Relaxation Properties of Cavitation Induced Tissue Lesions

T. L. Hall[1], G. R. Lee[2], C. A. Cain[2], and L. Hernandez-Garcia[2]

[1]Biomedical Engineering, University of Michigan, Ann Arbor, Michigan, United States, [2]University of Michigan

Introduction

High amplitude ultrasound can be used to create tissue disruption through cavitational effects[1]. Properly controlled, this disruption may be a useful means of non-invasive ultrasound surgery. To be clinically successful, any non-invasive surgical method requires imaging feedback on treatment efficacy to ensure that the entire target has been treated. Histologically, ultrasonically disrupted tissue appears as a liquid filled cavity with no discernable structure under light microscopy. MRI is sensitive to the chemical and physical structure of tissue and is frequently employed for soft tissue imaging where good contrast can be achieved to map the spatial extent of a malignancy. It was hypothesized that the homogenization produced by cavitational disruption of tissue should be detectable with MR and that this could provide spatial feedback on a non-invasive ultrasound surgical treatment. MRI has been used extensively for thermometry to guide tissue ablation procedures. Graham[2] has shown persistent changes in relaxation parameters after heating tissue to various temperatures. However, ultrasound disruption can occur with or without the presence of bulk tissue heating by varying the duty cycle of the applied ultrasound pulses.

Methods

Six samples of porcine liver obtained from a slaughterhouse within 6 hours of harvest were cut into sections approximately 8x8x3 cm and vacuum sealed in plastic bags. These prepared samples were then treated with ultrasound in two sets of experiments using varying parameters to create lesions through cavitation disruption of tissue. Four separate locations were treated in each sample with the experimental parameter varied for each location. A 512 element ultrasound transducer array capable of electronic focal steering was used to generate therapeutic effects[3]. Ultrasound was applied in a series of 50 cycle bursts at 1 MHz and 25 MPa peak rarefactional pressure in a 9x9x4 mm grid of 1 mm spaced spots for each lesion location. One burst was applied at each grid spot sequentially in a random order before repeating the set. For the first experiment, the total number of ultrasound bursts was varied (3240, 9720, 32400, or 97200) to create varying levels of tissue disruption with the pulse repetition rate (PRR) kept constant at 50 Hz. For the second experiment, the total number of bursts was kept constant at 64800 while the PRR was varied (10 Hz, 30 Hz, 100 Hz, or 200 Hz) to produce tissue disruption with different amounts of bulk heating (measured with an embedded thermocouple in some samples).

After ultrasound treatment, samples were placed in a 3T GE Signa scanner. High resolution T2-weighted fast spin echo images (TR=500 ms, TE=13.8ms, ETL=3) were collected to localize ultrasound treatment lesions. T1 and T2 maps were then created with the following scan parameters in common: 10-shot spiral readout, FOV=10 cm, matrix size = 64, 3 mm slice, fat saturation, NEX=4. The T2 map used a spin echo sequence with a 1.5 s TR and images acquired at 16 TE values between 8 and 83 ms. T1 maps used an inversion recovery preparation with 8 logarithmically spaced TI values between 20 and 2560 ms. Average T1 and T2 values were computed over 4x4 voxel regions of interest within each treated region as well as untreated tissue. After imaging, samples were fixed in formalin for 1-2 weeks and then sliced into thin sections for histologic evaluation.

Results and Discussion

Application of 9720 ultrasound bursts was sufficient to disrupt the majority of hepatocytes while leaving the collagen matrix intact. Additional bursts completely disrupted all tissue structure. Accordingly, the T2 relaxation time was observed to be significantly longer for treatments of at least 9720 bursts than surrounding untreated tissue. All PRRs produced a significant increase in T2. T1 was observed to decrease both with the number of bursts and PRR. Measured peak temperature for PRRs of 10, 30, 100, and 200 Hz were 39, 50, 65, and 72 C respectively.

In cavitation based ultrasound therapy, successive bursts of high intensity ultrasound cause the break down of tissue at a microscopic level. Structural and molecular changes associated with this process can be imaged quantitatively with MRI. Non-invasive, quantitative measurements of tissue damage provide necessary feedback for optimization of ultrasound therapy treatments. The observed increase in T2 closely follows the pattern of disrupted hepatocytes as seen histologically, and is therefore an indicator of microscopic homogenization of tissue structure. Furthermore, it allows high resolution T2-weighted images for targeting and volumetric measurement purposes. T1 relaxation time decreases with the number of bursts and PRR consistent with increases in maximum tissue temperature.

References

1. Roberts, et al, Journal of Urology, vol. 175, pp. 734-738, 2006.
2. Graham et al, MRM 39:198-203, 1998.
3. Hall and Cain, ISTU conference, S035, 2005.

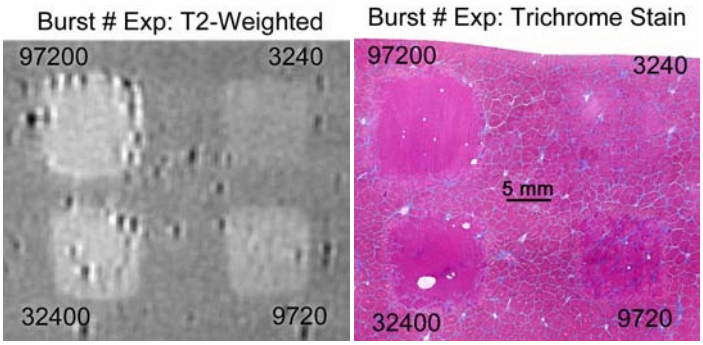

Image of ultrasound lesions (left) and corresponding histology (right) for varied burst number experiment. 3240 bursts produced limited disruption not visible macroscopically, 9720 bursts disrupted most hepatocytes while leaving collagen architecture intact, 32400 or 97200 bursts produced complete disruption.