Two-pool compartmental modeling of balanced SSFP and CEST

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Introduction: Chemical exchange saturation transfer has been used as a contrast mechanism for the imaging of cancer[1] and stroke[2], and is sensitive to the exchange rate between labile protons and unrestricted liquid water. Endogenously, several exchanging groups have been observed to contribute to the effect, mainly amide[1] and glycosaminoglycans[3] which have exchangeable groups that resonate within ~5ppm of the water frequency, and additionally contrast agents have been developed to exploit the CEST effect, including PARACEST[4] and which generally resonate on the order of 10-100 ppm shift from water. The standard CEST acquisition involves the application of a long RF saturation pulse such that a steady state is achieved between T1 recovery and saturation, with a resulting TR of 10s or longer. This is often referred to as the continuous wave (CW) CEST method. Several methods to reduce the scan time for CEST imaging have been introduced, including pulsed CEST[5-7]. This abstract simulates the utility of a balanced SSFP sequence for the characterization of chemical exchange, which promises a short TR and no waste of signal information due to spoiling.

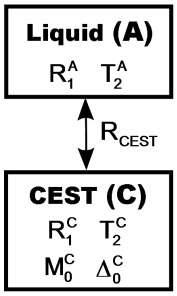

Figure 1.

Method: A simulation was developed which followed the behaviour of the liquid water and CEST proton magnetization vectors under the application of the balanced SSFP sequence. The spins were governed by a two-pool compartmental model of exchange (Fig. 1) in addition to effects of RF and T1, T2 relaxation[8]. The parameters which describe this model are as follows: M_{0c} (relative concentration of protons associated with the CEST pool), $T2_a$ and $T2_c$ (T2 of water and CEST pool respectively), Δ_{0c} (the frequency offset between the CEST pool and the free water pool) and R_{cest} (rate of chemical exchange between the CEST and free water pools). We modeled two different cases, simulating endogenous CEST from glycosaminoglycans (gagCEST) with M_{0c} = 0.007, $T2_c$ = 0.03s, Δ_{0c} = 1ppm = 128 Hz at 3T, R_{cest} = 1000 Hz and exogenous CEST from a hypothetical paraCEST agent with M_{0c} = 0.01, $T2_c$ = 0.08s, Δ_{0c} = 20ppm = 2550 Hz at 3T, R_{cest} = 2500 Hz. $T1_a$ and $T2_a$ were assumed to be 0.8 and 0.08s respectively. Two different approaches to the collection of CEST spectra with balanced SSFP were investigated: 1. Magnitude of the transverse magnetization as a function of RF phase[9, 10] 2. Magnitude of the longitudinal magnetization as a function of RF offset frequency (flip angle = 15° and TR = 12ms for both approaches). These were compared to a third experiment type, the standard CW CEST experiment (saturation pulse amplitude = 0.4 μT for 10s). For all experiment types it was assumed that enough repetitions had been performed so that the magnetization was at steady state.

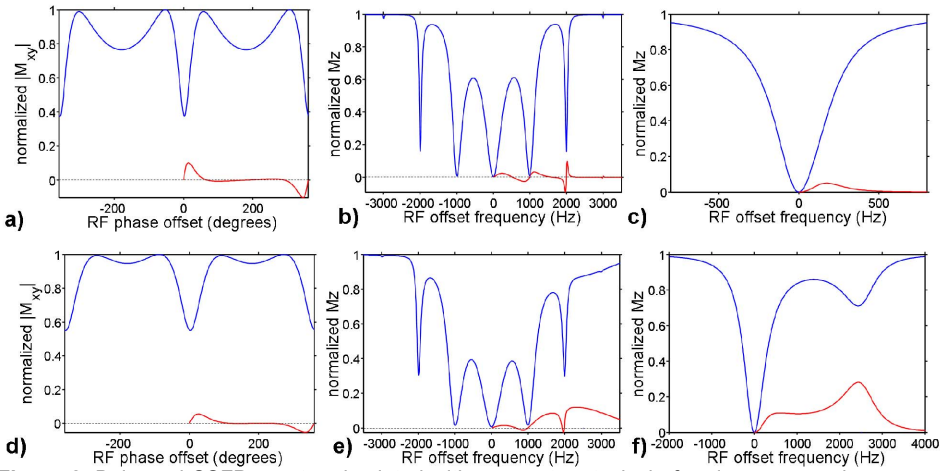

Figure 2. Balanced SSFP spectra simulated with parameters typical of endogenous and exogenous CEST and three experimental types. Simulations are shown for an endogenous gagCEST system for a) bSSFP signal vs. RF phase, b) bSSFP signal vs. RF frequency offset c) CW signal vs. RF frequency offset, and for a paraCEST system with d) bSSFP signal vs. RF phase, e) bSSFP signal vs. RF frequency offset f) CW signal vs. RF frequency offset. The asymmetry in the spectra (difference between signal at negative and positive offsets) is shown in red.

Results and Discussion: Asymmetry due to the presence of an off-resonance component in the spectrum and CEST is present in all the simulations (see Figure 2). It is apparent that the bSSFP sequence can achieve a similar amplitude of asymmetry to the CW sequence, with saturation arising from the repeated small flip angle excitations. This enables the acquisition of images with a TR of 12ms (Fig. 2 a-b, d-e) as compared to a TR of 10s (Fig. 2 c and f). We are aware of several features of this system which were not taken into account by the simulation but which would be present in experimental data. With such a short TR, the bSSFP sequence generally takes many iterations to reach steady state, requiring a number of dummy acquisitions which would be impractical. Consideration would need to be taken to account for the transient state of the signal. Additional sources of asymmetry are expected in experimental data, such as that due to frequency shifts from sequence-induced temperature changes and local susceptibility differences[11]. The contribution of magnetization transfer was neglected for these simulations but would be expected to have a significant impact on the shape of the spectra. Despite these considerations, it is still expected that the CEST asymmetry would be measurable *in vivo* by bSSFP and could be quantitatively described by the compartmental Bloch-equation model.

Conclusion: A quantitative model of CEST has been adapted to describe the signal observed with the bSSFP experiment. Balanced SSFP sequences show promise for the measurement of CEST asymmetry and can be performed with a TR a hundred times less than that required for traditional CW CEST experiments.

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