3D Whole Brain Pulsed CEST Acquisition at 7T

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Introduction: Chemical exchange saturation transfer contrast is created by selective saturation of exchangeable protons that reduces the intensity of the free water signal. Selective saturation has traditionally been accomplished by a long (>500 ms), low power saturation pulse followed by a long post-acquisition delay (>3*T1) for signal regrowth. Alternatively, a train of short, shaped pulses (e.g., Gaussian) can be used to obtain a similar affect. However, all current CEST sequences consist of temporally separate saturation and imaging modules, which hampers the acquisition efficiency. Two dimensional pulsed imaging was previously been shown in phantoms (1). In this paper we demonstrate a 3D whole-brain pulsed CEST technique employing steady state saturation, providing high resolution CEST images at 7T with limited to negligible interference of direct water or conventional magnetization transfer contrast (MTC). Whole brain acquisition per frequency point took only 20s, allowing 21 points to be acquired in 7 min.

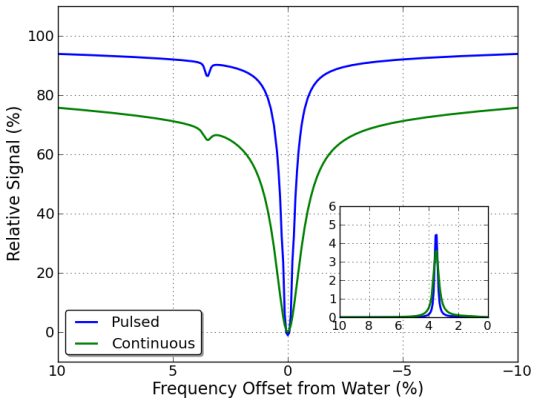

Figure 1: Bloch simulation of a pulsed vs a continuous saturation z-spectrum. Inset shows the traditional asymmetry measure with amide proton peak.

Methods: A 3-pool Bloch simulation (2) was used to determine the number of saturation pulses required for steady state and saturation pulse parameters for maximal amide proton transfer (APT) contrast at an offset of 3.5ppm from water. Previously published relaxation and exchange rates for free tissue water (T1/T2=1.7/0.048s) (3), macromolecular protons (T1/T2=1.7s/10μs, k=8Hz) (4) and amide pools (T1/T2=0.944/0.033s, k=28Hz, 3.5ppm) (5) were used in the Bloch simulations (relaxation times were adjusted for 7T). For all simulations the continuous pulse duration (for comparison) was set to 100 times the duration of the pulsed duration. The total acquisition time for one frequency offset for 2mm isotropic voxels was approximately 20s.

The pulsed CEST 3D-FFE pulse sequence was implemented on a 7T Philips MRI scanner TR/TE=65/6 ms, EPI-factor=7, and 2 mm isotropic (acquired) voxel. The readout was preceeded by a 25 ms, 1 μT single lobe sinc-gauss pulse for saturation. A whole brain volume was acquired at one saturation frequency followed by a 7s delay, to minimize signal saturated at one frequency bleeding through to the next frequency. A total of 68 volumes were acquired at saturation frequencies between -8 ppm and 8 ppm (Fig 2, red points). The acquired signal per voxel (z-spectrum) was fit to a Lorentzian based on a subset of points around the water frequency and a couple of points far downfield (Fig 2, green points) and shifted to correct for B0 inhomogeneity effects. The amide proton transfer (APT) signal was quantified as the difference between the acquired signal (Fig 2, blue points) and the Lorentzian fit (Fig 2, green line) between 3.3 and 3.7 ppm. A map of the mean APT signal was quantified.

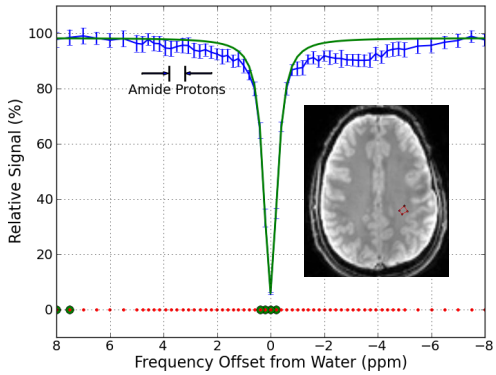

Figure 2: Mean signal intensity (blue) from a region in white matter (red ROI) and a Lorentzian fit (green).

Results and Discussion: Bloch simulations showed that the amide pool reached a steady state after approximately 3s of pulsing. For the 3D scan proposed here, the time to steady state is not a problem as it is reached while the high frequency components of k-space are acquired and therefore should not have a significant effect on the saturation efficiency of the data. Simulation of pulsed and continuous saturation (Fig. 1) showed the possibility to minimize MTC effects. The optimal saturation duration and power for maximal APT asymmetry and minimal MTC were 25 ms and 1μT.

Figure 2 shows a z-spectrum from a region of white matter (blue curve) using a pulsed CEST acquisition. As predicted by the simulations, there is limited MTC effect. However, when using this steady state acquisition, there are some strong effects of water saturation in the upfield (-5 – 0 ppm) range. These signals, attributed to lipid signal or Nuclear Overhauser Enhancement (NOE) (6) contributions prohibit asymmetry analysis. Though quantification is still achieved using the Lorentzian fitting of the direct saturation lineshape.

The amide proton transfer (APT) image was calculated at each voxel as the mean of the difference in signal between the acquired data and the Lorentzian fit between 3.3 and 3.7 ppm (Figure 3). The mean APT (from one slice) within WM = 2.66%±0.79% and within GM = 2.59%±0.90%. This signal is not corrupted by signal from upfield parts of the curve as the asymmetry method was not used. This should produce a more accurate representation of the actual amide proton transfer contribution in vivo. A whole brain map of the APT is shown in Figure 3.

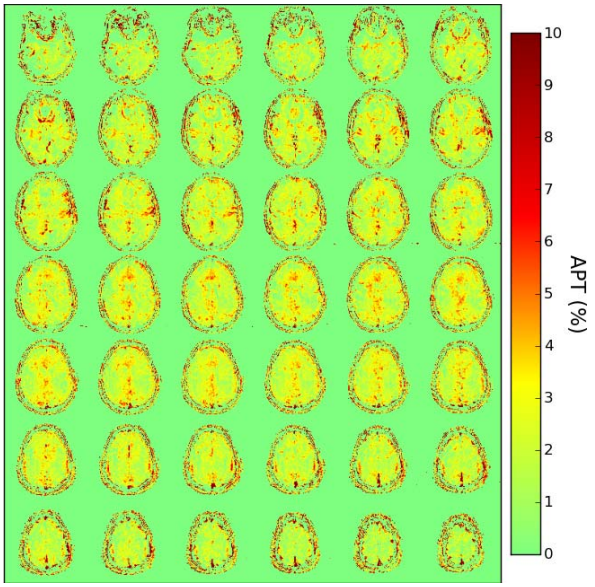

Figure 3: Whole brain APT asymmetry (%) from a 2mm isiotropic pulsedCEST acquisition acquired at 7T.

Conclusion: The pulsedCEST technique uses steady state saturation within a 3D readout to acquire whole brain volumes at given saturation frequency offset. The pulsedCEST acquisition is more power efficient as data is acquired interspersed throughout the saturation, and therefore it is possible on a SAR limited high field system such as the 7T. Bloch simulations showed the optimal saturation pulse parameters to be approximately 25 ms and 1 μT and this was found to reduce the strong MTC effects.

References: (1) Desmond et al., ISMRM Proceedings 4494, 2009; (2) Woessner MRM v53 2005 pp790, (3) Stanisz MRM v54 2005 pp 507, (4) Sled MRM v46 2001 pp 923, (5) Zhou MRM v51 2004 pp 945, (6) Ling et al. PNAS 2008;105:2266.