Eliminating MT Contribution in Z-Spectra using Dual Band Macromolecular Background Suppression (DBMS)

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Target: Those interested in developing and applying CEST techniques.

BACKGROUND Chemical Exchange Saturation Transfer (CEST) [1] and Nuclear Overhauser Enhancement (NOE) [2] effects have the potential to transform MRI into a molecular imaging technique. However the sensitivity to low concentration species is poor when the water saturation at the frequency of interest is overwhelmed by magnetization transfer from the semisolid pool. This problem can be reduced by using low power saturation pulses but at the cost of removing the flexibility required to be able to separate slow and fast exchanging species. Here we propose a new solution to the problem of MT contamination of CEST data. The solution is similar to macromolecular suppression in MRS: an RF saturation band is applied at a fixed off resonance to saturate the MT spectrum whilst a second saturation band is swept across the z-spectrum to interrogate CEST features. This can be achieved using a pulse that saturates two frequency bands simultaneously.

Aim: To demonstrate dual band macromolecular background suppression (DBMS) in phantom and human brain z-spectra for the first time.

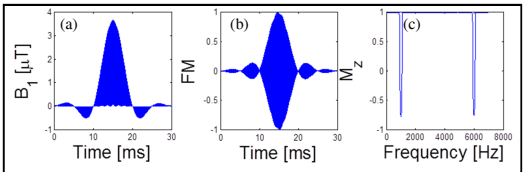

Fig 1 AM (a) and FM (b) profiles of an RF pulse designed to suppress simultaneously at 1kHz and 6kHz. (c) Bloch simulation of longitudinal magnetization response.

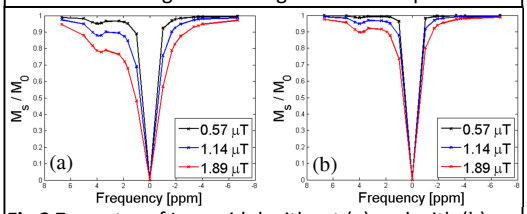

Fig 2 Z-spectra of Iopamidol without (a) and with (b) DBMS at 6kHz.

METHODS: Sequence: A DBMS pulse was designed to saturate two RF frequencies simultaneously by summing two Gaussian windowed sinc pulses, each frequency modulated to saturate a fixed bandwidth (BW=200 Hz) around a different central frequency (f_0 or f_1); the pulse behaviour was validated using Bloch simulations (fig. 1). The pulses were implemented so that it was possible to cycle the frequency offset f_1 (to interrogate the z-spectrum), whilst keeping f_0 constant at 6kHz (to provide suppression of the macromolecular contribution across the whole z-spectrum). The pulse sequence used consisted of a train of 20 DBMS pre-saturation pulses (pulse length=30ms, duty cycle 50%, B_{1rms}= 0.57, 1.14, 1.89 μT), followed by a gradient crusher to remove residual transverse magnetization, and a 3D TFE readout to measure the water saturation (S_{sat}) [3]. The control image (S_{nosat}) was acquired with a similar sequence but with a single pulse exciting 50kHz off resonance to overcome hardware errors related to gating on the RF amplifiers. Z-spectra were created by sweeping f_1 over a range of offset frequencies and measuring $MTR(f_1) = (S_{nosat} - S_{sat}^{f_1})/S_{nosat}$. Experiment: This sequence was tested on a phantom containing 14% Iopamidol with 2% Agarose to simulate macromolecule background and, on the brain of 1 healthy subject (age 24) with ethics approval. Scans were performed on a Philips Achieva 7 Tesla with a 32-channel receive coil array. Z-spectra were sampled at 15 values of f_1 -17 ppm and 17 ppm (-5kHz to 5kHz) with 3 varying saturation powers 0.57, 1.14 and 1.89 μT and with f_0 fixed at 6kHz.

RESULTS Using DBMS the main CEST peak at 4.2 ppm from amide protons in Iopamidol was much more pronounced because of the suppression of the MT background (fig 2b) compared to a standard CEST saturation scheme (fig 2a). The same effect was detected for the NOE peak in the human brain in both grey and white matter (fig 3 a and b). The NOE peak in the brain varied more linearly with RF saturation amplitude for DBMS suppression compared to conventional suppression, particularly in white matter where the MT contamination is larger (fig 3c); a similar variation with B1 was observed in the phantom containing Iopamidol.

DISCUSSION Here the DBMS pulse was optimized experimentally and Fig 2(b) suggests direct saturation is increasing with power. Further work is required to optimize the amplitude and frequency offset of the DBMS pulse, for instance it may be optimal to saturate the macromolecular pool simultaneously at two symmetric frequencies (requiring a triple frequency pulse). It is also likely that this technique could be used to suppress other confounds in the z-spectrum.

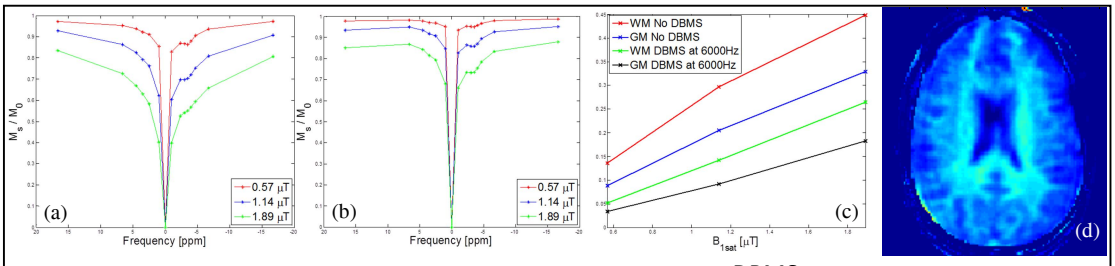

Fig 3 *In vivo* white matter (WM) Z-spectra measured without (a) and with (b) a DBMS pulse at 6kHz. (c) Measured peak difference at -3.5ppm with respect to the baseline in WM and grey matter (GM) (average over all GM and WM). 3(d) shows the NOE map resulting from fitting a function of three Lorentizan to the 1.89 μT z-spectrum.

CONCLUSION Dual band macromolecular background suppression (DBMS) provides a method to uncouple MT effects from other features of the z-spectrum which will simplify quantification and separation of different z-spectrum features.

REFERENCES [1] van Zijl 2011, MRM 65 (4). [2] van Zijl, 2013, NeuroImage 77. [3] Mougin 2013 NMR Biomed. **Acknowledgments**: This work was funded by the Medical Research Council.