and the Medical Research Council.

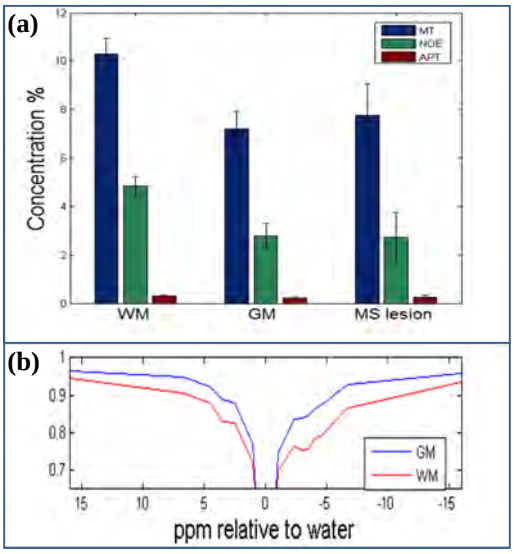

Figure 2 (a) Inter-subject mean and standard deviation of proton pool concentrations (b) WM and GM spectra