Amide Proton Transfer (APT) MRI: A 3T vs. 7T Comparison

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Introduction

Amide proton transfer (APT) imaging is a new protein and peptide-based MRI technique, and its contrast is quantified by the magnetization transfer ratio (MTR) between the amide proton pool belonging to protein and peptide backbones and the surrounding water pool, which is found to reflect the mobile protein and peptide concentration and the exchange properties of the amide protons [1]. APT MRI has been developed to detect the over-expressed proteins and peptides in brain tumors for evaluating tumor malignancy and inhomogeneity [2] and to detect cartilage glycosaminoglycan concentration [3]. The frequency difference between amide proton (3.5 ppm) and water resonance is 1043 Hz at 7T, much greater than 448 Hz at 3T, which may help reduce mixture of APT-MTR with the direct saturation effect to water signal. This study is to demonstrate and analyze the potential of 7T MRI to better facilitate the detection of APT effect than 3T using an egg phantom on clinical whole-body systems.

Material and methods

3T and 7T APT MRI The phantom consisted of an egg submerged in an oil-filled container. A smaller container was used in the center of an 8-channel knee coil in a 3 Tesla MR system (Achieva, Philips), and a larger container in a Nova knee coil at whole body 7T MR system (Achieva, Philips). APT images were acquired on a single slice covering the mid-section of the egg. TSE sequence was applied with the following parameters at both 3T and 7T: TR/TE = 5625/26 ms; TSE factor = 15; FOV = 165x165 mm^2; Matrix = 224x180; Slice thickness = 3 mm; NSA=1. TSE images were acquired with pre-saturation pulse at 33 frequency offsets (8 to -8 ppm with an interval of 0.5 ppm). S_0 was acquired by TSE image with maximum saturation frequency offset (100,000 Hz) allowed in the scanners. The pre-saturation pulse was composed of a train of sixteen 1400º block pulses with pulse length of 30 ms and saturation power of 130 Hz (~3.0 μT). The acquisition time for each frequency offset was 50.6 sec and the total acquisition time was 29 min.

Image processing The pixel-wised MT-spectrum from 33 frequency offsets were fitted by a least-square polynomial with the degree of 20 in IDL. From the fitted coefficients, the MT-spectrum was interpolated into 1601 offsets with an offset resolution of 0.1 ppm. The frequency at the minimum of the interpolated MT-spectrum at each pixel was defined as the water resonance frequency (B_0), which may be different from 0 ppm due to magnetic field inhomogeneitites. MTR_{asym} at 3.5 ppm without B_0 correction was calculated by directly subtracting TSE images at 3.5 ppm from the images at -3.5 ppm. MTR_{asym} at 3.5 ppm with B_0 correction was calculated by finding each pixel's B_0 and subtracting the data points at -3.5 ppm and 3.5 ppm with respect to B_0.

A new algorithm for 7T APTR The large frequency difference of 3.5 ppm at 7T enables easier separation of the saturation profile between amide proton and free water proton. An algorithm was developed by first fitting the free water saturation profile using a modified-Gaussian function from nine data points of the MT-spectrum (8, 7, 6, 5, 2, 1, 0.5, 0, -0.5, and -3.5 ppm). The difference between MT-spectrum and fitted water saturation profile was defined as the PT ratio (PTR), and the average PTR at the three data points (4, 3.5, and 3 ppm) were used as the APT ratio (APTR). The curve fitting used MPFIT function [4] in IDL, and overall 13 frequency offsets were used for APTR calculation.

Statistical analysis Regions of interest (ROI) were drawn on egg white, latebra, and egg yolk to evaluate MT-spectrum and new algorithm. The mean, standard deviation, and histogram of MTR value (MTR_{asym} at 3.5 ppm, and APTR) were analyzed for all pixels in a ROI.

Results

There is better separation between the amide proton saturation and free water saturation profiles and a clearer dip that reflects the APT effect in the MT-spectrum of egg white at 7T than at 3T (Fig. 1). APTR derived using the new algorithm showed the peak at 3.5 ppm (Fig. 2, upper plot). APTR in egg white ROI was 9.0% ± 1.2%, more homogeneous than MTR_{asym}(3.5ppm) without B_0 correction (6.8% ± 1.5%), as shown in Fig. 2.

Compared to 3T APT MRI, MT-spectrum of egg latebra at 7T more distinctively shows three type of saturation: amide proton at 3.5 ppm, free water proton at 0 ppm, and fat saturation at -3.5 ppm (Fig. 3). APTR in egg latebra was 5.7% ± 0.7% and MTR_{asym}(3.5ppm) was negative due to the artifact caused by larger fat saturation at -3.5 ppm.

Egg yolk that is more solid than egg white had low signal intensity in S_0 images at 3T and 7T. MT-spectrum of egg yolk showed weak saturation of free water and fat, and did not show positive values of APTR or MTR_{asym}(3.5ppm) (Fig. 3, lower plot).

Discussion and Conclusion

APT-MRI at 7T shows a better separation of amide proton, free water, and fat in MT-spectrum and a clearer APT effect than APT at 3T under the same saturation condition and allows the APT effect to be extracted from the free water saturation profile using a modified-Gaussian function. This study strongly suggests that the APT sequence should be extensively evaluated at ultra-high-field (7T) for tissue characterization.

References

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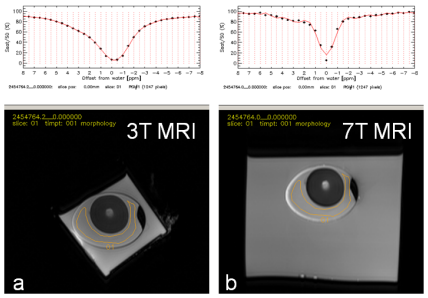

Figure 1. MT spectra at 3T and 7T. The red curves are the least-square polynomial fitted curve to MT-spectrum. The separation between amide proton saturation and free water saturation profile and the APT effect are more prominent at 7T.

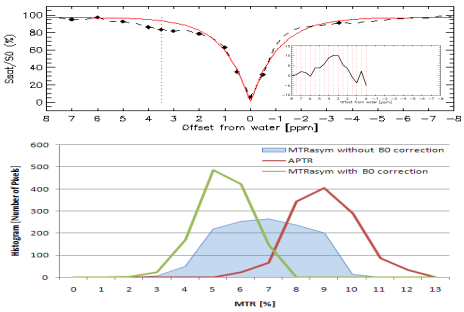

Figure 2. Upper plot: MT spectrum at 7T fitted by an inverted modified-Gaussian function (red curve). The inset plot is PTR versus frequency offset. Lower plot: Histograms of MTR_{asym} and APTR from the ROI in Fig 1 at 7T. APTR shows better homogeneity than MTR_{asym} without B_0 correction.

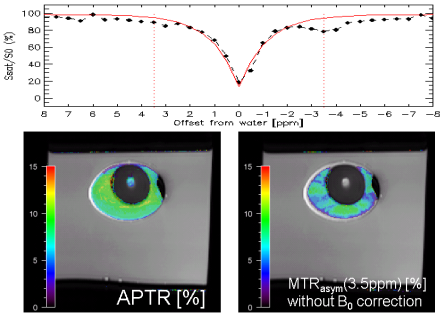

Figure 3. Upper plot: New algorithm at 7T MRI enables positive APTR in fat-rich latebra tissue. Fat saturation at -3.5ppm caused negative MTR_{asym}(3.5ppm) artifact. Lower plot: APTR map shows positive amide levels in latebra, which is not shown in MTR_{asym}(3.5ppm) due to fat saturation at -3.5 ppm.