Pulsed Saturation Transfer for quantifying CEST in the presence of MT

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Introduction: Chemical exchange saturation transfer (CEST) is an MRI technique which can detect the presence of labile protons associated with solute chemicals. It is similar to magnetization transfer (MT), in that the experiment involves an off-resonance saturation pulse in combination with readout at the resonant frequency of the water signal. The difference between CEST and MT is evident in the properties of the molecules which are exchanging with the bulk water; in the case of MT the effect is apparent over a wide range (hundreds of ppm) and symmetric about the water resonance, whereas with CEST the effect is off-resonance (asymmetric) and confined to a smaller bandwidth (several ppm). CEST measurements have been successfully employed in the determination of solute concentration [1], temperature [2] and pH [3], and there is movement towards applying these techniques in-vivo by exploiting the endogenous CEST effect from amide protons (APT [1]). The detection of the CEST effect in-vivo is complicated by the presence of immobile macromolecules, resulting in a large MT effect. In this situation, the CEST effect has been isolated from the MT effect by calculating the asymmetry value at the resonant frequency, Δ_{0c}, of the CEST protons: $Mz(\Delta_{0c}) - Mz(-\Delta_{0c})$. Several studies have questioned the validity of this method [4], [5], concluding that the magnitude of the CEST effect is modified by the properties of the MT pool. We propose a method by which the CEST and MT properties are determined independently and thus free of each other's influence.

Method: A set of three phantoms was constructed in pH 5 citric acid buffer: 1) 1M ammonium chloride representing CEST, 2) 2% agar representing MT, 3) 1M ammonium chloride and 2% agar representing both CEST and MT. Each phantom was measured at 22°C on a 3T GE Signa scanner by a pulsed magnetization transfer sequence [6] with TR/TE/flip angle = 200ms/4ms/15°. Four RF powers were employed for the saturation pulse, resulting in flip angles (mtflip) of 500°, 1000°, 2500°, 4394°, and for a spectrum of offset frequencies linearly spaced from -800 to 800Hz and logarithmically spaced from 800 to 200000Hz. The T1 was measured independently by an inversion recovery experiment (TR = 5s). Rough B0 correction was performed on the fly at the scanner as to minimize the signal at 0Hz offset, while fine correction was performed by fitting a spline to the spectra and again aligning the minima with 0 Hz offset. B1 mapping was performed by double-angle spin echo [7] and used to correct the mtflip angle as well as the readout flip angle. A three-pool compartmental model was used to fit the data, derived from the steady state solution to the Bloch equations modified to include exchange and off-resonance pulsed RF excitation [6].

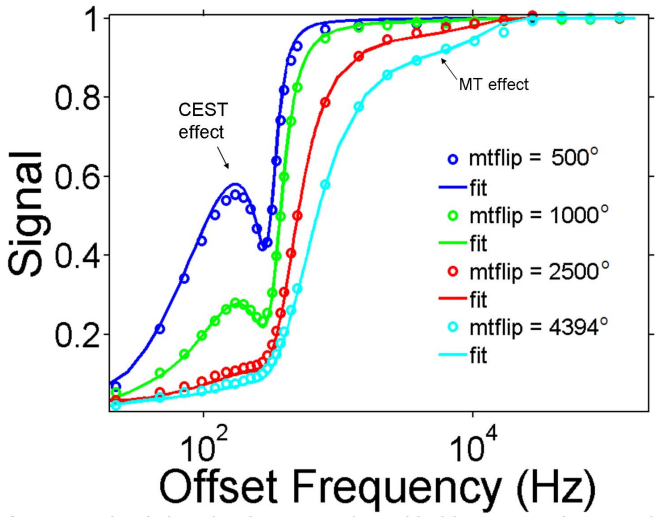

Figure 1: Fitted data for the ammonium chloride + agar phantom, for four different saturation RF powers resulting in flip angles of 500°, 1000°, 2500° and 4394°.

	Ammonium chloride (CEST)	Agar (MT)	Ammonium chloride + agar (CEST+MT)
$T2_a$ (s)	0.41	0.068	0.055
R (Hz)	-	60	68
M_{0b} (%)	-	0.85	0.89
$T2_b$ (s)	-	1.8×10^{-5}	2.2×10^{-5}
R_{CEST} (Hz)	300	-	280
M_{0c} (%)	4.5	-	5.4
$T2_c$ (s)	0.046	-	0.044
Δ_{0c} (Hz)	290	-	290

Table 1: Fitted CEST, MT, and bulk water parameters for the three-pool model. $T2_a$ is the T2 relaxation of the bulk water pool, R, $T2_b$, and M_{0b} are the exchange rate, T2 and fractional size of the semisolid MT pool, and R_{CEST}, $T2_c$ and Δ_{0c} are the exchange rate, T2 and resonant frequency of the labile CEST pool. The statistical errors from the fitting procedure were less than 7% in each of the parameters. All CEST and MT parameters from the combined sample are in very good agreement with independent MT and CEST measurements. Obviously, T2a differs due to different concentration of additives.

Results and Discussion: Figure 1 shows the result of the fit for the ammonium chloride and agar phantom. It is apparent that for an mtflip of 500° the MT effects are minimal, while at an mtflip of 4394° the CEST effects are likewise much reduced. This offers some insight into the design of an experiment where one wishes to limit the influence of either the CEST or MT pools. The resulting fitted parameters for the three phantoms are shown in Table 1. There is good agreement between the CEST parameters (R_{CEST}, $T2_c$ and Δ_{0c}) measured both with and without the presence of agar, which implies that the determination of CEST parameters by this method will not be heavily influenced by a changing MT component. We conclude that this method offers a robust means of determining both CEST and MT parameters simultaneously, using a sequence which is applicable in-vivo. The presented approach can be used instead of asymmetry methods which may slightly bias quantitative assessment of CEST [4].

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