10.1109/ULTSYM.2010.0356

A New Approach for Detecting Attenuation Changes During High-Intensity Focused Ultrasound

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Abstract - **The acoustic attenuation coefficient provides extremely valuable information for tissue characterization in general, and is needed for planning of High-Intensity Focused Ultrasound (HIFU) therapy in particular. The attenuation coefficient in tissue is sensitive to changes in temperature and to damage resulting from heating. To date, parametric images of attenuation coefficient from backscattered ultrasound have poor spatial resolution, and are thus inadequate for monitoring and assessment of HIFU. A novel method for detecting changes in attenuation using backscattered ultrasound was developed that could potentially be used for both monitoring and assessment of HIFU therapy. This approach compares the signal energy in an untreated region of sample located behind a region treated with HIFU. The technique was tested by using HIFU to treat a liver sample placed on top of a well-characterized tissue-mimicking phantom. The signal energy in the phantom was monitored using a clinical ultrasound scanner before, during, and after HIFU exposure of the liver. Results strongly depended on the presence of increased brightness in the sample. For cases without sample brightening, detected signal energy trended in a manner similar to the temperature. Also, a decrease in signal energy in the phantom after return to baseline temperature compared to initial conditions was detected in all cases, suggesting that the technique was sensitive to permanent changes induced by HIFU in the liver sample.**

Keywords- HIFU; therapy monitoring; therapy assessment; attenuation;

I. INTRODUCTION

High-Intensity Focused Ultrasound (HIFU) has shown promise as a non-invasive treatment modality. Despite the many advantages of HIFU for thermal therapy, obstacles remain in translating HIFU from the laboratory into clinical practice. Among these challenges is the limited success in developing non-invasive techniques to monitor changes in temperature and assess changes in tissue properties induced by HIFU. If an ultrasound-based technique could be developed, ultrasound would be ideally suited to these tasks due to its portability, low cost, and high spatial and temporal resolution. The acoustic attenuation coefficient is sensitive to changes in temperature [1], and to irreversible changes in tissue due to thermal damage [2]. Furthermore, knowledge of acoustic absorption is required to accurately predict heat deposition due to a known focused ultrasound field, and significant reduction in transmitted acoustic power have been associated with acoustic cavitation [3], which can make controlling HIFU difficult.

Current approaches to monitor temperature using ultrasound, including speed of sound and changes in backscattered energy, have important drawbacks. Thermal monitoring using changes in backscattered energy (CBE) [4] is limited to the hyperthermia temperature range (< 45°C), and the accuracy of speed of sound techniques generally degrades with sample motion [5]. Accurate estimation of the backscatter coefficient, which has been observed to vary with tissue temperature in liver [6], requires knowledge of the spatial variation of attenuation. For these reasons, high-resolution real-time estimates of attenuation that are relatively insensitive to motion of the sample would provide highly valuable information for monitoring HIFU exposure.

In this study, a novel approach is presented for estimating changes in attenuation of a tissue sample during exposure to HIFU. The technique was validated through experiments involving liver samples and well-characterized phantoms. In the technique, a well-characterized phantom was placed beneath the sample, and both the sample and phantom were monitored before, during, and after HIFU exposure.

II. EXPERIMENTAL METHODS

A. HIFU Exposure

Fresh samples of rabbit and rat liver were exposed to a single element 1 MHz F/1.1 transducer powered by an A150 55 dB power amplifier (ENI, Rochester, NY) excited by an arbitrary waveform generator (HP 33120a, Agilent Technologies, Santa Clara, CA). The exposure settings used in the experiments resulted in an intensity of 2600 W/cm^2 in degassed water, as measured using a needle hydrophone (Precision Acoustics, Dorchester, UK). A wire thermocouple (Omega, Stamford CT) was aligned with the focus of the HIFU

Sponsor: NIH R01- EB008992

transducer and moved into the sample at the location of the focus prior to each exposure. Motion control of the thermocouple was provided by a Daedal positioning system (Daedal, Inc., Harrisburg, PA) controlled through a PC running custom LabView (National Instruments, Austin, TX) software. Temperature data was captured using a National Instruments USB-TC01 interface, and recorded at 1 Hz. After exposure, the livers were sliced and inspected to determine if lesions were induced through the HIFU. Exposure conditions resulted in visible lesions for all data presented.

B. *Ultrasound Monitoring*

HIFU exposure was monitored using a Sonix RP (Ultrasonix, Richmond, BC, Canada) clinical ultrasound system with an L14-5/38 probe sampled at 40 MHz. The probe had a nominal center frequency of 7.5 MHz. An agar phantom containing glass beads was placed beneath the liver sample, and the Sonix RP acquisition was adjusted to capture both the liver sample and approximately 2 cm of the top of the phantom. RF data was acquired at 30 frames per second, and synchronized with the HIFU signal generator such that the image data were acquired between HIFU tone bursts. The acquisition was initiated and controlled by custom software for the Sonix RP. The Sonix RP array transducer was aligned to the needle thermocouple located at the focus, and alignment was verified by exposure of an agar phantom to HIFU, creating a clearly visible region at the focus in the B-mode display. The HIFU transducer and probe remained fixed with respect to each other for the duration of the experiment, and alignment was periodically verified.

Figure 1 shows the experimental setup for exposing rat liver. The rat liver exposures took place in degassed water maintained at 37°C using an YSI model 72 temperature controller (Yellow Spring Instrument Company, Yellow Springs, OH) and heating element. Rabbit liver exposures required a slightly modified setup, where the liver sample was fastened to the phantom, and the experiment took place in degassed saline at 37 °C.

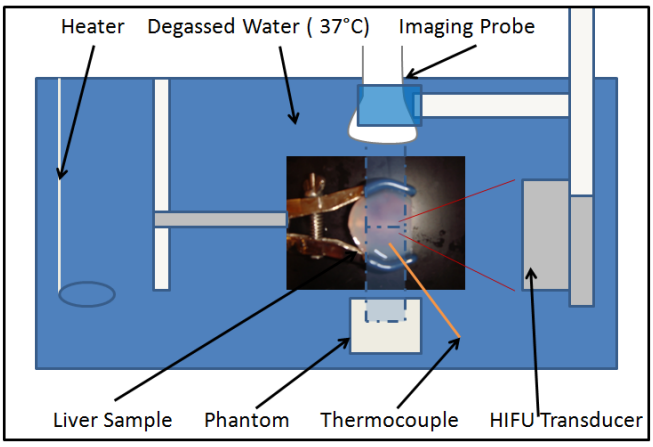

Figure 1. HIFU exposure experimental setup (Rat Liver)

III. Signal Analysis

Signal energy in the phantom was calculated before, during, and after the exposure in three spatial locations: directly beneath the focus, before, and after this location axially with respect to the HIFU transducer location. Figure 2 shows these locations, with the arrow representing the orientation of the HIFU transducer, and the green rectangle representing the phantom location beneath the focus. The signal energy ratio was calculated as:

$$ER[n] = \frac{\sum_m |x_n[m]|^2}{\sum_m |x_0[m]|^2} \qquad (1)$$

where x_n is the windowed signal in the phantom at time n, and x_0 is the signal in the same location before exposure.

IV. Results

A. *Rabbit Liver Results*

RF data collected during the HIFU exposure were used to generate sets of B-mode images, which were then used to guide the analysis. In the case of rabbit liver exposures, significant decreases in brightness in the phantom along with increased brightness in the locations of the HIFU focus were observed in images after the exposures (Figure 2). An initial smoothly increasing temperature trend was interrupted by sharp fluctuations, which has been observed during HIFU and attributed to cavitation by other authors [3].

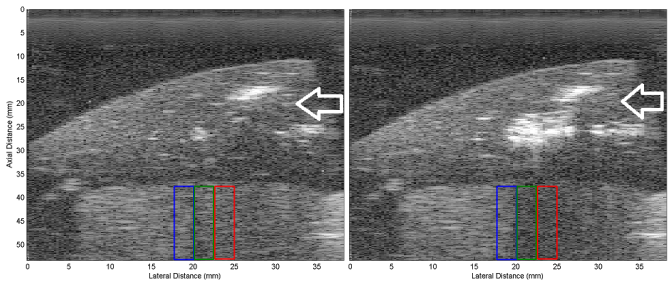

Figure 2. B-mode images of rabbit liver before (left) and after (right) HIFU exposure

Analysis of the signal energy (Figure 3) in the phantom region of the data revealed significant changes over time. In the case a rabbit liver, the signal energy ratio was observed to decrease rapidly after initiation of HIFU, indicating that the attenuation of the monitoring signal was substantial. In a rabbit liver exposure, the posterior region was observed to remain relatively unchanged. The focus and anterior regions decreased rapidly and signal energy remained low as the temperature returned to 37C.

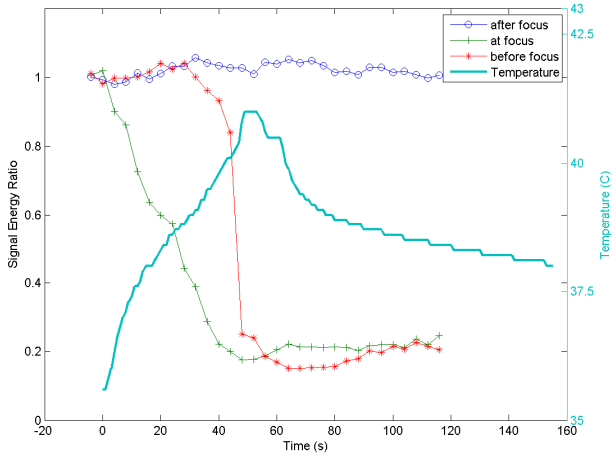

Figure 3. Signal energy ratio and temperature for rabbit liver exposure. Exposure ended at t=61 s.

B. Rat Liver Results

Exposures of rat liver samples resulted in two distinct cases. In the first case, brightening at the focus of the HIFU transducer and a significant visible decrease in the signal energy in the phantom were observed, similar to the rabbit liver exposures (Figure 4). Analysis of the phantom RF data revealed trends similar to the rabbit liver (Figure 5), although the signal energy also increased as the sample cooled.

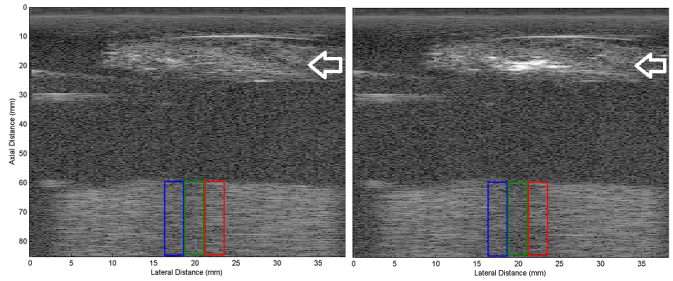

Figure 4. B-mode images of rat liver before (left) and after (right) HIFU exposure

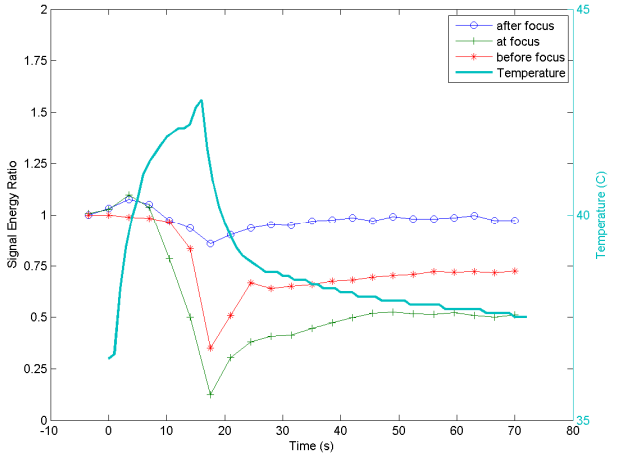

Figure 5. Signal energy ratio and temperature for rat liver exposure. Exposure ended at t=16 s.

A second series of measurements in which slightly different sample preparation was used resulted in little or no visible changes in either the sample or the phantom in B-mode images, despite identical exposure conditions (Figure 6). In this case, a primarily thermal mechanism for changes in signal energy was assumed, which was also evidenced by histological verification of a thermal lesion.

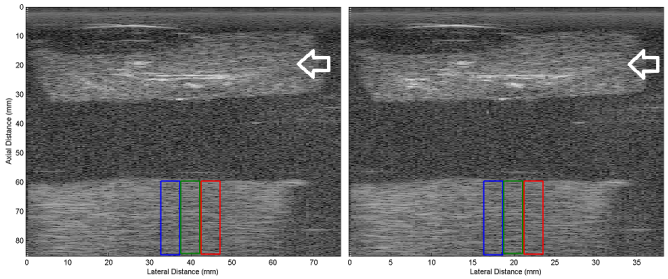

Figure 6. B-mode images of rat liver before (left) and after (right) HIFU exposure

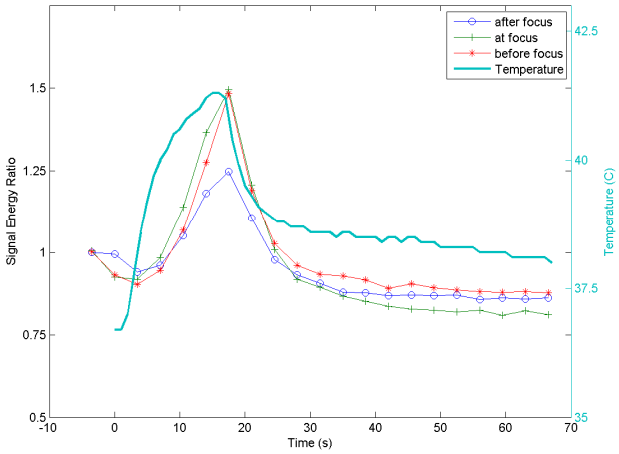

Figure 7. Signal energy ratio and temperature for rat liver exposure. Exposure ended at t=16 s.

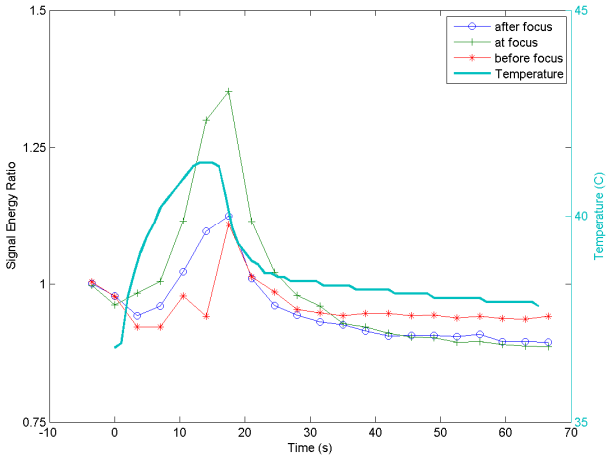

Figure 8. Signal energy ratio and temperature for rat liver exposure. Exposure ended at t=16 s.

In the rat liver case where the signal changes were assumed to come from purely thermal effects, increases in signal energies with increasing temperature in all three regions were observed, suggesting decreased signal attenuation (Figures 7 and 8). After turning off the HIFU, the signal energy increase was followed by a gradual decrease to a final value below the initial energy. These results suggest that the observed effect was temperature dependant and, in particular, that irreversible changes resulted in increased attenuation, which is consistent with measurements of attenuation of HIFU-induced lesions in the literature.

V. Conclusions

A novel method for monitoring changes in acoustic attenuation during HIFU exposure was developed and tested experimentally. Significant changes in the measured backscattered signal energy from a glass bead phantom using a real-time clinical system were observed due to HIFU exposure of a sample directly above the phantom. This approach measured changes in the signal energy in cases with and without a corresponding increase in brightness of B-mode images of the sample. In the case of no increase in B-mode image brightness, the changes in signal energy indicated decreasing signal attenuation with increasing temperature, and the final attenuation increased after return to baseline temperature. These observations are consistent with measurements in the literature for thermal lesions [1], [2].

The technique has several advantages over other techniques for monitoring of HIFU using ultrasound. First, this method does not rely on correlating the image data between samples in time, and so should be more robust to motion artifacts due to in-plane motion. Additionally, the experimental results demonstrated that the technique could be used for HIFU exposures resulting in tissue ablation. Therefore, the technique is not limited to hyperthermia applications. While the measured temperatures did not exceed 45°C, these measurements represented temperature outside of the actual focus, and so peak temperatures in the experiment were likely higher.

Although attenuation has been hypothesized to be responsible for the changes observed in backscattered signal energy, other explanations are possible, especially at elevated temperature. A thermo-acoustic lens effect occurs in non-uniform heating of tissue, as is present during HIFU exposure. This phenomenon could affect the amount of acoustic energy backscattered from the phantom in this experimental setup, and could therefore be responsible for some part of the changes observed in backscattered signal energy at elevated temperature. The results suggest that, regardless of the mechanism, the backscattered energy measured beyond a lesion may be useful in estimating temperature changes during HIFU. Furthermore, changes observed in signal energy behind the lesion of the rat livers suggests that this approach may be useful for assessing permanent changes in tissue due to HIFU therapy.

Acknowledgment

This work was support by a grant from the NIH, R01-EB008992. The authors would like to acknowledge Rita Miller, Goutam Ghoshal, and William Ridgway.

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