Amide proton transfer (APT) imaging using saturation transfer versus inversion transfer -- which is better?

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INTRODUCTION

In vivo amide proton transfer (APT) imaging is a particular type of chemical exchange saturation transfer (CEST) imaging that utilizes the exchange between labile amide protons and bulk water[1,2]. In addition, it has been shown that pH-sensitive APT imaging may provide complimentary information to commonly used CBF and DWI MRI for identifying ischemic tissue. For APT imaging, a CW pulse is commonly used to saturate labile protons for duration comparable to the bulk water T_1, followed by fast imaging (EPI). For clinical scanners, however, it is more common to use short RF trains due to hardware and RF duty cycle limit. In this work, we investigated and compared APT imaging using CW and rectangular RF pulse trains, and provided preliminary results for optimizing pulsed APT imaging of acute ischemia.

MATERIALS AND METHODS

All experiments were performed on 4.7T Bruker Biospec Imager. The phantom was a 1% poly-l-lysine (PLL, pH=7.4, T=20°C) solution. In addition, an acute ischemic animal 1hr post middle cerebral artery occlusion (MCAO) was studied using APT imaging with pulse trains irradiation. The RF power for pulse trains was varied from 0.5, 0.75, 1, 1.5, 3 to 5 μT. The RF duty cycle was 50% and the pulse durations were 2, 5, 8, 10, 12, 16 and 25 ms, with the total irradiation time being 4 sec. A CW-APT image (B_1=0.75 μT, duration 4 sec) was also acquired for reference. In addition, CBF (CASL), trace ADC (single-shot trace DWI), T_1 (inversion recovery) and T_2 (spin echo) maps were obtained after the pulsed APT imaging.

RESULTS & DISCUSSION

Phantom: The APT effect using pulsed RF was small initially, but increased to 10% at RF duration of 16 ms, compared to APTR=12% with CW pulse (B_1= 1 μT). For RF duration longer than 10 ms, the APTR decreased and remained at 5%. This can be attributed to spin longitudinal relaxation during the inter-pulse delay, which effectively reduces the saturation.

In vivo: Fig.1 shows CBF, ADC, T_1 and T_2 maps of an ischemic animal (top row) after unilateral MCAO . The CBF map shows severe cerebral hypoperfusion over the right side of brain, with a small ADC lesion over the right ventral pallidum (VP). In addition, the ADC lesion area also appears hyperintensive in the T_1 and T_2 maps and this can be attributed to the extensive delay between MCAO and the time when relaxation images were taken (~4hr). A B_0 map was derived by fitting the z-spectrum for the center frequency using high order polynomials (Matlab), as it is known that the center region of the z-spectrum is very sensitive to B_0 shifts. The data indicate that, within the brain, the B_0 was reasonably homogeneous (~0 Hz), with the most shift over the right cortex and left temporal lobe area. Such a small B_0 shift does not appreciably affect the APT imaging as the amide protons are at 8.3ppm (700 Hz at 4.7T), such a small B_0 shift does not affect measured MTR.

Representative APT images maps using pulse trains were shown in Fig. 1 (bottom row), with the reference APT image (CW saturation) shown on the right. The RF powers were the same (0.75μT) for easy comparison. For APT images with pulse trains, when the pulse duration increased from 2 to 5 ms, the lesion area became more hypointensive. At 8 ms, the contrast improved further, however there were noticeable banding artifacts over the contralateral normal area. At 10 ms, the MTR_{asym} became very similar as the reference APT map. Such a homogeneous APT contrast was expected as the animal had permanent MCAO and its CBF map showed large flow reduction over the right brain. The contrast between the contralateral normal and ischemic regions was studied as a function of the flip angle (Fig. 2). It initially improved with flip angle (α) for all powers. When the flip angle was increased further, the APTR of low RF powers (0.5 and 0.75μT) reduced and became even positive. On the other hand, for intermediate powers (1 and 1.5μT), the APTR continued to increase and peaked around a flip angle of 180°, as expected (Fig. 2b). When the minimal APTR of each RF power against its flip angle was investigated, it showed that the maximal APTR was about -4.6% at 1 and 1.5 μT with α=180°. (Fig. 2b) This contrast almost doubled that obtained using the CW APT imaging. Such an enhancement may be attributed to the fact that the amide protons were inverted (S_{amide}=-1) at the optimal condition for pulse train APT imaging in comparison with saturation (S_{amide}=0) using a CW pulse. At higher RF powers, however, the ischemic regions appeared heterogeneous (3 μT), and even hyperintensive (5 μT), which obscured the sought after APT effect (-2~3%), probably because of large saturation due to the asymmetric conventional MT effect and probably some direct water saturation

This study showed that the most APT contrast can be obtained at RF duration and power of 8-10 ms and 0.75-1.5 μT. However, it also appears that there can be severe artifacts at the condition for the maximal APTR (Fig.1, 8ms). Unlike solution phantom, there are concomitant asymmetric conventional MT effects for in vivo APT imaging[4]. In addition, the excitation bandwidth of pulse trains is broad, and it may label an ensemble of exchangeable protons. Moreover, it can affect both the label and reference images simultaneously, and introduce additional direct saturation compared to the CW pulse. Therefore, further study of the contrast and artifact of APT imaging using RF pulse trains is necessary.

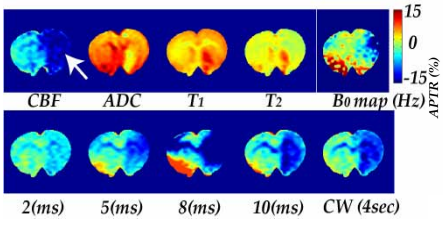

Fig. 1, CBF, ADC, T1, T2 and B0 field maps (top). Bottom shows pulsed APT images, CW APT is shown on the right.

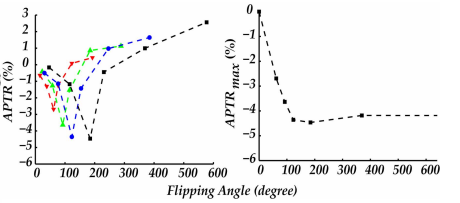

Fig. 2, APTR as a function of RF power and flip angle (left). The right shows the maximal APTR of each power as a function of its flip angle.

REFERENCES: 1) Zhou et al. Nat 2003;9:1085-90. 2)Ward et al. MRM 2000;44:799-02 3)Sun et al. 13thISMRM. 4)Pekar et al. MRM 1996;36(2): 217-24.