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Jeremy P. Kemmerer, Goutam Ghoshal, and Michael L. Oelze

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Quantitative Ultrasound Assessment of Thermal Damage in Excised Liver

Jeremy P. Kemmerer, Goutam Ghoshal, and Michael L. Oelze

Bioacoustics Research Laboratory, Department of Electrical and Computer Engineering, University of Illinois at Urbana-Champaign, 405 N. Mathews, Urbana, IL 61801 USA

Abstract. Quantitative ultrasound (QUS) is a novel approach for characterizing tissue microstructure and changes in tissue microstructure due to therapy. In this report, we discuss changes in QUS parameters in liver tissues after being exposed to thermal insult. Effective scatterer diameter (ESD) and effective acoustic concentration (EAC) from the normalized backscattered power spectrum were examined in rat liver specimens heated in a degassed saline bath. Individual liver samples were bisected, with half of each sample heated to a therapeutic temperature of 60 °C for 10 minutes and the other half held at 37 °C. The ultrasonic backscatter and attenuation coefficient were then estimated at 37 °C from both halves. ESD was observed to decrease by an average of 34% in exposed compared to unexposed sample sections, EAC increased by 18 dB, and the attenuation coefficient increased by 70%. Histological slides from these samples indicate cell size and/or concentration may be affected by heating. This work was supported by NIH R01-EB008992.

Keywords: HIFU, quantitative ultrasound, backscatter coefficient
PACS: 43.80.Ev, 43.80.Sh, 43.80.Vj

INTRODUCTION

Conventional B-mode ultrasound is limited in its ability to detect disease and assess therapy because of low contrast between most soft tissues, as well as a dependence of the outcome on the skill of the ultrasound technician. Quantitative ultrasound (QUS) refers to a set of techniques which make fuller use of ultrasound data by removing instrument and operator dependency. Parametric images can be formed from QUS estimates, and these images are hypothesized to quantitatively relate to tissue microstructure and mechanical properties. QUS estimates may be a new source of tissue contrast. Quantitative ultrasound has been successfully used to discriminate tumors in both animal and human models [1-4].

Non-invasive assessment of High-Intensity Focused Ultrasound (HIFU) therapy is essential for successful therapy application, as treatment feedback is needed to determine if further exposure is required. Bush et al. [5] assessed the viability of using speed of sound, attenuation coefficient, and backscattering coefficient to detect HIFU lesions in pig liver, and concluded that attenuation was the most useful. Elastrography techniques [6] have shown potential to differentiate between HIFU lesions and surrounding tissues based on differences in their mechanical properties. However, an ultrasound-based technique which can be readily employed on a clinical device with demonstrated capability to grade treatment regions *in vivo* is still needed. A goal of

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this work is to investigate how QUS may meet this unsolved challenge of rapid and accurate assessment of HIFU therapy.

EXPERIMENTAL METHODS

Saline Bath Heating of Liver

Liver samples were excised from Sprague-Dawley rats and scanned ultrasonically within 2 hours of euthanization to avoid sample degradation. Rat liver samples were treated in a saline bath at 60 °C for 10 minutes to ensure that each sample was uniformly treated. Each liver sample was cut in half lengthwise, and half of the sample was treated as described, while the other half was placed in saline at 37 °C. This treatment regime was chosen to simulate and isolate the thermal effects of a controlled HIFU exposure. The sample halves were pinned to a thin Plexiglas holder and placed in a tank of degassed saline at 37 °C on top of a Plexiglas reflector (fig. 1).

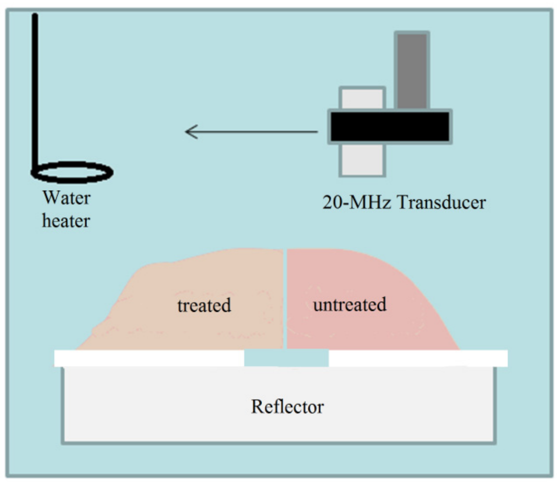

FIGURE 1. Saline bath heating experiment

Ultrasonic Methods

Ultrasonic scans were performed on both treated and unheated halves of liver tissue samples by single-element transducers having a nominal center frequency of 20 MHz. Transducers were excited using a Panametrics 5900 pulser-receiver (Olympus NDT, Waltham, MA) connected to a 14-bit PC A/D card with a 250 MHz sampling frequency. Scan lines were spaced approximately half of a beam width apart (150 μm for 20 MHz f/4) and consisted of at least 100 time averages. Transducer positioning was achieved using a Daedal (Harrisburg, Pa) positioning system controlled by a PC running custom LabView software. A reference scan was taken for all data sets collected using the same equipment and settings. Reference scans consisted of the measured reflection from a planar Plexiglas reflector at normal incidence. Reference waveforms were obtained with the transducer positioned such that measurements were taken over the depth of field of the transducer with an axial step size of 100 µm.

B-mode images of livers generated from ultrasonic scans were segmented and processed to estimate QUS parameters. Independent, non-overlapping data blocks of size 1 mm x 1 mm were selected near the top surface of the liver, and care was taken to avoid blood vessels. An estimate of the backscatter coefficient (BSC) was obtained for each data block. Effective scatterer diameter (ESD) and effective acoustic concentration (EAC) were estimated for each data block using a spherical Gaussian model [7]. Example QUS parametric images are shown in figure 2.

Insertion loss measurements were performed for liver samples in the saline bath heating experiments in order to estimate changes in attenuation coefficient with heating. A pulse-echo single-element transducer measurement of the reflection from a planar surface was obtained with the sample placed between the transducer and the reflector. Several such measurements were acquired over the same lateral region as the backscatter measurements. A reference measurement was taken in the starting location of this scan with the sample and holder removed, but all other settings maintained.

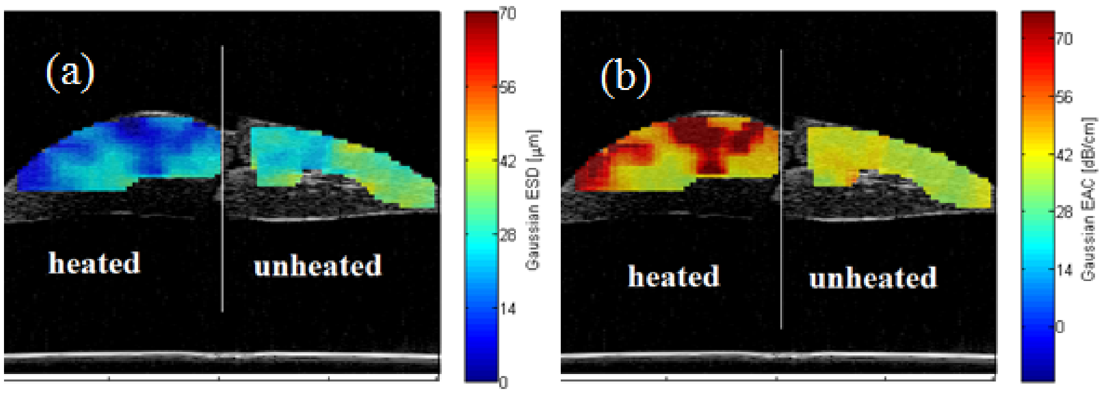

FIGURE 2. QUS parametric images of (a) ESD and (b) EAC in rat liver

EXPERIMENTAL RESULTS

From the experimental results, an average increase in attenuation coefficient of 70%, an average decrease in ESD of 34%, and an average increase in EAC of 18 dB were observed in heated compared to unheated liver samples. These differences were statistically significant for every sample ($p<0.05$). Figure 3 shows the mean and standard deviation of the attenuation coefficient estimated from seven samples using an insertion loss technique, where a prominent increase can be observed with heating. Figure 4 shows average BSCs for each sample and demonstrates a clear separation between heated and unheated estimates. Average ESD and EAC estimates for each sample are shown in figure 5, again indicating a clear separation between heated and unheated estimates.

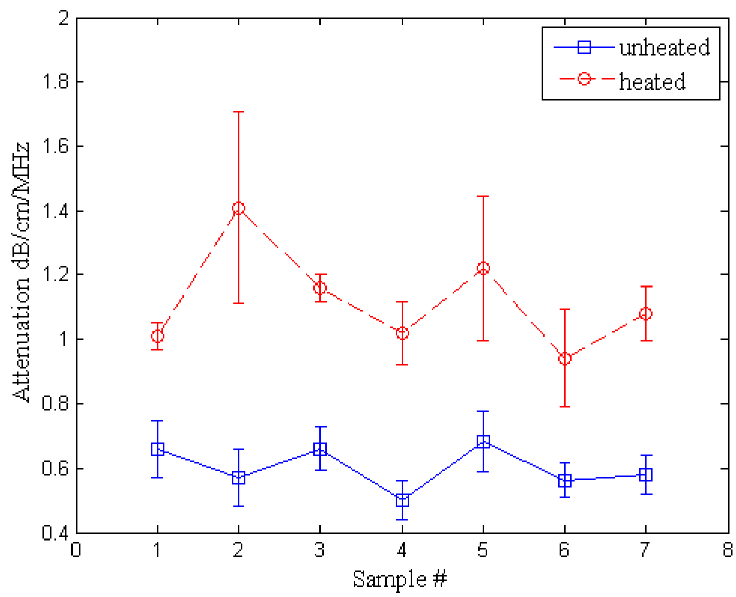

FIGURE 3. Attenuation coefficient estimates for rat liver

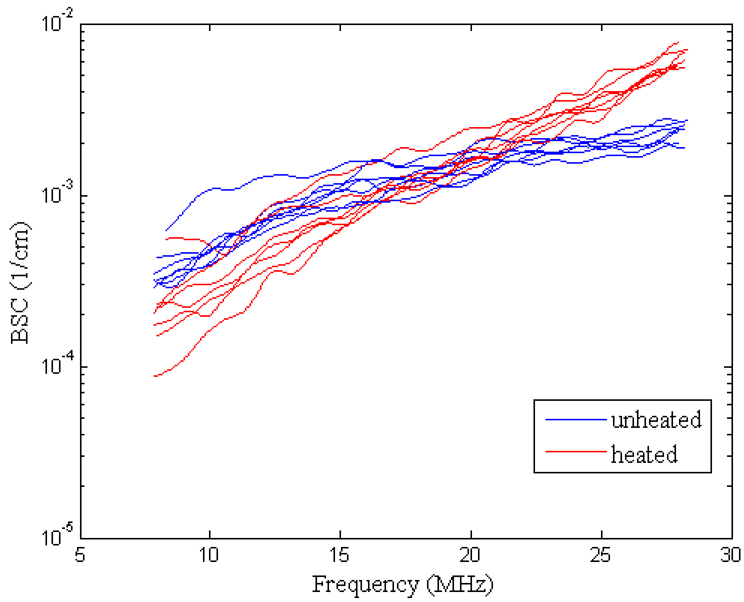

FIGURE 4. BSC estimates for rat liver

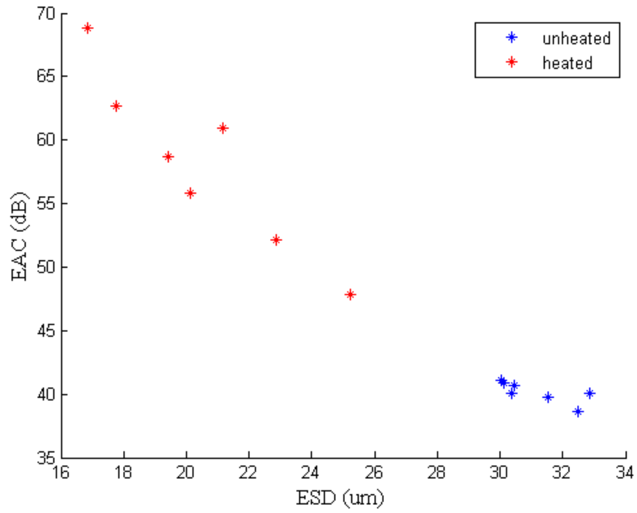

FIGURE 5. QUS estimates for rat liver

Histological analysis was performed on heated and unheated regions of rat liver samples. After the ultrasound scans, samples were preserved by fixation in 10% formalin for at least three days, after which they were stained with hematoxylin and eosin (H&E), mounted in paraffin, and sliced to create microscope slides. Figure 6 shows digitized images of histology slides from an untreated and a treated sample. Both images include a circle sized to the average ESD estimated for that type of sample. Dilation of the liver sinusoids was observed in the heated compared to unheated liver, suggesting that ESD may be sensitive to changes in tissue structure, as also indicated by measurements.

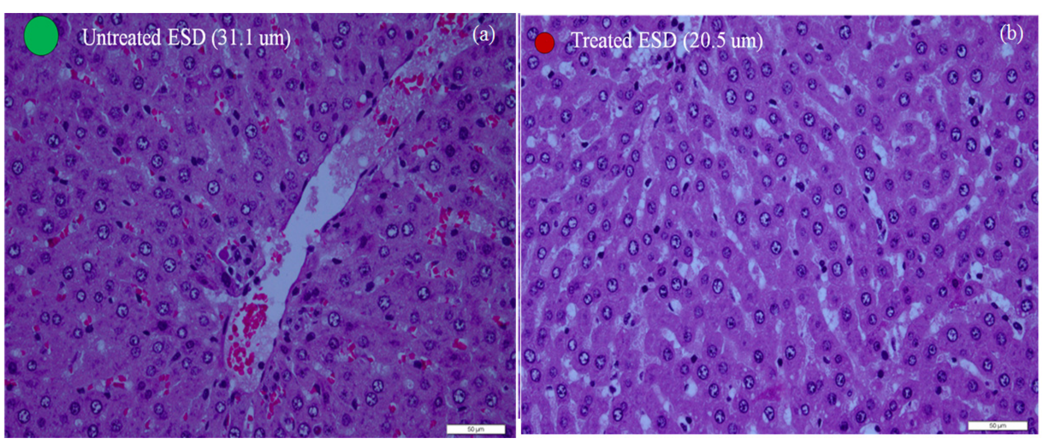

FIGURE 6. Histology images (a) untreated and (b) treated rat liver

CONCLUSIONS

A series of saline bath heating experiments were conducted as an important preliminary step in determining the extent to which changes in liver tissue properties with heating could be estimated ultrasonically. The saline bath experiments yielded substantial changes in estimates of sample attenuation with heating, as well as significant and consistent changes in BSCs in liver with heating. Scattering models applied to the measured changes in BSCs yielded an average decrease in ESD with heating of 34%, and an average increase in EAC of 18 dB.

Preliminary attempts to measure the size of cells from these histology images yielded inconclusive results. However, apparent structural changes associated with dilation of liver sinusoids appeared in the heated images. Further experiments will be conducted by varying the exposure conditions in order to better determine how structural changes can be correlated to ultrasonic measurements and ultimately modeled as a function of thermal exposure. This information will be critical in developing a non-invasive ultrasonic technique for assessing thermal damage in tissues.

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