

Amide proton transfer (APT) imaging for the monitoring of heating treatment by high intensity focused ultrasound (HIFU): phantom experiments

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Introduction

Chemical exchange saturation transfer (CEST) imaging gives the contrast of exchange rate between solute protons and bulk water protons [1]. Amide proton transfer (APT) imaging, a variation of CEST where the interaction between protons from free water and the amide groups, is recently developed for brain tumor detection [2, 3], pH weighted imaging [4], and so forth. In a typical APT experiment, the saturation pulse is applied at ± 3.5 ppm and the two resulting images are subtracted to get APT-weighted magnetization transfer asymmetry (MTR_{asym}). In our study, we use APT contrast to detect the protein denaturation in a phantom with and without the high intensity focused ultrasound (HIFU) treatment. The results show consistently that MTR_{asym} is lower in the region of denatured protein by 21% to 28%.

Material and Methods

The phantom setting (Fig. 1) was designed to compare the APT effect between protein and denatured protein treated by HIFU heating, where the surrounded water is the control and its MTR_{asym} at ± 3.5 ppm theoretically is zero. The image acquisition was performed on a 3T Philips Achieva system using APT pulse sequence with turbo-spin-echo (TSE) at two offsets (± 3.5 ppm relative to the water frequency), where echo train length = 11, TR = 3 sec, TE = 39 msec, matrix size = 256x256, FOV = 230 mm, RFOV = 35%, slice thickness = 3 mm, NEX = 16 to increase the SNR. The saturation RF pulse duration was 1000 msec with irradiated power of 2 μ T. A control image (S_0) (Fig. 2(a)) without the saturation RF pulse was also acquired.

We used the equation: $MTR_{asym}(3.5\text{ppm}) = 100\% \times (S_{sat}(-3.5\text{ppm}) - S_{sat}(+3.5\text{ppm})) / S_0$ to calculate the MTR_{asym} for each voxel. Three regions of interest (ROI) (Fig. 2(b)) were analyzed. The mean MTR_{asym} of each ROI was calculated and the MTR_{asym} ratio, the region of denatured protein to that without HIFU heating process, was used to evaluate the contrast between the region with and without HIFU treatment.

Results

The control image is shown in Fig. 2(a). The signal intensity between water and protein shows little difference, and there is slight contrast between the region of protein with and without HIFU treatment. Fig. 2(b) shows the image within the red rectangular region in Fig. 2(a), obtained from a subtraction of the image acquired at the offset -3.5ppm from that acquired at +3.5ppm. The water signal is seen to be suppressed, with the contrast between the protein with and without HIFU treatment enhanced. The red rectangular region in Fig. 2(b) was analyzed to show the MTR_{asym} map (Fig. 2(c)), where the MTR_{asym} in the regions of denatured protein at about 12~13% level, is seen to be lower than that of protein without HIFU treatment (MTR_{asym} about 17~18%). Table 1 lists the average MTR_{asym} values from the three ROIs for two experiments, where the values of protein with HIFU treatment are consistently lower than that without HIFU treatment. The MTR_{asym} ratio obtained from the two experiments range from 0.72 to 0.79, which means the MTR_{asym} in the regions of denatured protein is consistently less than that of protein without HIFU treatment by 21% to 28%.

Discussion and Conclusion

The difference in MTR_{asym} between the denatured protein and that without HIFU treatment can be depicted by the APT imaging technique. The MTR_{asym} mapping results suggest that the region of denatured protein seems to contain more protons from free water. During the heating process by HIFU, the regional protein is heated and denatured, possibly causing protein solidification and deposition from water, meaning that the proton environment of the protein has been altered. Therefore, the proton exchange rate between the denatured protein and the protein without heating process becomes different, leading to the enhanced contrast using the APT imaging technique. Due to protein deposition from water in the heating region, the relative amount of free water protons, which shows no MTR_{asym} at ± 3.5 ppm during image acquisition, increases as compared with protein without HIFU treatment. For this reason, the MTR_{asym} level of denatured protein is less than that of the protein without HIFU treatment.

We conclude that the APT imaging technique offers good contrast between nature and denatured protein with about 20~30% difference in the MTR_{asym} . Based on such results, APT imaging provides an opportunity to help monitor the process of HIFU treatment in vivo.

References

- [1] Ward, K. and R. Balaban, *Magn. Reson. Med.* **44** (2000) 799-802. [2] Zhou, J., et al., *Magn. Reson. Med.* **50** (2003) 1120-1126. [3] Jones, C., et al., *Proc. Intl. Soc. Mag. Reson. Med.* **14** (2006) 428. [4] Zhou, J., et al., *Nature Medicine*, **9** (2003) 1085-1090.

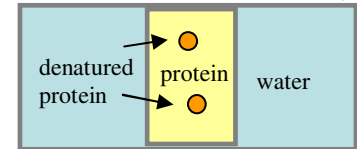


Fig1. Phantom setting: the protein is solved in gel and the denatured protein is treated by HIFU.

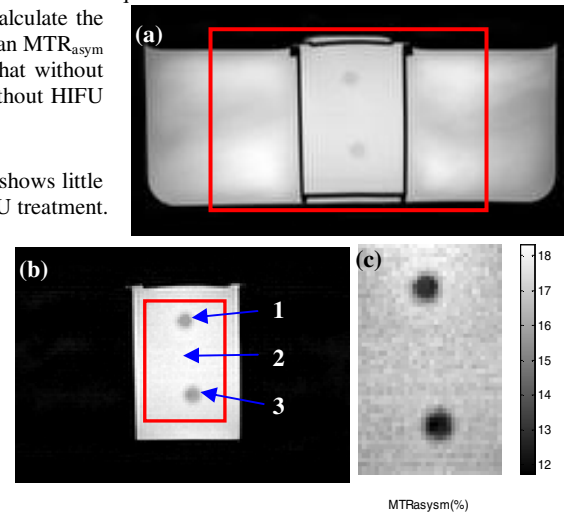


Fig2. (a) Control image (S_0) of the phantom. (b) The resulting image within the red rectangular region from (a) is subtracted from the images acquired at two offsets (± 3.5 ppm) with NEX = 16. ROI 1 and 3 are the regions in the gel with protein with HIFU treatment, and ROI 2 is that without heating processing between ROI 1 and 3. (c) MTR_{asym} map, which is within the red rectangular region from (b), shows the MTR_{asym} difference between the protein phantoms with and without HIFU treatment, and the region with HIFU treatment displays the lower MTR_{asym} than that without HIFU treatment.

Table 1. List of MTR_{asym} for denatured protein regions (ROI1 and 3) and the region without HIFU treatment (ROI2), where protein without HIFU treatment shows higher MTR_{asym} than that of the denatured protein. In MTR_{asym} ratio, it shows about 21~28% difference between these two kinds of protein.

		Exp. 1		Exp. 2	
		MTR_{asym} (%)	MTR_{asym} ratio*	MTR_{asym} (%)	MTR_{asym} ratio*
Denatured protein region	ROI1	13.3	0.79	11.1	0.72
	ROI3	12.7	0.75	11.2	0.73
Protein without HIFU	ROI2	16.9		15.4	

* MTR_{asym} ratio = $(MTR_{asym_denatured\ protein}) / (MTR_{asym_protein\ w/o\ HIFU})$