Amide Proton Transfer Imaging of Human Brain at 3T

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Introduction

Amide protons of proteins and peptides resonate at a frequency (~8.3 ppm) different from water protons (~4.75 ppm) and exchange with water protons approximately 30 times per second. [2] In APT imaging, a long magnetization transfer (MT) off resonance pulse is applied to saturate these amide protons, after which an imaging sequence is used to measure the free water signal. The proton exchange creates a measurable MR signal intensity change of on water, due to the chemical exchange saturation transfer (CEST) sensitivity enhancement effect[1]. The APT signal is a function of amide proton concentration, exchange rate k, T_1 of free water, and the concentration of free water, which allowed the study of pH changes in an ischemia model[2] and protein/peptide content changes in a tumor model[3]. Therefore, APT imaging on a clinical system has the potential to diagnose disease populations and progression for example, stroke[2] or tumors. [3] The goal of this study was to implement this technology on a clinical scanner and to show initial results in normal brain and application to brain tumors.

Methods

Z-spectra, in which the relative water intensity loss (S/S_0) is measured as a function of irradiation frequency, were acquired using a whole body 3T Intera scanner (Philips Medical Systems, Best, The Netherlands). The MT pulse was 3s with an amplitude of 3μT and each image was a single-shot acquisition with TR=5s. To take advantage of the SENSE technology, experiments were done with two different coils: 1) a transmit-receive head coil which allowed a 3 second MT pulse, and 2) a SENSE head coil for reception and body coil for transmission, this combination allowed a 500 ms MT pulse. For the z-spectra in normal volunteers 35 offsets were acquired at ω = 0, 64, -64, 128, -128,…, 1024, -1024 Hz, with 0 being the water frequency and 128 Hz = 1ppm. The MT asymmetry was calculated as the signal ratio (S/S_0) difference between the positive and negative offsets in the z-spectrum. For the brain tumor studies, a reference scan and two sets of frequency offsets ω = 448, -448 Hz (+/- 3.5 ppm with respect to water) were used.

Results and Discussion

Z-spectra and corresponding MT asymmetry curves for white matter regions in normal volunteers from each coil were similar for 500ms duration MT pulse (Fig.1). The total MT effect for the 3s MT pulse was greater, as expected, but the MT asymmetry for white matter was relatively insensitive to the total MT effect. On the other hand, there was an increase in MT asymmetry in the tumor example (infiltrating astrocytoma, Fig.2) compared to contra-lateral normal appearing white matter. Figure 3 shows the APT contrast compared to a standard T2w, FLAIR and post-gadolinum MPRAGE images. Based on previous work in animals,[3] it was hypothesized that the APT image would be sensitive to protein and peptide content and that this would be higher in tumors. Interestingly, such a hyperintense area was found in the APT image (Fig.3), while not change/enhancement was found on the post-gad image. Similar results were found in other tumor patients.

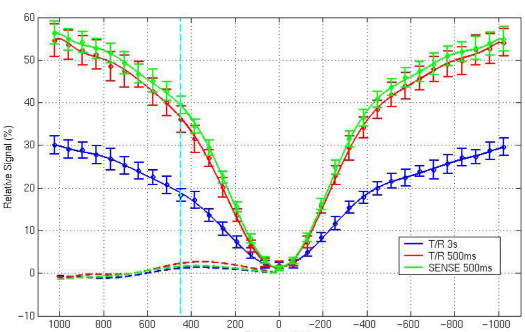

Figure 1: Z-spectra and MT asymmetry curves for a white matter ROI from a normal volunteer acquired with a T/R head coil (blue and red) and SENSE head coil (green).

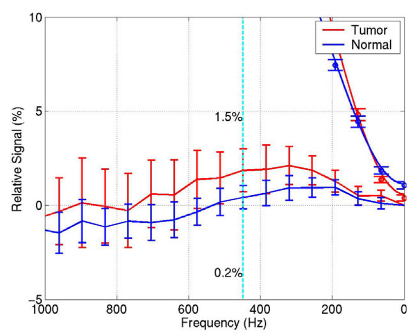

Figure 2: MT asymmetry curves from tumor and contralateral normal appearing white matter of an infiltrating astrocytoma tumor (WHO grade III).

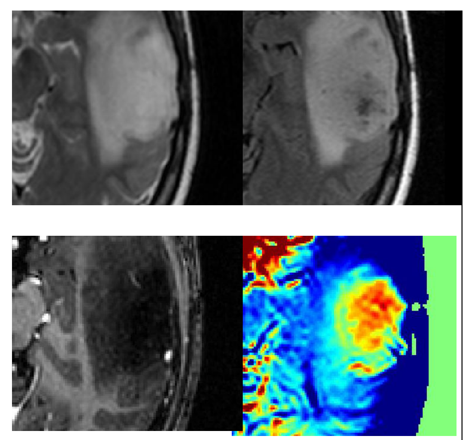

Figure 3: T2w (top left), FLAIR (top right), post-gad MPRAGE (bottom left), and APT (bottom right) images of an anaplastic astrocytoma (WHO grade III).

Conclusions

APT imaging was implemented on a whole body 3T scanner and white matter asymmetry results were consistent with those found in rat studies. Initial APT imaging in patients with brain tumors reveals information not available from other sequences and may provide a unique biomarker for diagnosis and therapeutic monitoring. Preliminary results from the SENSE head coil confirm the asymmetry curves calculated from images from the transmit/receive head coil were similar to those acquired using the SENSE head coil and a shorter MT pulse.

References: (1)Ward, et al., JMR 2000 Mar;143(1):79ff, (2) Zhou J, et al. Nat. Med. 2003;9:1085, (3) Zhou J, et al. MRM 2003 Dec;50(6):1120ff.