Towards an Optimized and Standardized Amide Proton Transfer (APT) MRI Sequence and Protocol for Clinical Applications

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Target audience: Basic scientists and clinical scientists who are interested in the development of APT and CEST imaging technology.

Purpose

Amide proton transfer (APT) imaging is a novel molecular MRI technique that generates image contrast based on endogenous cellular proteins in tissue. However, the current APT-weighted (APTw) imaging protocols vary substantially among institutes, far from being optimized, due to scanner hardware constraints (particularly amplifier duty cycle) and specific absorption rate (SAR) requirements. The time-interleaved, parallel RF transmission (pTX) method proposed recently is capable of reducing amplifier limitations and detecting appreciable APT-MRI effects on clinical scanners[1]. As such, this approach may be a suitable choice for standardization of clinical APT imaging sequences. Towards this end, we quantitatively assessed conventional (continuous wave) and pTX-based APTw imaging, the latter with different fast readout sequences.

Methods

Experiments were performed on a 3T scanner (Achieva, Philips) using body coil transmit and a prototype 32-channel phased-array coil for reception or a transceiver (TR) head coil. A bottle of homogenous eggwhite solution with 10% protein concentration, healthy human subjects (n = 5), and a patient with a glioblastoma were imaged.

Two RF saturation schemes were used to compare signal-to-noise ratios (SNRs) and APTw signal intensities: 1) a continuous-wave long block pulse (CW, as usually used in animal scanners), and 2) a pTX-based, pseudo-CW pulse train with a sinc-gauss pulse shape. The same saturation time (1.6 sec) and power (2 μT, mean for pTX) were used. For pTX, ten different 3D fast imaging schemes were used: turbo field echo (TFE factor = 110) with flip angles of 10° (pTX-TFE[1]), 20° (pTX-TFE[2]), and 30° (pTX-TFE[3]); turbo field echo (TFE factor = 183) with flip angles of 10° (pTX-TFE[4]), 20° (pTX-TFE[5]), and 30° (pTX-TFE[6]); turbo spin echo (TSE) with TSE factors of 55 (pTX-TSE[1]), 110 (pTX-TSE[2]), and 183 (pTX-TSE[3]); and GRASE with a TSE factor of 22 in the right-left direction and an EPI factor of 7 in the superior-inferior direction (pTX-GRASE). Imaging parameters used were: FOV=212×186 mm^2 with 2.2×2.2 mm^2 resolutions; 15 slices of 4.4 mm thickness. CW-APT imaging with a long block saturation pulse was performed with a single slice acquisition due to restrictive RF specifications. A nine-offset protocol (±3, ±3.5 twice, ±4 ppm, M_0) was acquired twice and averaged.

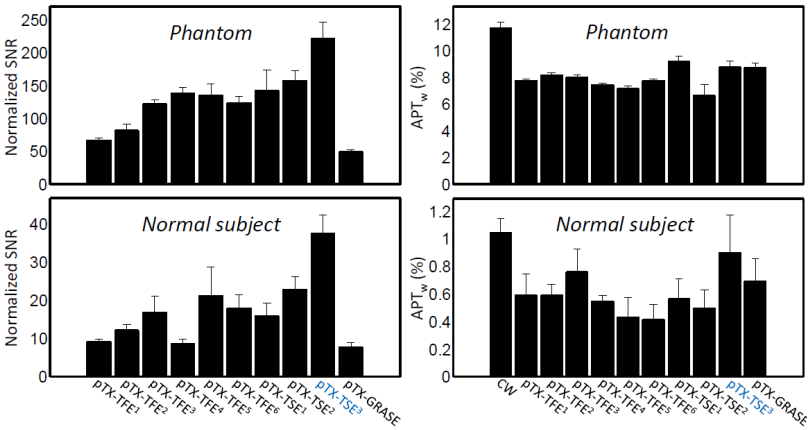

Fig. 1. Normalized SNRs and APTw signals from different MRI sequences.

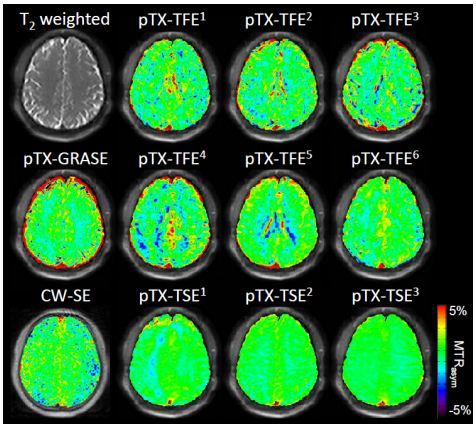

Fig. 2. APTw images for a normal subject.

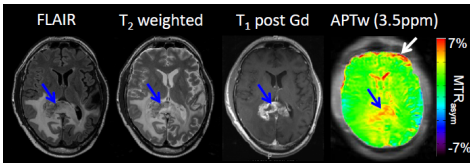

Fig. 3. Conventional and APTw image for a patient with a glioblastoma (blue arrow: tumor core, white arrow: artifact).

The acquired data were corrected for the B_0 inhomogeneity effect on a pixel-by-pixel basis with the water saturation shift referencing[3]. APTw images were quantified using the magnetization transfer-ratio asymmetry at 3.5 ppm from water, namely, MTR_{asym}(3.5ppm). The SNR values were measured using two +3.5-ppm saturated image that were acquired consecutively. Based on a selected ROI, the signal intensity was calculated from the average image, and the noise level was estimated by the standard deviation of the intensities of the difference image in the same region. SNR values were further normalized to √dynamic time for each sequence.

Results and Discussion

Fig. 1 compares normalized SNRs and APTw signal intensities acquired on the homogenous eggwhite and white matter regions in the healthy subjects. The CW-APT sequence (single slice and TR coil) had the largest APTw signals, as expected. All ten 3D pTX-based sequences were associated with similar APT effects, which were smaller than the CW case. Notably, pTX-TSE[3] (TSE factor of 183) showed the highest normalized SNR values (Fig. 1) and the most homogenous APTw images (Fig. 2). The GBM patient scanned using pTX-TSE[3] had an SNR (=33.6 ± 1.3) that was comparable to normal subject studies. The APTw image identified an area of APTw hyperintensity (feature of active tumor), which was much smaller than T_2w and FLAIR, and larger than T_1w post Gd (Fig. 3). The APTw signal intensity of the Gd-enhancing tumor core (up to 7%, much higher than the previous results [2]) was significantly higher than that of the normal tissue.

Conclusions

Time-interleaved pTX sequences, particularly using the TSE acquisition, can maximize SNRs and APT-MRI effects on clinical scanners by avoiding RF amplifier limitations to the saturation pulses, while staying within the SAR limitation (3.2 W/kg). The pTX-based 3D sequence can equally be applied to other CEST imaging applications.

References: [1] Keupp, J. et al. 19th ISMRM (2011)710. [2] Zhou, J. et al. JMRI 2013;38:1119-28. [3] Kim M et al., MRM 2009;61:1441-50