

Interleaved Parallel Transmission Saturation Scheme for 3D Amide Proton Transfer Imaging of Brain Tumors at 3 Tesla

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Introduction

Amide proton transfer (APT) imaging¹ can provide endogenous contrast related to mobile protein content in tissue, through saturation labeling of exchangeable backbone amide protons, followed by chemical exchange of saturated protons with water protons. For APT imaging on animal systems, RF saturation is typically applied using a continuous pulse of several seconds to maximize saturation effects. On clinical systems, however, restrictive RF specifications (amplifier duty cycle and unblank time) typically limit lengths of RF pulses to less than about 500 ms. Although pseudo-continuous RF saturation pulses (a train of pulses separated by brief delays²) can accommodate part of the limitations, typically only 35-45% of the potential APT contrast is obtained. Recently, a new method based on time-interleaved, parallel RF transmission (pTX) was proposed for enhanced sensitivity in APT imaging.³ In principle, this approach allows arbitrarily long RF saturation pulses. In this study, the pTX technique was applied to 3D APT imaging of brain tumors at 3 Tesla.

Materials and Methods

Experiments were performed on a Philips Achieva 3T pTX scanner, equipped with a 32-channel phased-array head coil for reception. A fast gradient- and spin-echo (GRASE) 3D APT-MRI sequence (Fig. 1) was used.² The RF saturation section ($t_{\text{sat}} = 2$ sec) consisted of 20 time-interleaved block pulses on two RF transmit channels (100 ms duration; 2 μT amplitude). The GRASE 3D image acquisition was configured with TSE = 22 in RL and EPI = 7 in FH. FOV = 212 (AP) \times 186 (RL) mm^2 with 2.2×2.2 mm^2 resolutions; 15 points (slices) of 4.4 mm thickness covered 66 mm in FH; SENSE acceleration = 2 in RL; TR = 3 sec; SAR < 2.85 W/kg. APT sequence parameters (saturation time; saturation power) were optimized for maximum APT effect in phantom experiments (a box of homogenous eggwhite with 10% protein concentration) and scans of normal subjects. The optimized protocol was tested on three brain tumor patients, who provided written informed consent as required. In the phantom experiments, a full z-spectrum with 26 frequency offsets (-6 to 6 ppm from water, interval 0.5 ppm) was acquired. In the patient scans, APT imaging was acquired with a six-offset protocol ($\pm 3, \pm 3.5, \pm 4$ ppm; 2, 8, 2 averages, respectively).⁴ The total scan time was 10 min 42 sec. APT signals were calculated using a magnetization transfer ratio-asymmetry analysis at ± 3.5 ppm, including B_0 inhomogeneity corrections.

Results and Discussion

Fig. 2 shows z-spectra and MTR_{asym} spectra acquired on the homogeneous eggwhite (10% protein), using the new pTX-based 3D GRASE sequence ($t_{\text{sat}} = 2$ sec; amplitude = 2 μT). The pTX-APT sequence produced uniformly large APT effects (black arrow) across all slices. The average APT signal [i.e., $\text{MTR}_{\text{asym}}(3.5\text{ppm})$] was $14.8\% \pm 0.6\%$, much higher than the previous results (5%–6%) on the similar phantom using the pseudo-continuous RF saturation pulses ($t_{\text{sat}} = 0.8$ sec).³ We found that the eggwhite APT signals (if normalized to $\text{TR}^{1/2}$) started to decrease at $t_{\text{sat}} \sim 2$ sec. We chose 2 μT as power level, because the measured APT-MRI signal of the normal brain tissue is almost nulled due to the negative conventional MTR asymmetry, which allows us to better visualize lesions. To show that the new approach can be used *in vivo*, Fig. 3 shows an example of pTX-based APT and conventional MR images for a patient with suspected recurrent glioma versus radiation necrosis. Conventional $T_2\text{w}$ and FLAIR images showed a large area of hyperintensity (compared to contralateral). Post-contrast $T_1\text{w}$ images revealed two heterogeneously enhancing regions. The APT signal has recently been shown to have potential as a biomarker for active tumor that can help distinguish between active glioma and radiation-induced necrosis more accurately, a radiologic dilemma that has remained for decades.¹ In this patient, when compared to the MRI exam three months ago, region 1 (red arrow) had an increased size, and region 2 (white arrow) was unchanged to minimally decreased in size. This suggests that region 1 is very likely associated with tumor recurrence, and region 2 associated with radiation necrosis. As expected, on APT images, region 1 showed APT hyperintensity (feature of active tumor), while region 2 had a low APT signal (feature of radiation necrosis).

Our results demonstrate that time-interleaved pTX can maximize APT-MRI effects on clinical scanners by avoiding RF amplifier limitations to the saturation pulses, while staying within SAR limits. The pTX-based 3D sequence can be applied equally to other CEST imaging applications.

References: (1) Zhou et al. Nat. Med. 2011;17:130. (2) Zhu et al. MRM 2010;64:638. (3) Keupp et al. ISMRM 2011, p.710. (4) Zhou et al. MRM 2008;60:842.

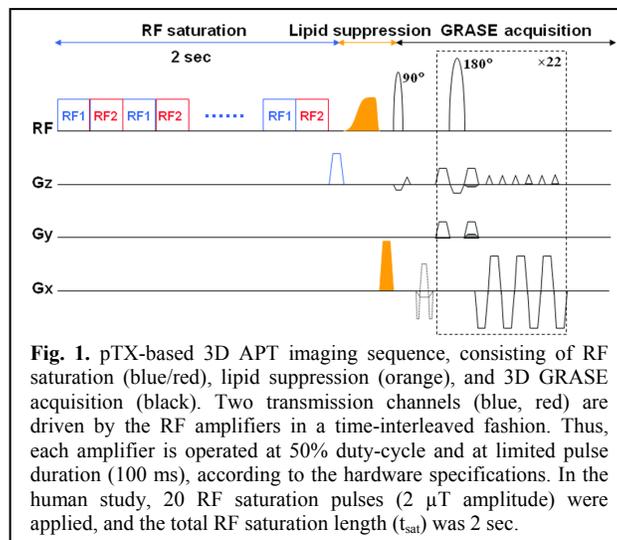


Fig. 1. pTX-based 3D APT imaging sequence, consisting of RF saturation (blue/red), lipid suppression (orange), and 3D GRASE acquisition (black). Two transmission channels (blue, red) are driven by the RF amplifiers in a time-interleaved fashion. Thus, each amplifier is operated at 50% duty-cycle and at limited pulse duration (100 ms), according to the hardware specifications. In the human study, 20 RF saturation pulses (2 μT amplitude) were applied, and the total RF saturation length (t_{sat}) was 2 sec.

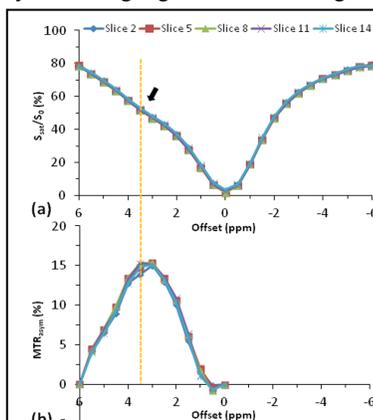


Fig. 2. z-spectra (a) and MTR_{asym} spectra (b) from a homogenous eggwhite phantom. Five of 15 slices are shown.

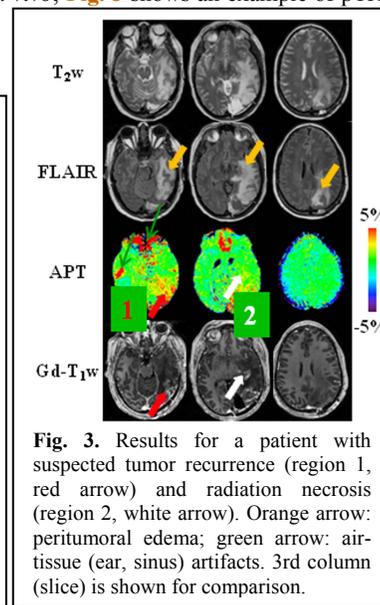


Fig. 3. Results for a patient with suspected tumor recurrence (region 1, red arrow) and radiation necrosis (region 2, white arrow). Orange arrow: peritumoral edema; green arrow: air-tissue (ear, sinus) artifacts. 3rd column (slice) is shown for comparison.