Imaging Acute Ischemic Tissue Acidosis using a Relaxation-Compensated multi-slice Amide Proton Transfer (APT) MRI

P. Z. SUN[1], Y. Murata[2], J. Lu[2,3], X. Y. Wang[2], E. H. Lo[2], and A. G. Sorensen[1]

[1]Radiology, A. A. Martinos Center for Biomedical Imaging, Charlestown, MA, United States, [2]Neurology, Massachusetts General Hospital, Charlestown, MA, United States, [3]Radiology, XuanWu Hospital, Beijing, China, People's Republic of

INTRODUCTION CEST imaging provides a sensitivity enhancement mechanism that enables MRI, which usually detects bulk water signal only, sensitive to certain labile metabolites and their byproducts. In particular, the chemical exchange between bulk water and endogenous amide protons is pH-dependent, which has been dubbed amide proton transfer (APT) imaging. As ischemic tissue pH decreases subsequent to abnormal glucose/oxygen metabolism, pH-weighted APT imaging may serve as a surrogate metabolic imaging marker, in complementary to perfusion and diffusion MRI for delineation of ischemic tissue. One limit for previous pH-sensitive APT imaging is that they are all single slice only. Given that pathologies such as stroke and cancer are spatially heterogeneous, APT imaging with sufficient volume coverage is necessary in order to fully evaluate the diagnostic power. Here, we propose a fast volumetric APT imaging approach that acquires multi-slice CEST images immediately after a single long CW RF irradiation, and the relaxation-induced loss of APT contrast is compensated during post-processing. The proposed technique is verified by numerical simulation and validated with a tissue-like dual pH phantom. When translated to image acute animal stroke, the proposed technique detected heterogeneous distribution of PWI, pH and DWI lesions, permitting future study to fully elucidate the diagnostic value of pH-weighted APT MRI.

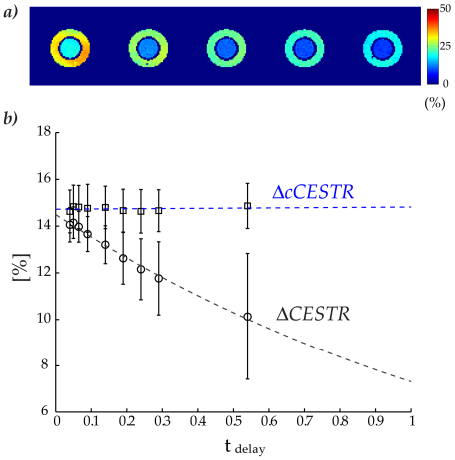

Fig. 1 a) multi-slice CEST imaging from a tissue-like dual pH phantom, showing loss of CEST contrast due to relaxation. b) CESTR (circle) before correction and cCESTR (squares) after the proposed relaxation compensation.

Fig. 2, a fused PWI-APT-DWI lesion from a representative embolic stroke animal, 2 hr after stroke. It shows large PWI-DWI mismatch, while the APT approximates PWI lesion.

THEORY For the case of a long CW RF irradiation, the CEST ratio (CESTR) is given as,

$$CESTR = k_{ws} / r_{1w} \cdot \alpha \cdot (1-\sigma) \cdot \left(1 - e^{-r_{1w} t_{irad}}\right).$$

where α is the labeling coefficient, σ is the spillover factor, t_{irad} is the RF irradiation duration, $k_{sw,ws}$ are the chemical exchange rates from labile proton to bulk water and vice versa, with $r_{1w,s}=R_{1w,s}+k_{ws,sw}$, $r_{2w,s}=R_{2w,s}+k_{ws,sw}$, in which $R_{1w,s}$ and $R_{2w,s}$ are the intrinsic longitudinal and transverse relaxation rates of bulk water and labile groups, respectively. After the labeling RF pulse, magnetizations recover toward equilibrium state as,

$$CESTR(t) = k_{ws} / r_{1w} \cdot \alpha \cdot (1-\sigma) \cdot e^{\left(-r_{1w} + k_{sw} k_{ws} / (r_{1s} - r_{1w})\right) t}$$

It can be shown for dilute labile protons of intermediate chemical exchange, the relaxation rate is approximately equal to the intrinsic bulk water relaxation time, and thus, the compensated CESTR (cCESTR) can be obtained as,

$$cCESTR \approx CESTR(t) \cdot e^{R_{1w} t}$$

MATERIASL AND METHODS The dual-pH gel phantom contains creatine (150 mM) and low gelling point Agarose (3%) mixture, with the inner and exterior compartment pH titrated to 5.6 and 6.6, respectively. All animal experiments were carried out in accordance with guidelines approved by Small Animal Research Committee of Massachusetts General Hospital (SARC, MGH). Adult male Wistar rats weight 280-360 grams (n = 7) with embolic stroke received MRI at 4.7 T, with two animals (n=2) excluded from image analysis due to hardware malfunction and clot autolysis.

RESULTS Fig. 1a shows representative multi-slice CEST images of a dual-pH phantom with an inter-acquisition time of 250 ms; the delay time between acquisition and irradiation RF was 26, 267, 507, 747 and 988 ms for the five slices, respectively. The CEST contrast for the outer and inner compartment was 32 ± 3% and 19 ± 2% for the first slice (TE=26 ms), and it decreased to 18 ± 1% and 9 ± 1% for the fifth slice (TE=988 ms), respectively. Fig. 1b shows the mean of experimentally obtained CESTR (circles) and relaxation-compensated cCESTR values (squares) for five slices as a function of the delay time. The decay rate obtained from the least square fitting of Fig. 1b was 0.34 s^{-1}, in good agreement with the directly measured longitudinal relaxation rate of 0.37 s^{-1}. It is worthwhile to note that the extrapolated ΔCESTR and ΔcCESTR nearly converged at zero delay time, being 14.5% and 14.7%, respectively. Fig. 2 shows fused PWI-APT-DWI lesions from a representative embolic stroke animal acquired 2 hr after clot injection. It shows that PWI and APT lesions are approximately equal, while both are significantly larger than DWI lesion. The CBF, APT and ADC for the contralateral normal area is 1.2 ± 0.47 ml/(g·min), 2.94% (normalized) and 0.76 ± 0.05 μm²/ms, respectively, while the corresponding values for the ipsilateral ischemic area is 0.35 ± 0.33 ml/(g·min), 0.6%±0.7% and 0.57 ± 0.06 μm²/ms.

REFERENCES 1)Zhang S et al, JACS 2003; 2)Aime S et al, MRM 2003; 3)Zhou J et al. Nat Med. 2003. 3)Sun PZ et al. MRM 2007. 4)Sun PZ et al. JCBFM 2007.