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USE OF MRI TO VISUALIZE MECHANICALLY FRACTIONATED LESIONS GENERATED BY BOILING HISTOTRIPSY IN TISSUE

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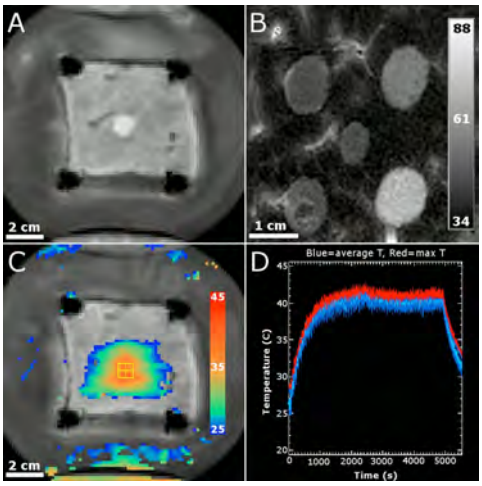
Boiling histotripsy (BH) is a novel high intensity focused ultrasound (HIFU) treatment method to generate mechanically fractionated lesions in target tissue. The method utilizes repetitive millisecond-long pulses with high amplitude shocks, rapid boiling in tissue within each pulse caused by shock-induced heating, and interaction of shocks with the resulting vapor cavity. Ultrasound (US) imaging methods have been used to target and visualize the BH treatment in real time based on scattering from boiling bubbles that form in the HIFU focus. However, it is still technically difficult to visualize the final lesion and to evaluate the mechanical bioeffect with US imaging. The objective of this study was to test the feasibility of using MR imaging methods to target, monitor, and characterize BH treatments with regard to lesion volumes and associated bioeffects. Samples of degassed ex vivo bovine liver (6x6x3 cm) were placed in deionized, degassed water and sonicated using a clinical MR-HIFU system (Sonalleve, Philips Healthcare, Vantaa, Finland). Volumetric lesions of various shapes and sizes were produced within the samples by electronic steering of the HIFU beam generated by a 256-element array transducer. Sonications were performed at a frequency of 1.2 MHz with 10 ms-long pulses, pulse repetition frequencies of 1–10 Hz, and an acoustic power of 250 W, which corresponded to an estimated in situ shock amplitude of about 65 MPa. Continuous exposures were used to generate thermal lesions for comparison with fractionated ones. A standard clinical MRI system (Achieva 3T, Philips Healthcare, Best, the Netherlands) was used for simultaneous real-time monitoring of lesion formation and temperature elevation using a fast-field-echo (FFE) -based MRI sequence and the proton resonance frequency shift (PRFS) -method for temperature mapping. In addition, MRI was used to visualize and characterize the final lesions using standard T2-weighted imaging and T2-mapping. It was found that BH lesions of various shapes and sizes could be created and visualized in ex vivo samples using a clinical MR-HIFU system. Lesions were visualized in real time during sonications; final lesions were also visible on MR images. As shown by gross analysis of the lesions, purely mechanical fractionation was obtained for exposures at 1 Hz pulse repetition rate; combined mechanical and thermal effects were observed at higher pulse repetition rates (>3 Hz). The lesions were characterized by a permanent and positive change (max ~70%) in signal intensity in real-time FFE images (Fig. A) as well as in post-treatment T2-weighted images. In these post-treatment images, BH lesions were clearly distinguishable from lesions caused by thermal ablation and from normal bovine liver tissue. In quantitative T2 maps, mean T2 values were 69 ms for mechanically fractionated BH lesions, 51 ms for thermal lesions, and 39 ms for normal tissue (Fig. B). In addition, temperature maps were acquired in real-time during a BH sonication with a 5% duty factor (Fig. C), demonstrating that MR can be used to monitor BH exposures and provide feedback on thermal effects both within the target location (Fig. D) as well as in the surrounding region. Lesions in ex vivo liver are visible and can be monitored by real-time MR-imaging during BH sonications; moreover, final lesions can also be imaged and characterized quantitatively in a similar way. MRI is sensitive to the fractionation of liver tissue into a liquid-like consistency, which is a goal of histotripsy treatments. Work supported by NIH EB007643, K01 EB 015745-01, T32 DK007779, and NSBRI SMST03402.



A) A real-time FFE magnitude image showing preferential signal enhancement in the BH targeted location at the end of a sonication. B) A T2 map showing higher T2 values for the purely mechanically fractionated BH lesion, as compared to thermal lesions and normal tissue. C) A temperature map (color scale) overlaid on the FFE magnitude image, showing the temperature distribution at the end of a BH sonication. D) Mean and maximum temperature within the BH target region over a 4860 s sonication, followed by a cool-down time.