Simultaneous Monitoring of Temperature and Magnetization Transfer during HIFU Transmission: in vivo rabbit investigations

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Introduction

Recent development of high intensity focused ultrasound (HIFU) technology has offered a potentially new approach to the local ablation of cancer [1] or myoma. The utilization of MRI for guiding HIFU beams not only increases the localization accuracy during HIFU procedures but also allows evaluation of HIFU-induced lesions after treatment [2]. During the past few years, temperature measurement procedure using phase mapping was developed based on the temperature dependence of the water proton chemical shift [3]. This is called the proton resonance frequency (PRF) shift method. In addition, the changes in magnetization transfer (MT) contrast of tissues after heat treatment was also evaluated in a previous study [4]. A real-time evaluation method, that includes temperature monitoring as well as MT contrast of thermal damage during sonication, should be helpful to improve the heating efficiency of HIFU procedures and to avoid the damage of adjacent normal tissues. In our previous study [5], a sequence which can simultaneously monitor temperature change and magnetization transfer effect at 2-sec temporal resolution during HIFU heating was demonstrated on *ex vivo* porcine muscle tissue. In this study, we further apply this method to rabbit thigh muscle to investigate the feasibility for *in vivo* experiments.

Methods and Materials

A single-element focused piezoelectric transducer (central frequency 1.85 MHz, 10 cm diameter, 12.5 cm curvature, Imasonic, Besancon, France) was immersed in 37 ^{o}C degassed water and was used as the source of sonication. Continuous wave HIFU pulses with power of 40 Watt were applied on the thigh muscle tissue of two adult New Zealand White rabbits (3.8~4 kg) for 52 sec (in total four heated spots). Rabbits were sedated using isoflurane and was placed in a right-lateral position (Fig. 1). Serial MR images were acquired at pre-heating (t=0~21 sec), heating (t=22~73 sec) and post-heating time (t=74~218 sec). All MR images were acquired on a 3T clinical imager (Siemens Trio, Erlangen, Germany). The pulse sequence used a dual gradient-echo design, with ON and OFF of the MT pulse interleaved [5], such that the phase images from the two gradient echoes could be used to estimate PRF shift in response to temperature change, and the first echoes from two consecutive TR could be used to derive MT ratio (MTR = 1-(M_{MT}/M_0), where M_{MT} and M_0 are the signal intensity of magnitude images with and without off-resonant MT pulse, respectively) on a pixel-by-pixel basis. Imaging parameters were TR=27 msec, TE=3.61/7.55 msec, flip angle=20^{o}, FOV=240x240 mm^2, matrix size=128x96, slice thickness=3 mm, off-resonance frequency of MT pulse = −1200 Hz. Temporal resolution of about 2.6 sec for monitoring temperature change and observing MTR change was achieved simultaneously. To further enhance visualization of the heated spots, we subtracted the baseline MTR values, which were calculated from the mean of all pre-heating MTR maps, from the instantaneous MTR values to yield series of ΔMTR maps. In addition, a temporal mean filter was applied to smooth the fluctuation noise in the ΔMTR maps. To characterize the time courses of temperature and ΔMTR with respect to the heating time, two ROIs were selected in the heated and non-heated regions (2 cm from the heated area) from the ΔT map (dotted lines in Fig. 2a).

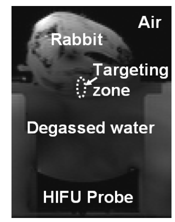
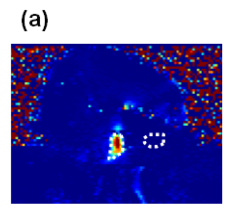


Fig.1. The set-up of HIFU system and the rabbit. A single-element HIFU probe was immersed in 37 ^{o}C degassed water. The sedated rabbit was placed in a right-lateral position.

Results

The time course of temperature change in the heated and non-heated areas for one rabbit were shown in Fig. 2b. The mean temperature change within the heated region reached a peak at 38 ^{o}C at the end of heating, whereas that in the non-heated region remained zero during the entire course. As shown in Fig. 2c, ΔMTR in the non-heated zone was varying slightly around 0%. In the heated region, ΔMTR first decreased during the HIFU transmission. After turning-off the HIFU pulses, ΔMTR increased gradually to 5%, which was distinguishable from that in the non-heated zone. The mean ΔMTR from t=178s till the end of acquiring images for heated and non-heated regions were 4.29%±0.41% (mean±standarder deviation) and -0.19%± 0.30%, respectively. Fig. 3 showed the ΔT map at the end of HIFU transmission (t=73) and the ΔMTR map at the end of image acquisition.



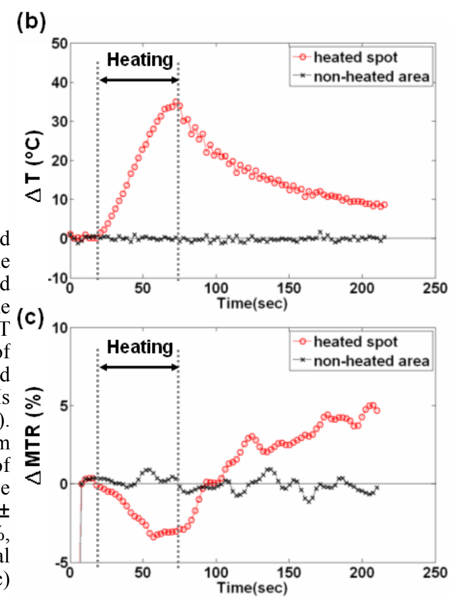


Fig.2. (a) ROIs (white dotted lines) were selected in the heated and non-heated regions (2 cm from the heated area) from the ΔT map. The time courses of temperature change and ΔMTR within the two ROIs were shown in (b) and (c). The mean ΔMTR from t=178s till the end of acquiring images for these two regions were 4.29% ± 0.41% and -0.19% ± 0.30%, respectively. The two vertical lines shown in (b) and (c) denote the heating duration.

Discussion and Conclusions

Monitoring temperature change and magnetization transfer in response to tissue damage of a tissue under HIFU treatment is crucial to the evaluation of treatment efficiency, as they provide complimentary information regarding temporary and permanent thermal alterations of tissue characteristics, respectively [5]. In this study, we have verified the *in vivo* feasibility of simultaneous MR measurement of temperature change and MT effect during HIFU procedures on rabbit thigh muscle. Using this method, we found that the temperature change rose immediately after the heating procedure and fell immediately after turning off HIFU (Fig. 2b), underlining the high sensitivity of the PRF method. ΔMTR began to increase after the heating duration and remained elevated, consistent with *ex vivo* results [5] (Fig. 2c). The ΔMTR first decreased during HIFU transmission, which was somewhat different from *ex vivo* findings [5], suggesting possible temperature dependency of the MTR derivation which needs to be further investigated. In conclusion, MRI with simultaneous temperature and MTR mapping is potentially an effective technique to evaluate tissue damage upon HIFU treatments *in vivo*, as demonstrated on rabbit thigh muscle. Although current ΔMTR maps (Fig. 3b) suffer from relatively high noise influence, the immunity to phase variations and off-resonance effects (in contrast to temperature mapping derived from phase images) plus the unique capability clearly distinguishing heated spot and non-heated region (Fig. 2c) after turning-off HIFU pulses suggest that the simultaneous temperature and MTR mapping technique should worth further explorations.

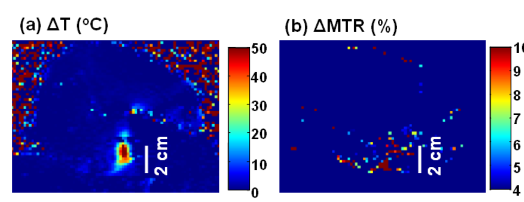


Fig.3. The ΔT map (a) at the end of HIFU transmission (t=73) and the ΔMTR map (b) at the end of image acquisition were shown. The ΔMTR map provided complimentary information to ΔT map although currently suffered from higher noise.

References

1. Cheng et. al, J Cancer Res Clin Oncol 1997, 123: 219-223. **2.** Vykhodtseva et. al, Ultrasound in Med & Biol 2000, 26: 871-880. **3.** Ishihara et. al, Mag Reso Med 1995, 34: 814-823. **4.** Graham et. al, Magn Reson Med 1999, 42: 1061-1071. **5.** Peng et. al, J Magn Reson Imaging 2009, 30: 596:605.