

Study of Chemical Exchange Effect on Water MR Frequency Shifts using CEST

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Introduction: Contrast in phase images of human and animal brains, obtained with gradient-recalled echo MRI, provides unparalleled tissue resolution and holds great promise for in vivo study of biological tissue structure (1). However possible mechanisms responsible for this contrast are still under debate. Among others, they include anisotropic relationship between local Larmor Frequency and tissue microstructure at cellular and sub-cellular levels (2) and water-protein exchange (3, 4). In a study using bovine serum albumin solution, the exchange effect on water resonance frequency was estimated as approximately half of the susceptibility effect, but with the opposite sign (3). Another in vitro tissue study using reference chemicals (TSP and Dioxane) reported the same trend (5). However, it is very difficult to provide direct in-vivo validation of the role of liable NH (amide) and OH (hydroxyl) groups in protein and macromolecules. One approach is to saturate each group by frequency selective irradiation (CEST) (6) and to evaluate its effect on tissue frequency shift. In this study we provide theoretical treatment of such an experiment and compare it with in vivo experiments.

Methods: Standard Bloch equation describing two-pool exchange with chemical shift has been established. The T1 decay of the system and intrinsic T2 decay for tissue water pool do not contribute significantly to the results and are ignored. The following parameters were used in the simulations: chemical shift of 3.5 ppm (NH) and 2.6 ppm (OH); intrinsic T2 of protons of 0.5 ms (NH) (8) and 10 ms (OH); exchange rate to tissue water pool as 100 sec⁻¹ (NH) (7) and 1000 sec⁻¹ (OH) (8). All experiments were performed on a 3.0 T Siemens Trio scanner using three healthy volunteer subjects. Global frequency selective saturation RF pulses were applied before a standard Siemens multi-echo GRE 2D sequence: TR of 500 ms, TE of 7 and 17 ms, FOV of 256 × 192 mm², slice thickness of 4 mm and a sampling matrix of 192×144. We used a bandwidth of 170 Hz for the saturation RF pulses and a bandwidth of 1500 Hz for the excitation RF pulses. As a result, the proton groups of interest were excited during imaging. To determine the absolute frequency shift effect from a single proton group, two images were acquired in an interleaved manner: one with RF saturation and another as control. The absolute tissue frequency differences between the CEST-prepared and the control images were calculated.

Results: Figure 1 shows the simulation result on tissue absolute frequency shift and tissue signal amplitude (T2 effect) from NH and OH groups. The proton pool size ratio was assumed to be 1:100. NH proton exchange mainly contributed to the tissue apparent T2 decay, while the contribution to water frequency shift was very small (<0.2 Hz at TE~10 ms). Although the potential contribution from OH group could be considered significant (between 0.3 and 0.4 Hz at TE>10 ms), the difference detectable by CEST is very small for TE>5 ms. Maximum frequency difference (0.13 Hz) occurred at TE of 1.5 ms.

Fig. 2 shows the relative frequency contrast maps of the control and after the application of NH and OH saturation RF pulses. No apparent changes were detected. Fig 3 illustrates the absolute frequency shift by CEST effect from amide protons during the two acquisitions (differed by spatial resolution). The amplitude was much smaller than that observed GM/WM frequency contrast without any recognizable anatomical pattern, possibly originating from imaging artifacts, or limited by SNR. Because the SNR of the GRE image about 200, the error on frequency estimation corresponded to 0.08 Hz.

Discussions: In this study, we investigated the effect of proton exchange of NH and OH groups on water MR frequency shift through Bloch simulations and by selective saturation during in-vivo experiment. Both results indicate that the chemical exchange effect on water proton resonance frequency is difficult to be resolved by CEST approach, unless the phase evolution profile of the MR signal can be acquired with sub-millisecond echo time. The study of frequency shift effect by hydroxyl groups at such short time scale may potentially lead to the same sensitivity as CEST.

References: 1. Duyn, et al., PNAS 2007;104:11796; 2. He and Yablonskiy, PNAS 2009; 106:13558; 3. Zhong, et al., Neuroimage 2008;40:1561; 4. Luo, et al., JMR 2009; 202:102; 5. Shmueli, et al., MRM 2010; on-line; 6. Ward, et al., JMR 2000;143:79; 7. Liepins and Otting, MRM 1996; 35:30. 8. Mougin, et al., Neuroimage 2010; 49:272;

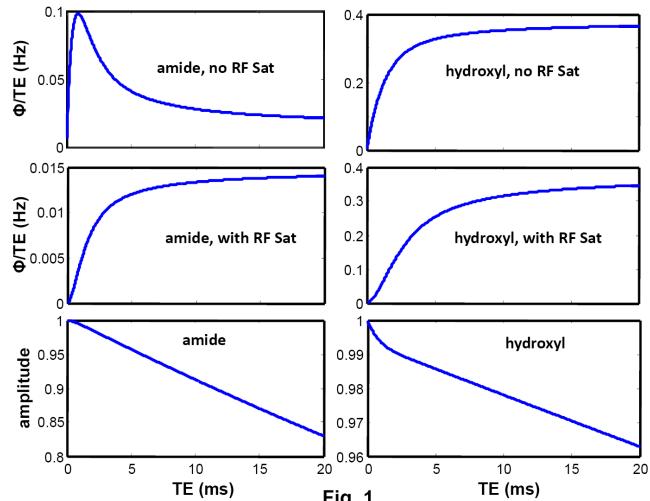


FIG. 1

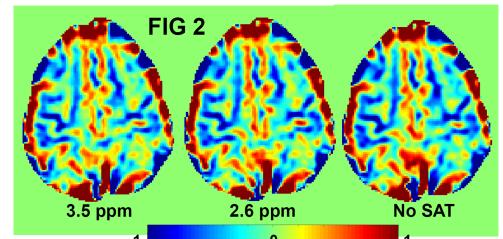


FIG 2

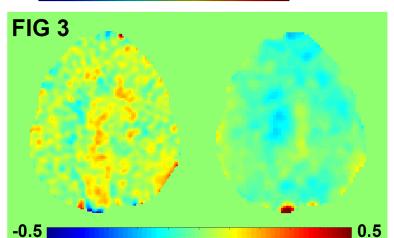


FIG 3