Introduction

CEST imaging is an important molecular MRI technique that can generate contrast based on the saturation transfer between bulk water protons and low-concentration solute labile protons. Because RF radiation to saturate the solute labile protons induces large direct water saturation and conventional MT from semi-solid macromolecules, the quantitative CEST measurement and theoretical simulation are complicated. In this study, we investigated the mixed MT, APT, and NOE effects in a multi-pool proton exchange model with the a priori fitted two-pool MTC information.

Methods

Six human glioblastoma-bearing adult Fisher 344 rats were scanned on a horizontal bore Bruker 4.7 T. CEST image data were obtained using a fat-suppressed spin-echo pulse sequence with a single-shot EPI readout (TR = 10 s; TE = 30 ms; matrix size = 64 x 64 mm2; FOV = 32 x 32 mm2; slice thickness = 1.5 mm; and RF saturation time = 4 s). Two sets of z-spectra with 26 frequency offsets were acquired to quantify conventional MT, NOE, and APT effects, using three RF saturation powers (0.5, 1.3, and 2.1 μT): (1) Z_{21−21ppm} 21 to -21 ppm at intervals of 1.75 ppm for MT modeling with the super-Lorentzian lineshape; (2) Z_{6−6ppm} 6 to -6 ppm at intervals of 0.5 ppm for the quantification of NOE and APT effects. The wide-offset data were fitted to two-pool MT model with the super-Lorentzian lineshape. Data points of small frequency offsets between 7 and -7 ppm in B0-corrected Z_{21−21ppm} were excluded (Z_{21−21ppm}) to avoid APT and NOE contributions prior to MT modeling. Next, a multi-pool exchange model was analytically solved with the fitted two-pool MT information, and the parameter fitting was performed using the minimum norm estimate. The post-hoc test was performed for p < 0.05: <: significantly smaller; >: significantly larger; not indicated: no significant difference.

Results and Discussion

The two-pool MT model accurately behaved the semi-solid MT system for wide frequency offsets as shown in Fig. 1. The MT parameters (except T_{2m}) were significantly different between the normal tissue and the tissue in the tumor center or rim as shown in Table 1. Four-pool APT and NOE exchange model fitted the Z_{6−6ppm} behavior very well as shown in Fig. 2. As expected (Table 2), the APT-related pool sizes of the tumor center and the tumor rim were significantly larger than that of the normal tissue, while the NOE-related pool sizes of the tumor center and the tumor rim were significantly smaller than that of the normal tissue.

Further, by subtracting experimental data (Z_{6−6ppm}) or simulated four-pool data from Z_{EMR}, APT^s and NOE^s signals could be obtained (Fig. 3). The APT^s signals in all ROIs were lowest at the RF saturation power of 0.5 μT and seemingly peaked at 1.3 μT, while the NOE^s signals were lowest at 2.1 μT. The APT^s signals of the tumor center and the tumor rim were both significantly higher than those of the normal tissue across all power levels (p < 0.05). The NOE^s signals were generally lower in the tumor center and rim than in the normal tissue, which reached statistical significance (p < 0.05) in the tumor center at 1.3 μT.

Conclusions

Four-pool fitting using extrapolated semi-solid MTC parameters as prior known information could reduce the over-fitting errors. The quantitative results would provide some insight into the mechanisms of APT and NOE effects in tissue.

References