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An Acoustic Backscatter-based Method for Estimating Attenuation towards Monitoring Lesion Formation in High Intensity Focused Ultrasound

Siavash Rahimian and Jahan Tavakkoli

Abstract. This work investigated the transient characteristics of tissue attenuation coefficient before, during and after HIFU treatment at different total acoustic powers (TAP) in ex vivo porcine muscle tissues. Dynamic changes of attenuation coefficient parameters were correlated with conventional B-mode ultrasound images over the whole HIFU treatment process. Two-dimensional pulse-echo radiofrequency (RF) data were acquired to estimate the changes of least squares attenuation coefficient slope ($\Delta g_{533}$) and attenuation coefficient intercept ($g_{3020}$) averaged in the region of interest, and to construct $g_{533}$, $g_{3020}$, and B-mode images simultaneously. During HIFU treatment, bubble activities were visible as strong hyperechoic regions in the B-mode images, causing fluctuations in $\Delta g_{533}$ and $g_{3020}$ estimations during treatment. $\Delta g_{533}$ and $g_{3020}$ increased with the appearance of bubble clouds in the B-mode images to values in the range of 1.5-2.5 [dB/(MHz.cm)] and 4-5 [dB/cm], respectively. After the treatment, $\Delta g_{533}$ and $g_{3020}$ gradually decreased, accompanied by fadeout of hyperechoic spot in the B-mode images, until they were stable at ranges of 0.75-1 [dB/(MHz.cm)] and 1-1.5 [dB/cm], respectively. In conclusion, $g_{533}$ and $g_{3020}$ images outperformed B-mode images in detecting HIFU thermal lesions by having significantly higher contrast to speckle ratios at all investigated TAP values.

Keywords: HIFU, Thermal Lesion, Tissue Attenuation Coefficient, B-mode Image, Contrast to Speckle Ratio

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INTRODUCTION

Currently, one of the most common and promising noninvasive modality for high-temperature thermal therapy is high intensity focused ultrasound (HIFU). The purpose of monitoring HIFU treatment is to ensure that the target volume is completely treated (thermally damaged), and to ensure the safety of sensitive structures near or outside the target volume. Monitoring should be conducted in real-time and using a closed loop system. X-ray imaging, magnetic resonance imaging (MRI), and ultrasound imaging have all been used as noninvasive methods for monitoring and assessment of tissue thermal damage in HIFU surgeries [1].

In studies conducted on changes in ultrasound tissue attenuation coefficient as a function of temperature or thermal dose [2-4], it was observed that as the temperature of tissue rose, and ultimately, as the tissue coagulated, there was a dramatic increase in ultrasound attenuation slope, $\beta$, and ultrasound attenuation intercept, $\alpha_0$. This provided the possibility that changes in the frequency dependent ultrasound attenuation as a function of temperature and thermal dose might be exploited for monitoring HIFU procedures, and gaining more information about the location and size of the thermal damage within the tissue [3, 5-9]. In monitoring HIFU using ultrasound attenuation estimation, ultrasound attenuation slope and attenuation intercept measurements are directly applied to the region of interest in the tissue through analysis of the RF backscattered ultrasound signal, resulting in differentiation of normal and thermally coagulated regions of the tissue.
In this study, a system capable of acquiring backscattered ultrasound RF data in the pre, during, and post phases of HIFU procedures was designed and developed. In addition, two frequency domain algorithms were developed to estimate attenuation slope and attenuation intercept. The two algorithms were capable of quantitatively estimating changes in tissue attenuation using the acquired backscattered ultrasound RF data. The purpose of the study was to show that changes in the attenuation of HIFU lesions can be estimated with respect to initial attenuation of normal tissue, using the acquired backscattered RF data. Using the two algorithms, the transient characteristics of tissue attenuation coefficient parameters \( \Delta \beta \) and \( \Delta a_0 \) as a function of HIFU exposure time, at different total acoustic powers in \textit{ex vivo} porcine muscle tissues, were investigated. Finally, \( \Delta \beta \) and \( \Delta a_0 \) images (attenuation maps) were generated, and correlated with B-mode images. The HIFU lesion imaging performance of these attenuation maps were compared with each other and with conventional B-mode imaging.

**MATERIALS AND METHODS**

The experiments were conducted on fresh \textit{ex vivo} porcine muscle tissues. The muscle specimens were cut and trimmed to 20×80×100 mm, and stored in degassed, deionized water at 5°C for 12 hours prior to conducting the experiment. This ensured that most preexisting gas bubbles were transferred from the tissue into the degassed water. The HIFU transducer was installed inside a water tank filled with degassed deionized water at room temperature. The imaging probe was installed confocally through an opening at the center of the HIFU transducer (Fig. 1(f-g)). The specimens were mounted on a tissue holder for HIFU treatment. The tissue in the tissue holder was then submerged in the tank at the focal region such that it would cover the entire focal area. Enough time was allocated for the tissue inside the water tank to reach room temperature. An acoustic absorber was placed at the end of the water tank to absorb acoustic waves, and prevent any reverberations within the water tank.

A single element HIFU transducer (Model 6699A101; Imasonic S. A., Voray sur l'Ognon, France) with a resonant frequency of 1 MHz was used throughout this study. The transducer had a 125 mm diameter of aperture, and a 100 mm geometric focal length (radius of curvature). The measured axial and lateral focal width of the HIFU transducer were 8 mm and 2 mm at full width at half maximum (FWHM), respectively. The radio frequency (RF) signal driving the HIFU transducer was generated by an arbitrary function generator (Model AFG3010; Tektronix, Beaverton, OR, USA). The RF signal was amplified by a class-A broadband RF power amplifier (Model A150; E&I, Rochester, NY, USA). The efficiency of the transducer was measured to be 64% for input electric powers in the range of 0.8 W to 157 W. For total acoustic powers (TAP) of 34, 37, 39, 44, and 49 W, used in this study, the HIFU transducer generated free field (in water) spatially averaged focal intensities \( (I_{SA}) \) of 737, 801, 845, 961, and 1068 W/cm², respectively.

An ultrasound imaging system (SonixRP® scanner, Ultrasonix Inc., Richmond, BC, Canada) and an endocavity array probe (EC9-5/10, Ultrasonix Inc., Richmond, BC, Canada) with 128 elements, a center frequency of 7 MHz, and bandwidth of 3 MHz, were used for acquisition of B-mode images, and RF backscattered data. In order to acquire RF backscattered data throughout all phases of treatment, a micro-controller (Model M68HC11; Motorola, Inc., Schaumburg, Illinois, USA) was used to synchronize various components of the experimental setup. RF data were acquired pre, during, and post HIFU treatments to estimate the initial, transient, and final
acoustic properties. RF data were also acquired 10 minutes after the completion of HIFU treatment.

**FIGURE 1.** (a) Schematic diagram of the image-guided HIFU experimental setup (b) the experimental setup in the laboratory (c) SonixRP® Ultrasound Imaging System (d) 2D B-mode image during HIFU treatment (e) tissue in the tissue-holder submerged in the water tank in front of the HIFU transducer (f) HIFU transducer (g) Imaging Array Probe.

The HIFU exposure duration was fixed at 40 s. During HIFU treatment, the RF data frames were obtained by briefly interrupting the HIFU transducer in order to avoid acoustic and electrical interferences. The duration of interruption was fixed at 120 ms (OFF-Time), allowing for the capture of two RF data frames. The HIFU ON-Time was fixed at 400 ms, resulting in a duty cycle of 77%. The RF data were acquired at a sampling rate of 40 MHZ. The acquired RF data consisted of many individual frames, each frame in turn consisting of many individual echo lines corresponding to individual elements of the ultrasound imaging transducer array.

Following is a mathematical description of the steps implemented in the attenuation slope algorithm in order to estimate $\Delta \beta$ for one window of signal with respect to a reference window, at location $z$, in frequency domain [10],

\[
P(f,z)_{signal} = P_0(f) \exp[2.7 \gamma_T(f) \cdot z] \tag{1}
\]

\[
\ln P(f,z)_{signal} = \ln P_0(f) + 2.7 \gamma_T(f) \cdot z \tag{2}
\]

\[
S_{signal}(f) = -\Re[\ln P_0(f) + 2.7 \gamma_T(f) \cdot z] \tag{3a}
\]

Substituting, $\gamma_T(f) = -\alpha(f) - i\delta(f)$[10], in equation 3a yields,

\[
S_{signal}(f) = -\Re[\ln P_0(f)] + 2.7\alpha(f)_{signal} \cdot z \tag{3b}
\]

Similarly, the reference obtained at $T_0$ ($T = 0s$) is,

\[
S_{reference}(f) = -\Re[\ln P_0(f)] + 2.7\alpha(f)_{reference} \cdot z \tag{4}
\]

Subtracting $S_{reference}$ from $S_{signal}$ results in,

\[
\Delta S(f) = S_{signal}(f) - S_{reference}(f) \tag{5a}
\]

\[
\Delta S(f) = 2.7 z \cdot (\alpha(f)_{signal} - \alpha(f)_{reference}) \tag{5b}
\]

Using the linear approximation of attenuation coefficient, $\alpha(f) = \alpha_0 + \beta(f - f_c)$ [5],

\[
\Delta S(f) = 2.7 z \cdot (\Delta\alpha_0 + \Delta\beta(f - f_c)) \tag{5c}
\]

\[
\Delta S(f) = 2.7 z \cdot \Delta\alpha_0 + 2.7 z \cdot \Delta\beta, (f - f_c) \tag{5d}
\]

Fitting a line to $\Delta S(f)$, and then dividing the slope of the fitted line by $2z$ yields $\Delta \beta$. In the attenuation intercept algorithm, after the acquisition of $\Delta S(f)$, in equation 5d, the value of $\Delta S(f)$ at the center frequency, $f_c$, is evaluated as follows:
\[ \Delta S(f_c) = 2z \Delta \alpha_0 \]  
\[ \frac{\Delta S(f_c)}{2z} = \frac{2z \Delta \alpha_0}{2z} = \Delta \alpha_0 \]  

\( \Delta \alpha_0 \) and \( \Delta \beta \) maps were generated using a moving Blackman window function of length 5\( \lambda \), with \( \lambda = \frac{c}{f_c} \), where \( f_c \) was the imaging center frequency (during this study \( f_c = 4 \text{ MHz} \)). The moving window was shifted by (2.5)\( \lambda \) at every iteration, resulting in \( \Delta z = 0.96 \text{ mm} \).

**RESULTS**

![Figure 2](image_url)

**FIGURE 2.** (a) Dynamic changes of \( \Delta \alpha_0 \) and (b) Dynamic changes of \( \Delta \beta \) (spatially averaged in ROI) in ex vivo porcine muscle tissue during HIFU treatment, for monitoring duration of 10 min, duty cycle was 77% for a total HIFU treatment time of 40 s, and TAP values were 34, 37, 39, 44, and 49 W.

Fig. 2 (a-b) show the dynamic changes of attenuation intercept and attenuation slope, respectively, as functions of HIFU treatment time in ex vivo porcine muscle tissue at different input electric powers. These figures provide a quantitative assessment of the changes in \( \alpha_0 \) and \( \beta \) for duration of 10 minutes.

The visualization of lesion formation is directly correlated with the B-mode images formed from the pulse-echo RF data, shown in Fig. 3(a), with the HIFU transducer being on top. Fig. 3(b) shows the corresponding \( \Delta \alpha_0 \) images, and Fig. 3(c) shows the corresponding \( \Delta \beta \) images generated using the same RF data. Every frame represents a 2-D map of change in attenuation intercept (\( \Delta \alpha_0 \)) and least squares attenuation coefficient slope (\( \Delta \beta \)), respectively.

After the treatment, the bright hyperechoic region in the focal region visible in the B-mode images gradually fades, and after 10 minutes it is hardly visible. However, after 10 minutes, the high intensity regions in the \( \Delta \alpha_0 \), and \( \Delta \beta \) images remain visible. To quantitatively compare the performance of the attenuation slope (\( \Delta \beta \)) and attenuation intercept algorithms (\( \Delta \alpha_0 \)) with each other, and further with conventional B-mode imaging, the contrast to speckle ratios (CSR) [11] of all three different modes of generating images in this study are investigated. The CSR is defined as:

\[ \text{CSR} = \frac{S_{\text{in}} - S_{\text{out}}}{\sqrt{\sigma_{\text{in}}^2 + \sigma_{\text{out}}^2}} \]  

where, \( S_{\text{in}} \) is the mean signal measured inside the region of interest, \( S_{\text{out}} \) is the mean signal measured from same-sized regions outside the region of interest, and \( \sigma_{\text{in}}^2 \) and \( \sigma_{\text{out}}^2 \) represent the
variances of the signal within and outside of the region of interest, respectively [11]. Fig. 4 shows CSR values for lesions created at different total acoustic powers for frames acquired less than 10 minutes after the end of HIFU treatment (representing steady state conditions due to the absence of boiling bubbles, and no temperature rise).

**FIGURE 3.** Lesion growth in degassed ex vivo porcine muscle tissue in (a) conventional B-mode images (b) $\Delta\alpha_0$ images, and (c) $\Delta\beta$ images, where the duty cycle was 77%, resulting in TAP of 49 W, and average focal intensity of 1068 W/cm$^2$ at the HIFU treatment site, for a total HIFU treatment time of 40 s

**FIGURE 4.** Comparison of contrast to speckle ratios at various total acoustic powers, less than 10 minutes after the end of HIFU treatment

**CONCLUSIONS**

We have obtained preliminary data for the changes in attenuation coefficient induced in ex vivo porcine muscle tissues due to coagulation. Changes in attenuation coefficient slope ($\Delta\beta$) and attenuation coefficient intercept ($\Delta\alpha_0$) are both potentially reliable indicators of tissue thermal damage.
The transient characteristics of attenuation coefficient slope and attenuation coefficient intercept were simultaneously investigated in a novel approach. In this new approach, based on a simplified model, $\Delta\beta$ and $\Delta\alpha_0$ values for any given location were estimated as functions of time and location, with respect to pre-treatment values of $\beta$ and $\alpha_0$ at that same location, before, during and after HIFU treatment at different HIFU powers, using pulse-echo ultrasound RF signals.

The rapid increases in attenuation slope and intercept were generally accompanied by some fluctuations due to rapid rises in temperature and the bubble activities. Violent bubble activities were evident as hyperechoic regions in the B-mode images at the HIFU treatment sites. The performance of the B-mode images relied more on the effects of bubble activities than that of the $\Delta\beta$ and $\Delta\alpha_0$ images. The dynamic changes of attenuation coefficient parameters ($\Delta\beta$ and $\Delta\alpha_0$) may be employed in the development of real-time monitoring and guidance of HIFU therapies, and evaluation of HIFU-induced lesions. Further studies are necessary to determine the relative contributions of bubble activities and thermal tissue damage to the dynamic changes in attenuation coefficient parameters ($\Delta\beta$ and $\Delta\alpha_0$) in HIFU-induced lesions.

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REFERENCES