Comparison of chemical exchange saturation transfer (CEST) and T1ρ MRI for measurement of proton chemical exchange between metabolites and water at 7T

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Introduction: Chemical exchange between labile protons of proteins and water protons can make Magnetic Resonance Imaging (MRI)sensitive to information about the concentrations of endogenous proteins and their environments. Chemical Exchange Saturation Transfer (CEST), a technique which uses the attenuation of bulk water magnetization through magnetization exchange with saturated labile protons, has become a popular method for measurement of metabolites with exchangeable protons[1,2]. While CEST has been well established over the past decade as method for measuring proton exchange, spin-lattice relaxation in the rotating frame ($T_{1\rho}$) is another technique which is sensitive to proton exchange but has yet to be thoroughly investigated [3-5]. In this abstract, we compare the sensitivity of CEST and $T_{1\rho}$MRI for imaging proton exchange and showed that at 7T, $T_{1\rho}$MRI has a higher sensitivity.

Theory: In order to remove the direct water saturation which plagues CEST imaging, CEST proton transfer ratio (PTR) is thus quantified by

$$CEST\ \%\ Contrast = \frac{M_{sat}(-offset) - M_{sat}(+offset)}{M_O} * 100\% \quad (1)$$

where [M_{sat} (+offset)]/ [M_{sat} (-offset)] are the magnetization signal at the positive (labile proton saturation site) and negative (no labile proton saturation) offsets with respect to water respectively and M_0 is the control magnetization signal without selective irradiation[6].
For $T_{1\rho}$imaging, applying a low amplitude spin-lock (B_1) results in relaxation highly dependent on chemical exchange. However, when a high amplitude spin-lock is applied, the chemical exchange effects are minimized. Thus by subtracting $T_{1\rho}$ maps acquired at high($T1\rho_{Low\ B1}$) and low spin-lock($T1\rho_{Low\ B1}$) amplitudes, the effect of the chemical exchange can be isolated.We thus define the effect due $T_{1\rho}$ PTR as

$$T1\rho\ \%\ Contrast = \frac{T1\rho_{HighB1} - T1\rho_{LowB1}}{T1\rho_{HighB1}} * 100\% \quad (2)$$

Method: A sample of Lysine, which has an amino group (-NH_2) capable of exchanging protons with bulkwater, was prepared at a concentration of 20 mMin deionized water at a pH of 6.0. Lysine –NH_2has a resonance frequency of 3 ppm relative to water resonance. Imaging experiments were performed onSiemens 7.0T whole body MRI scanner using a custom built radiofrequency coil. Imaging was performed using a CEST/ $T_{1\rho}$magnetization preparation pulse followed by a turbo spin echo (TSE) readout. CEST magnetization preparation utilized a long irradiation pulse. CEST Images were acquired with a 3000 ms saturation pulse at +3 ppm/-3ppm at various B_1 in order to determine a maximum CEST effect. The $T_{1\rho}$ magnetization preparation pulse consisted of a 90º RF pulse which tips the longitudinal magnetization into the transverse plane followed by two spin-lock pulses of equal length and amplitude. The spin-lock pulses are phase alternating in order to refocus the effect of an inhomogeneous B_1 field. $T_{1\rho}$ maps where constructed for high (2000 Hz) and low (100 Hz) spin-lock amplitudes from images acquired at various spin-lock lengths.

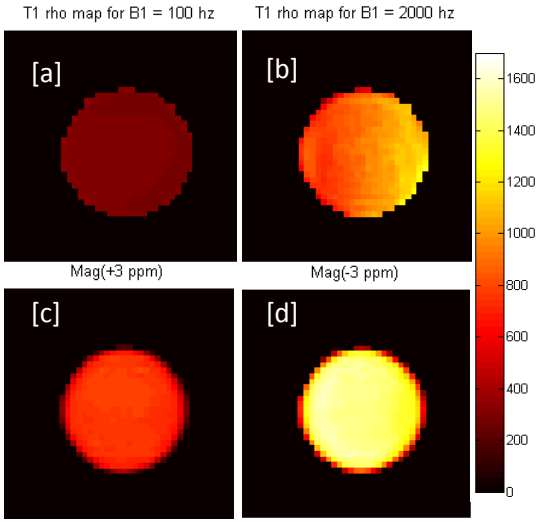

Figure 1: $T_{1\rho}$ maps taken [a] low (150 Hz) and [b] high (2000 Hz) spin-lock amplitudes. CEST images at [c] +3 ppm and [d] -3 ppm. [a,c] show images that exhibit proton exchange while [b,d] are baseline images that were unaffected by proton exchange. Images show only the 20 mM lysine sample at a pH of 6.0

Results and Discussion: Figure 1 shows $T_{1\rho}$ (a,b) images and CEST (c,d) maps of the lysine sample only with (a,c) and without (b,d) the presence of chemical exchange. As seen from the figures, both techniques are sensitive to chemical exchange however $T_{1\rho}$ imaging shows higher sensitivity. This is further exhibited in figure 2 which shows the % change due to chemical exchange for each respective method computed using the images in Figure 1 and equations (1) and (2). Images in figure 2 also show the de-ionized water, in which the NMR tubes containing the lysine samples were held. CEST shows an average change of 37.2 % while $T_{1\rho}$ shows an average change of 67.0%. Equally important to % change due to chemical exchange, both images show that there were minimal differences in the water between images taken to include and exclude the presence of chemical exchange. Small differences can be due to noise and magnetic field inhomogeneities. However, the lack of difference seen in the water proves that differences seen in the lysine samples are due to chemical exchange and not to intrinsic properties of the techniques themselves.
Imaging at higher static magnetic fields is very important for imaging of proton exchange in both of these methods.For CEST imaging this higher sensitivity is explained by a larger chemical shift difference between solute and water which decreases the effects of direct saturation of water. Additionally, the T_1relaxation rate of water decreases as field strength increases. This prolongs the storage of transferred saturation in the water pool thus resulting in an increase in PTR. For T1p imaging, relaxation rates scale as the square of the difference in proton chemical shift. As this difference increases linearly with magnetic field, $T_{1\rho}$ chemical exchange effects vary quadratically with the static magnetic field.

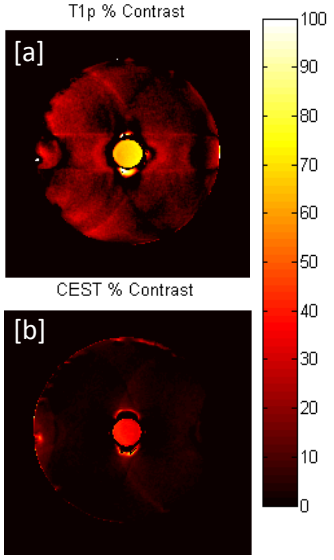

Figure 2: Percent change due to proton exchange with [a] $T_{1\rho}$ imaging and [b] CEST imaging. Images show a 20 mM lysine sample surrounded by deionized water.

Conclusion: In this study we demonstrated that while both CEST and $T_{1\rho}$imaging can be used to image proton exchange between solutes with exchangeable protons and water, $T_{1\rho}$imaging is more sensitive to these processes. Specifically, in the lysine sample studied here, the $T_{1\rho}$ method has roughly a factor of two higher sensitivity compared to CEST. Further, this sensitivity differences are expected to depend on the chemical exchange rates of the exchangeable protons. Further studies are in progress to model these effects and determine the optimal experimental conditions applicable to each method.

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