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 (with frequency Δ) in combination with readout at the resonant frequency of the water signal. The saturated protons transfer their magnetization to the bulk water, thereby reducing 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 of Δ (a hundred 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]), or through the development of paramagnetic contrast agents which serve as shift reagents (PARACEST [4]). 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 is typically isolated from the MT effect by calculating the asymmetry value at the resonant frequency, Δ, of the CEST protons: Mz(Δ) – Mz(-Δ). This method makes the assumption that the CEST effect is unchanged by the presence of MT. In this work we will explore the validity of this assumption.

Method: We used a two pool (CEST) and three pool (CEST+MT) compartmental model, and derived the steady state solution to the Bloch equations modified to include exchange and off-resonance continuous wave (CW) excitation. We then evaluated the behaviour of the asymmetry for representative values of the model parameters at 3T chosen from the literature, and compared the results of the CEST-alone model to the CEST+MT model. The CEST exchange rate, R, was modelled as a function of pH according to the following relation: $R(Hz)=5.57\times10^{pH-6.4}$ [5].

Results:

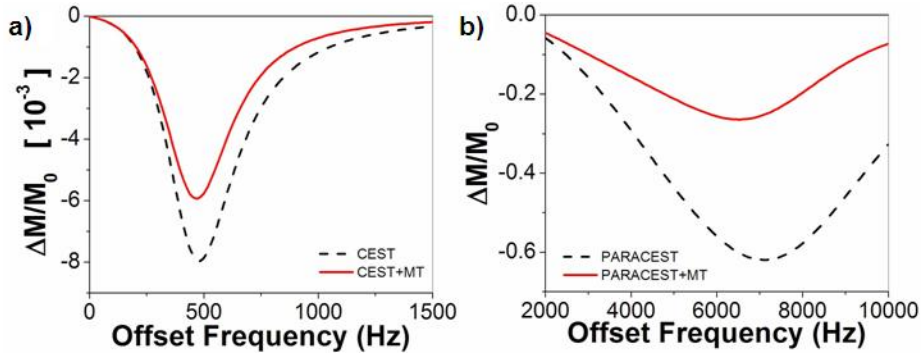

Figure 1 *The CEST asymmetry, calculated for parameters similar to those involved in an (a) APT stroke experiment and (b) PARACEST experiment, in the absence and the presence of an MT effect typical of normal gray matter. Please note the scale difference in the y-axes.*

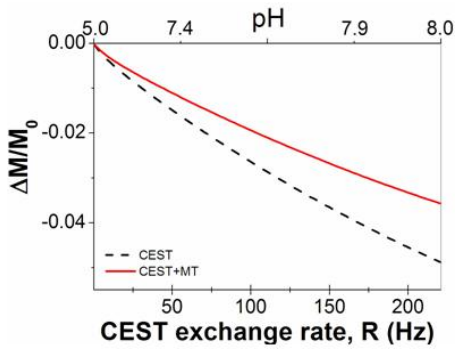

Figure 2 *The CEST asymmetry, evaluated at the resonant frequency of the solute, for varying values of the CEST exchange rate (a function of pH). Results shown for parameters characteristic of an APT experiment.*

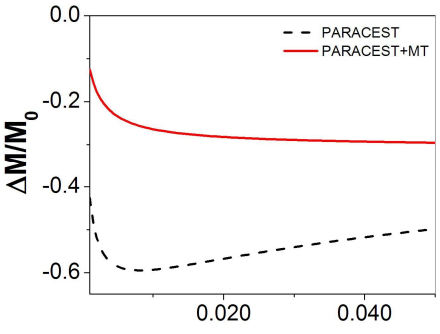

Figure 3 *The CEST asymmetry, evaluated at the resonant frequency of the solute, for varying values of the CEST proton concentration. Results shown for parameters characteristic of a PARACEST experiment.*

Discussion: The asymmetry value derived from the CEST model (Fig. 1a) differed from the CEST+MT model by at most 0.2% of the initial magnetization, M_0, which would be well below the noise threshold in a typical in-vivo experiment at 3T. However, the CEST effect itself is less than one percent at this field strength, such that any attempts to measure it via the asymmetry parameter would be severely impacted by the presence of an MT component. In the case of PARACEST imaging, this error was accentuated (Fig. 1b), and the true CEST effect could be underestimated by a factor of three. Figure 2 illustrates the effect of changing the pH (changing R) on the asymmetry value. In Fig. 3, the asymmetry value as a function of changing PARACEST concentration is shown. In both of these cases, any variation in the properties of the MT pool had a significant impact on the measured CEST effect. A description of the CEST effect in terms of asymmetry alone may result in its underestimation, leading to errors in the calculation of physiological quantities including pH and solute concentration.

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