3D Amide Proton Transfer (APT) Imaging of the Whole Brain at 3T

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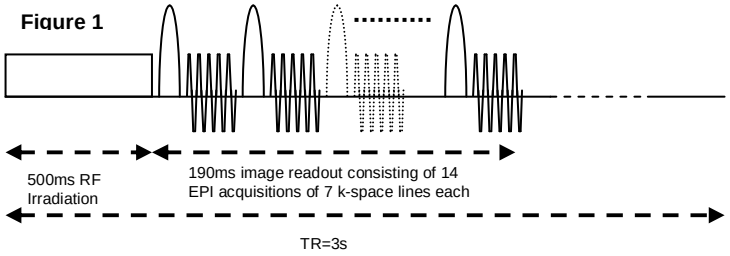
Introduction

APT imaging[1] is an *in vivo* Chemical Exchange Saturation Transfer (CEST) method.[2-4] Its contrast is determined by a change in bulk water magnetization due to chemical exchange of water protons with saturated amide protons of endogenous mobile proteins and peptides. This technique has the potential of mapping protein and peptide levels in the brain noninvasively. However, *in vivo* implementations of APT imaging to date have only been single-slice, which limits clinical application. The reasons for this limitation include long scan time, sensitivity to B_1 and B_0 inhomogeneity, and potentially high RF power deposition. The purpose of this abstract is to address these issues, and to explore the feasibility of whole-brain APT imaging within a clinically acceptable scan time.

Materials and Methods

The whole-brain APT imaging sequence, abbreviated as 3D-APT, consisted of a 500ms block pre-pulse of frequency-selective saturation, followed by fourteen 3D gradient-echo EPI image acquisitions (Fig.1). Each image acquisition segment contained a small tip excitation pulse (10°), phase-encoding gradients in two directions, and EPI image readout of seven k-space lines. The entire data acquisition section was about 190ms long, acquiring 98 k-space data lines. The number of EPI acquisitions after RF saturation was chosen to limit the length of the image acquisition period to under 200ms, so the maximal recovery of saturation state was less than 10% and thus the maximal APT loss would be as small as 0.2-0.3%. Image field of view (FOV) was 212mm x 175mm with 2.2 mm x 2.2mm in-plane resolutions. To cover the entire brain (12~16 cm), 30 slices were prescribed with a slice thickness of 4.4 mm (Fig.2a). Using an RF saturation power of 3μT and a saturation time of 500 ms, SAR was 0.9 w/kg for TR = 3s, well within FDA guidelines. *In vivo* experiments were performed on a Philips Achieva 3T MRI scanner (R2.5.3) using a body coil for RF transmission and an 8-channel phase array coil for reception.

Figure 1



A full z-spectrum, showing water saturation as a function of irradiation frequency, was acquired using 25 frequency offsets (-6 to 6ppm, in steps of 0.5ppm, NSA = 1) for each voxel (S_{sat}). One unsaturated volume was acquired for intensity normalization (S_0). With a SENSE factor of 2.5, the total scan time to image 30 slices for 26 dynamics was about 19 min. Three healthy subjects participated in this study with written informed consent as required. The z-spectra were corrected for the B_0 inhomogeneity effect on a pixel-by-pixel basis according to the procedure previously reported in the literature.[5] The APT effect was quantified using an MT-ratio asymmetry parameter at the offset of 3.5ppm: $MTR_{asym}(3.5ppm) = 100\% \times [S_{sat}(-3.5ppm)-(S_{sat}(3.5ppm)]/S_0$.

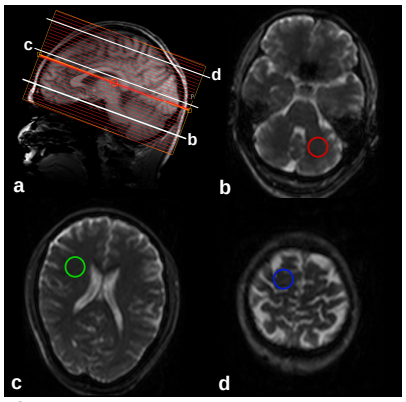


Figure 2

Results and Discussion

Fig.2a shows an example of the location of the 3D volume covering the whole brain. Three saturated images acquired at frequency offset 3.5ppm for slices b, c, and d are shown, where ROI locations (cerebellum, white matter, gray matter) are marked. z-spectra and MTR_{asym} spectra at these ROIs are plotted in Fig.3. The fact that MTR_{asym} for GM and WM did not reach maximum at 3.5ppm can be attributed to the conventional MT asymmetry,[6] as clearly seen at offsets greater than 5ppm. $MTR_{asym}(3.5ppm)$ showed negligible difference in all cerebrum locations in each of these healthy subjects. In cerebellum, $MTR_{asym}(3.5ppm)$ was significantly higher (t-test, $p < 0.04$) (2.2%±0.3%) than in GM (1.0%±0.3%) and WM (1.1%±0.3%).

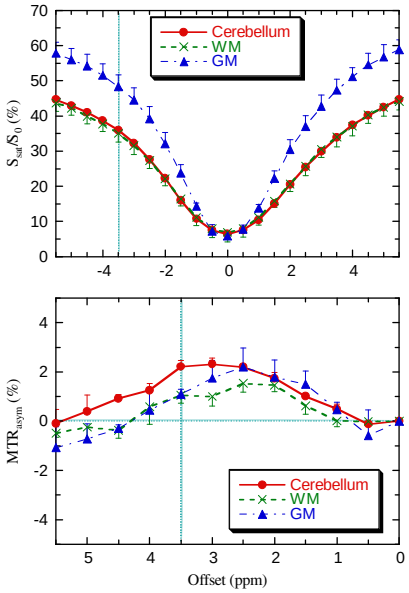


Figure 3

APT imaging is most compatible with 3D acquisition where each line of k-space data contributes to all reconstructed images in the whole volume. Multi-slice acquisition, on the other hand, would suffer from different inherent contrasts from slice to slice caused by time dependent saturation loss.[7] The scan time of 3D-APT imaging is acceptable at present stage, but can be further reduced with a 32-channel phased array coil allowing SENSE acceleration in two phase encoding directions. At 3T, the effective saturation bandwidth was approximately 2ppm (as determined by the Bloch equations), which was larger than the offset interval (0.5ppm) and the B_0 field spread (< 0.8ppm). Therefore, the possibility that the local amide protons were partially missed by a saturation pulse is extremely low, even when the standard two-offset (±3.5ppm) acquisition protocol is used. Further applications of 3D-APT to patients with brain tumors are in progress.

References: (1) Zhou and van Zijl Progr. NMR Spec. 2006;**48**:109. (2) Ward et al. JMR 2000;**143**:79. (3) Zhang et al. JACS 2001;**123**:1517. (4) Aime et al. MRM 2002;**47**:639. (5) Zhou et al. MRM 2008;**60**:842. (6) Jun et al. MRM 2007;**58**:786. (7) Sun et al. MRM 2008;**59**:1175. Grant **Support:** NIH-NCRR P41015241; Dana Foundation.