# Simultaneous Monitoring of Temperature and Magnetization Transfer during HIFU Transmission: *ex vivo* experiments

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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], so-called 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], we have investigated the accuracy of estimating temperature change and the feasibility of monitoring MT contrast on pre-heating phantom. In this study, we further applied our sequence on *ex vivo* porcine liver tissue so that we can simultaneously estimated temperature change and the increase of magnetization transfer ratio (MTR) during HIFU heating.

## Materials and Methods

Pulsed-wave HIFU pulses with power of 83 Watt were performed on porcine liver tissue, immersed in 25° C degassed water. Serial MR images were acquired at pre-heating (t=0~19 sec), heating (t=20~122 sec) and post-heating time (t=123~223 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 MTR on a pixel-by-pixel basis [4]. Imaging parameters were TR=29 ms, TE=3.61/7.57 ms, flip angle=20°, FOV=160x120 mm$^2$, matrix size=128x85, slice thickness=3 mm, off-resonance frequency of MT pulse=−450 Hz. Temporal resolution of about 1.85 sec for monitoring temperature change and observing MTR change was achieved simultaneously. To evaluate the consistence of the values of MTR due to protein denaturation, this sequence was performed again 2 min after turning off the HIFU heating pulses for 32sec. To characterize the time course of temperature and MTR with respect to the heating time, several ROIs were selected in the heated and non-heated areas (2 cm from the heated area) from the phase and magnitude (with MT pulses) images.

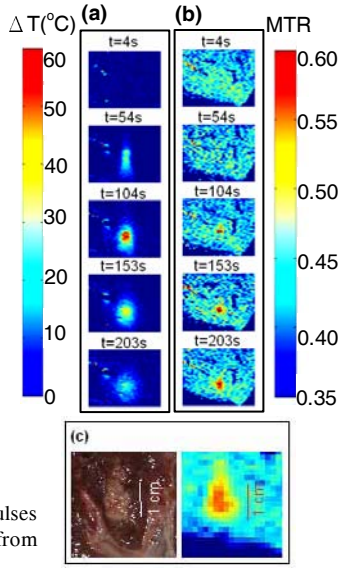


Fig. 1: Pseudo-colored maps of temperature change (a), and MTR (b). Each picture represents different time points before HIFU heating (t=4s), during heating (t=54s, 104s) and after heating (t=153s, 203s). Comparison of optical images of cut face of the heated tissue and the MTR map 2 min after turning off of HIFU (c).

## Results

The measured temperature changes and MTR were rendered in pseudo-color maps (Fig. 1a and b). In these maps, the HIFU pulses were applied from the bottom upward. The maps of temperature change (ΔT) showed a successive change in distribution of ΔT from pre-heating (t=4 sec), heating (t=54 sec, 104 sec) to post-heating (t=153 sec, 203 sec) phases. The MTR maps showed a gradual increase in the area of elevated MTR after 104 sec (Fig. 1b). Comparison between optical images of the cut face of the heated tissue and the MTR map two min after turning off the HIFU heating showed a comparable shape of the burned lesions (Fig. 1c). The time course of temperature change in the heated and non-heated areas were shown in Fig. 2a. The temperature change in the heated areas reached a peak at 58 °C at the end of heating, whereas that in the non-heated areas remained zero during the whole course. As shown in Fig. 2b, MTR in the non-heated areas was 43.5%. In the heated areas, MTR increased gradually from 45% to 52%, and stayed rather constant after 150 sec. The increase in MTR in the heated areas measured about 16%, which was distinguishable from that in the non-heated areas. Such elevation of MTR still maintained 2 min after turning off the HIFU pulses (Fig. 2c).

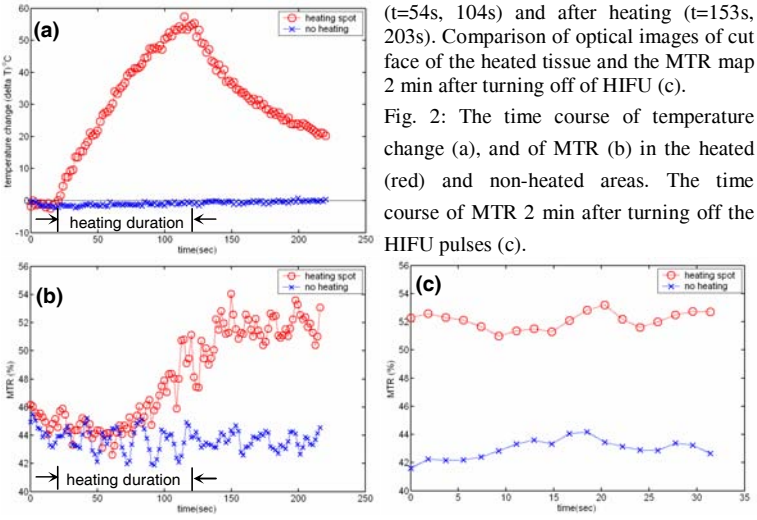


Fig. 2: The time course of temperature change (a), and of MTR (b) in the heated (red) and non-heated areas. The time course of MTR 2 min after turning off the HIFU pulses (c).

## Discussion and Conclusions

Monitoring temperature change and protein denaturation of a tissue under HIFU treatment is crucial to the evaluation of treatment efficiency. In this study, we have verified the feasibility of simultaneous MR measurement of temperature change and MTR during HIFU procedures. Using this method, we found that the temperature change rose immediately after the heating procedure and fell immediately after turning off HIFU (Fig. 2a), underlining the sensitivity of the PRF method. We also found that MTR began to increase 60 sec after the heating and reached a plateau at about 150 sec and stayed unchanged up to 250 sec (Fig. 2b and c). This implies that even heat disperses quickly after heating procedure, the change in MTR due to protein denaturation does not diminish. Furthermore, geometrical consistency between MTR maps and optical images of the burned tissues suggests that MTR might be an effective *in vivo* imaging marker for protein denaturation (Fig. 1c). In conclusion, MRI with simultaneous temperature and MTR mapping is an effective technique to monitor local heating conditions and progress of protein denaturation during HIFU treatment. The proposed mapping method could potentially improve HIFU heating efficiency and reduce unwanted heating damage. Histological comparison will be carried out to clarify the relationships between tissue damage and the values of temperature change and MTR.

## References

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