Different Indication of FLAIR, Contrast-Enhanced, and MTR Images on Tissues Ablated by High-Intensity Focused Ultrasound

Shih-Chieh Lin[1], Teng-Yi Huang[2], Wen-Shiang Chen[3], Jyun-Ming Tsai[2], Meng-Ju Wang[3], Wen-Yih Isaac Tseng[4], and Hsu-Hsia Peng[1]

[1]Department of Biomedical Engineering and Environmental Sciences, National Tsing Hua Univisity, Hsinchu, Taiwan, [2]Department of Electrical Engineering, National Taiwan University of Science and Technology, Taipei, Taiwan, [3]Department of Physical Medicine and Rehabilitation, National Taiwan University Hospital, Taipei, Taiwan, [4]Center for Optoelectronic Biomedicine, Medical College of National Taiwan University, Taipei, Taiwan

Introduction: The potential development of high intensity focused ultrasound (HIFU) on thermal treatments of tumors has been reported in previous study [1]. By using real-time MR image-guiding technology, patient's safety and the efficiency of treatment can be maintained. Real-time monitoring of temperature changes as well as the determination of tissue damage is crucial for evaluation of treating efficacy. In our previous studies, a designed pulse sequence which can evaluate temperature and magnetization transfer effect (MT) simultaneously during HIFU transmission has been performed on *ex vivo* porcine muscle studies [2] and *in vivo* rabbit thigh muscle studies [3]. T1-weighted contrast-enhanced (CE) images are usually used to indicate neovessels and neovascularization [4, 5]. As for the pulse sequence of fluid attenuation inversion recovery (FLAIR), it can be utilize to demonstrate edema or lesions [6,7]. In this study, we aim to compare the complimentary information provided by MT effect and above routine images. The FLAIR images, T1-weighted CE images, and MT-weighted images were acquired in long-term follow-up experimental design. Different indication of above three kinds of image contrast is demonstrated in this study.

Methods and Materials: A single-element focused piezoelectric transducer (central frequency 1.85 MHz, 10 cm diameter, 12.5 cm curvature, Imasonic, Besancon, France), used as the source of sonication, was immersed in 37 ^{o}C degassed water. HIFU pulses with power of 40 watt were applied on thigh muscle to 12 adult New Zealand White rabbits (2.8~3.2 kg) for 34 sec (in total 17 heated spots). Rabbits were sedated using isoflurane and were placed in a right- or left-lateral position. All MR images were acquired on a 3T clinical imager (Siemens Trio, Erlangen, Germany). The follow-up experiments were performed on Day 1 (the day of HIFU sonication), Day 8, Day 15, and thereafter every two-week. Several pulse sequences were performed for long-term evaluation of ablated regions: (1) FLAIR images (TR/TE=7000/79, TI=2218 msec); (2) 3D MT images (TR=27 msec, TE=3.61/7.55 msec) (MT ratio is calculated as 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); (3) T1-weighted CE images (TR/TE=500/9.7 msec). The areas of ablated cores were determined manually on above three kinds of images.

Results: The Day 1 and follow-up (Day 8, Day15) of FLAIR images and MTR maps of one rabbit were shown in Fig.1. The heated regions were shown as central cores (hypointensity) and peripheral zones (hyperintensity) in FLAIR images. As for MTR maps, cores (higher MTR) were delineated by peripheral zones (lower MTR). As demonstrated in Fig. 1(a), central cores of FLAIR images are larger than those of MTR maps on Day 1. However, on the other two follow-up days, areas of central cores displayed on FLAIR images and MTR maps tended to be consistent (Figs.1 (b,c)). In Fig. 2(a), heated regions shown on CE images were displayed as dark cores delineated with thin brighter margins. On Day 1, the heated cores as well as heated extent shown on CE images were not as evident as on FLAIR images (Fig.2(a)), implying that CE images may not be able to properly identify ablated regions on the day of performing sonication. As for on Day 8 and Day 15, cores with hypointensity on CE images were clearly enhanced (Figs.2 (b,c)). Nevertheless, inconsistent areas of dark central cores on FLAIR and CE images were perceptible. Fig. 3(a) displayed long-term follow-up of volume of cores shown on FLAIR images, CE images, and MTR maps. Since these three kinds of image contrast provide different information of heated regions (cores and peripheral zones), different volume of cores were shown. Nevertheless, the volumes of regions affected by ablation measured from MTR maps and CE images showed high correlation (Fig.3(b); $R^2 = 0.95$).

Discussion and Conclusions: Evaluation of longitudinal tissue property alterations following HIFU ablation is important in the monitoring of therapeutic effects. For cancer treatment in particular, differentiation of tumor recurrence from heating-induced secondary changes, such as possible increases in micro-vascular permeability, would be crucial for deciding subsequent treatment plans. In this study, a long-term follow-up of MT effect showed persistently increased MTR values in heated spots on Day 1, Day 8, and Day 15 with the least changes in volume, suggesting the value of MT effect in consistently depicting the area of initial HIFU treatment. In comparison, CE and FLAIR images as routinely used for indicating regional vascularity and edema, respectively, demonstrated continuously reduction in volume of hyperintensity, which seems to suggest spontaneous post-ablation tissue recovery process in the healthy animals included in our study. As shown in Fig.1 (a), heated cores shown on FLAIR images and MTR maps on Day 1 were inconsistent (arrows). However, on Day 8 and Day 15, core regions on these two images tended to be consistent, suggesting gradual clearance of the edema surrounding the actual heated core at about two weeks following HIFU ablation. Moreover, the peripheral tissue with lower MTR, delineating clearly the extent of heated region, underlines the advantage of long-term follow-up with usage of MT effect to evaluate the efficacy of HIFU treatment. In Fig. 2, the discrepancy of core areas between FLAIR and CE images was displayed on the three days. On Day1, the peripheral zones in CE were not as evident as on FLAIR images, because FLAIR demonstrated an immediate response of edema and CE images showed the delayed response of neovascularization. In conclusion, three kinds of image contrast performed for long-term follow-up after HIFU treatments may present complimentary physiological information for evaluation of ablated cores and peripheral zones. CE images provide the neovascularization of neovessels and FLAIR images demonstrate the information of edema. These two technologies may not provide sufficient information for cell death which is crucial for tumor treatments by HIFU. Comparing the information provided by CE images and FLAIR images as well as MTR maps can help determine the proper boundary between heated cores and peripheral zones and can improve the efficacy and efficiency of HIFU treatments. Further histological studies are needed to comprehend the pathology of cores and peripheral zones shown on three different kinds of image contrast.

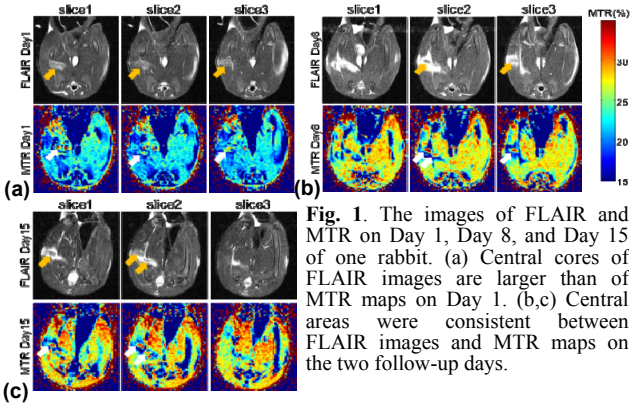

Fig. 1. The images of FLAIR and MTR on Day 1, Day 8, and Day 15 of one rabbit. (a) Central cores of FLAIR images are larger than of MTR maps on Day 1. (b,c) Central areas were consistent between FLAIR images and MTR maps on the two follow-up days.

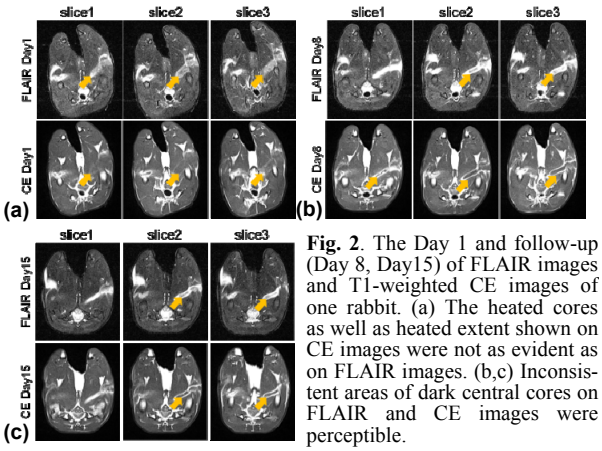

Fig. 2. The Day 1 and follow-up (Day 8, Day15) of FLAIR images and T1-weighted CE images of one rabbit. (a) The heated cores as well as heated extent shown on CE images were not as evident as on FLAIR images. (b,c) Inconsistent areas of dark central cores on FLAIR and CE images were perceptible.

References: **1.** Cheng *et al.,* J Cancer Res Clin Oncol, 123:219–223 (1997). **2.** Peng *et al.,* J Magn Reson Imaging, 30: 596-605 (2009). **3.** Peng *et al.*, ISMRM, 2011. **4.** Calcagno *et al.,* Arterioscler Thromb Vasc Biol 28:1311-1317 (2008). **5.** Yuan *et al.*, J Mag Reson Imaging, 15:62–67 (2002). **6.** Po *et al.,* PLoS ONE 6: e25451 (2011). **7.** Ashikaga *et al.,* Neuroradiology 39: 239–242 (1997).

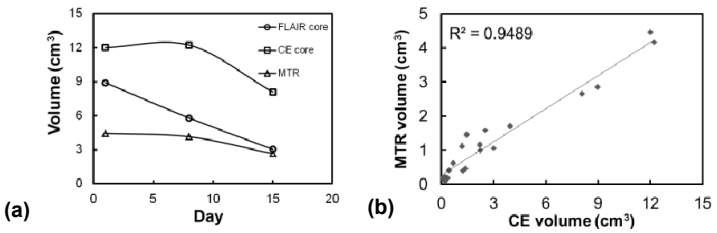

Fig. 3. (a) Long-term follow-up of volume of cores shown on FLAIR images, CE images, and MTR maps. Different volume of cores implied these three kinds of image contrast may provide different information of heated regions. (b) The volumes of regions affected by ablation measured from MTR maps and CE images showed high correlation.