Power Optimization of In-vivo Chemical Exchange Saturation Transfer (CEST) contrast for pH weighted Imaging

P. Z. Sun[1,2], J. Zhou[1,2], J. Huang[3], P. van Zijl[1,2]

[1]Russel Morgan Radiology Department, Johns Hopkins University, Baltimore, MD, United States, [2]F.M.Kirby Center, Baltimore, MD, United States,

[3]Neurosurgery Department, Johns Hopkins University, Baltimore, MD, United States

INTRODUCTION

Chemical exchange saturation transfer (CEST) imaging provides a unique contrast through the exchange between solute protons and bulk water protons [1]. It can detect tissue acidosis and elevated protein content in acute ischemia and animal tumor models [2,3]. Conventionally, a continuous wave (CW) RF pulse is applied at the solute proton frequency and the saturation is transferred to the bulk water. The obtained MT-type contrast depends on the exchange rate and chemical shift of the labile solute protons as well as experimental parameters such as the duration and strength of the irradiation pulse [4]. The in vivo endogenous CEST effect, also called the amide proton transfer (APT) contrast [2,3], is only a few percent. Therefore, it is necessary to maximize the CEST sensitivity by optimizing the irradiation pulses. It has been reported previously that the CEST effect in poly-l-lysine solution is irradiation power dependent, and there are significant direct saturation effects on bulk water (spillover effects) [5, 6] when the pulse is stronger than the optimal power. The in-vivo CEST process is further complicated due to the presence of conventional MT effects. We model the CEST process using an empirical formula considering both the saturation transfer and spillover effects at low to intermediate power. The model is shown to be able to correctly describe the effects of irradiation on endogenous CEST process and allowed us to achieve a significant improvement of the contrast when using pH-weighted imaging in an acute ischemia animal model.

MATERIALS AND METHODS

Adult male Wister rats (n = 3) received MRI one hour after permanent middle cerebral artery occlusion (MCAO) at 4.7 T. Multi-parametric imaging including cerebral blood flow (CBF), APT, apparent diffusion constant (ADC), and T_2 maps were acquired to delineate the ischemic area. Single slice images were acquired using one shot EPI (slice thickness 2 mm, FOV 32x32 mm^2, matrix 64x64). In the CEST experiments, exchangeable amide protons at the offset of +3.5ppm from the water resonance were selectively saturated (CW pulse, 4s) and the irradiation power varied from 0.25, 0.5, 0.75, 1, 1.5, 2, to 3 μT. A reference MT image at the offset -3.5ppm and a control image (S_0) without the RF saturation pulses were also acquired. The pH weighted image were processed using the equation: $MTR_{asym}(3.5ppm) = 100\% \times (S_{sat}(-3.5ppm) - S_{sat}(3.5ppm))/S_0$.

RESULTS

The APT contrast between the contralateral brain and CBF deficit area was analyzed as a function of irradiation power (Fig. 1). This contrast increased initially with the RF power to 2.5%, then decreased with further power increase, which we attribute to concomitant direct water saturation (spillover) and conventional MT effects. Ensemble exchange rate and pool ratio were fitted to be 13.6 s^{-1} and 746, respectively, in agreement with reported values[2]. It shows that the maximal APT contrast (2.5%) during acute ischemia can be acquired with an irradiation power of 0.75 μT at 4.7T. It is a significant improvement over previously reported value (1.9%) acquired at suboptimal conditions (1.5 μT). Fig. 2 shows the CBF and pH-weighted maps using the optimal irradiation pulse on a representative animal. The CBF map showed significant flow reduction across the ischemic right cerebral hemisphere. The pH-weighted image reflects pH reduction across the CBF deficit area (hypoperfused area with CBF two standard deviations or more reduced from the mean of the contralateral area). Area with most severe CBF reduction (red arrows) appeared as hypointense on the pH-weighted image. pH-weighted images acquired at suboptimal conditions showed much reduced contrast both within CBF deficits areas and between deficits and contralateral area.

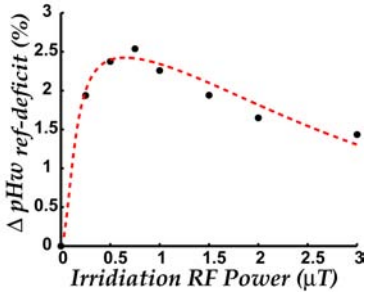

Fig. 1, RF power dependence of the pHw contrast. Red line represents a least square fit against a 2-pool model.

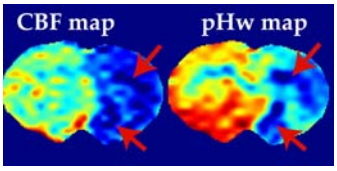

Fig. 2, CBF and pHw, MRIs show deficits over the right ischemic hemisphere post MCAO operation. Arrows show areas of the most severe CBF and pH deficits.

DISCUSSION

The in-vivo CEST process is very complex with conventional MT and concomitant spillover effects in addition to the CEST process. Therefore, it takes at least a 3-pool model[7] to reasonably describe it and it is not easy to quantify some of the key parameters. However, because conventional MT effects are mainly symmetric, it may be treated with bulk water as an ensemble pool when the spillover effects are considered during in-vivo endogenous CEST contrast imaging. It is expected that the sensitivity of CEST imaging can be improved at high field at which non-specific saturation effects reduce. Furthermore, this optimization reduces the experimental duration and energy deposition, which is suitable for clinical applications.

REFERENCES

1)Ward & Balaban MRM 2000;44:799-802 2) Zhou et al. Nat Med 2003;9:1085-1090 3) Zhou et al. MRM 2003;50:1120-6. 4) Graham & Henkelman JMRI 1997;7:903-912. 5) Spencer et al. JMRB 1993; 101:294-296. 6) Sun et al. JMR 2005;175:193-200. 7) Adler et al. JMR 1996;110:1-8.