Correcting for Focusing when Estimating Attenuation for Tissue Characterization based on Gaussian Approximations of the Beam Profile

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***Abstract*— Tissue attenuation has shown potential for characterizing soft tissues for many years, but natural biological variability has limited its effectiveness in many applications as a sole indicator of tissue health. Recently however, there has been increased interest in measuring tissue attenuation due to the need to compensate for frequency-dependent attenuation when quantifying scatterer correlation length and scatterer concentration. Correlation length and concentration might be capable of distinguishing benign from malignant tumors if attenuation can be accurately estimated. In this study, the traditional attenuation-estimation algorithm based on measuring the down-shift in center frequency of the ultrasound backscattered signal with propagation depth was modified to correct for focusing along the beam axis. Whereas previous approaches required a reference phantom to correct for the focusing, which is more challenging at higher frequencies, this approach corrected for the focusing by assuming that the field pattern along the focal zone could be approximated by a Gaussian function. Based on this approximation, a correction term was introduced to compensate for the effects of focusing when estimating attenuation in the focal region. The algorithm was verified using computer simulations and an ex vivo tissue sample, both of which used a 33-MHz spherically focused transducer with a focal length of 9 mm and an f-number of 3. The algorithm was validated in computer simulations by moving the region of interest used to obtain the attenuation through the focal region. The algorithms' sensitivity to noise was also assessed by varying the frequency bandwidth used in the Gaussian fit to find the spectral-peak frequency from 15 to 50 MHz. The accuracy of the attenuation estimate in the computer simulations was on the order of 10% for all of the cases while the precision of the estimates varied from 5 to 35% depending on the available bandwidth. Similarly, the attenuation of the ex vivo tissue sample was 2.6±0.6 dB/cm-MHz using the developed algorithm compared to 2.5±0.4 dB/cm-MHz as measured using an insertion loss technique.**

Keywords- Attenuation estimation, tissue characterization

I. INTRODUCTION

Estimates of tissue attenuation are critical in many different tissue characterization applications involving estimates of correlation length and acoustic concentration. Over the years many algorithms have been proposed for making *in vivo* estimates of the attenuation from backscattered ultrasonic signals. The most common algorithms are based on assuming that the backscattered signals have a Gaussian power spectrum and that the ultrasonic attenuation linearly increases with frequency, thus allowing the attenuation to be determined from the downshift in center frequency of the backscattered spectrum [1-8]. When using the downshift in center frequency to estimate the *in vivo* attenuation of backscattered ultrasonic signals using focused sources, it is critical to compensate for the effects of focusing [3, 8]. Otherwise, windowed regions in front of the focus will result in an underestimate of the attenuation and windowed regions beyond the focus will overestimate the attenuation. Previous approaches required a reference phantom to correct for the focusing which is more challenging at higher frequencies.

In our study, we compensated for diffraction or focusing by approximating the field along the beam axis in the focal region by a Gaussian function. Earlier studies have demonstrated that the Gaussian approximation is sufficiently valid when estimating spectral properties for the purpose of tissue characterization [9, 10]. Based on this approximation, a correction term was introduced to compensate for the effects of focusing when estimating attenuation in the focal region. The accuracy and precision of our implementation of the algorithm was then validated by computer simulations and an experiment performed on an *ex vivo* tissue sample from a rat cervix

II. SUMMARY OF ALGORITHM

The expected backscattered amplitude spectrum from the tissue, $E\left[\left|V_{refl}(f)\right|\right]$, is proportional to

$$E\left[\left|V_{refl}(f)\right|\right] \propto \begin{pmatrix} f^2\left|V_{plane}(f)\right|\left(F_\gamma\left(f,a_{eff}\right)\right)^{1/2} \\ \cdot e^{-2\alpha_{eff} z_T}\, \mathrm{e}^{-2\alpha f z_o}\, \mathrm{e}^{-2\left(\frac{z_o^2}{w_z^2}\right)} \end{pmatrix}, \qquad (1)$$

where $\left|V_{plane}(f)\right|$ is the amplitude spectrum returned from a rigid plane placed at the focal plane in a water bath. For the other variables, α_{eff} is the effective attenuation along the

propagation path from the transducer to the focus, z_T is the distance from the aperture plane to the focal plane, $F_\gamma\left(f, a_{eff}\right)$ is a form factor that accounts for the frequency dependence of the ultrasonic backscatter at the focus [11], z_o is the distance of the windowed region from the focus, α is the slope of ultrasonic attenuation versus frequency in the focal region that we are attempting to estimate, and w_z is the effective Gaussian depth of focus that results from approximating the field with a Gaussian function. w_z depends linearly on wavelength and is given by $w_z = 6.01\lambda\left(f\#\right)^2$ for an ideal spherically-focused source where *f*# is the f-number of the source [10]. Assuming that the backscattered spectrum can be approximated by $\exp\left(-\left(f-\tilde{f}_o\right)^2 \Big/ 2\tilde{\sigma}_\omega^2\right)$, Eq. (1) can be written as

$$E\left[\left|V_{refl}\left(\omega\right)\right|\right] \propto e^{\left(-\frac{\left(f-\tilde{f}_o\right)^2}{2\tilde{\sigma}_\omega^2} - 2\alpha f z_o - 2\left(\frac{z_o^2}{w_z^2}\right)\right)} \qquad (2)$$

where $\tilde{f}_o$ and $\tilde{\sigma}_\omega$ are the spectral peak frequency and Gaussian beam width of the backscattered signal.

Therefore, the impact of focusing can be removed by multiplying the received amplitude spectrum (i.e., magnitude of the Fourier Transform of windowed signal) at every window location by $\exp\left(2z_o^2/w_z^2\right)$ prior to finding the center frequency of the spectrum of the signal. The ultrasonic attenuation of the medium can then be calculated by finding the change in spectral peak frequency, f_{peak} , with depth into the tissue using

$$\alpha = -\frac{1}{2\tilde{\sigma}_\omega^2}\frac{\partial f_{peak}}{\partial z_o}. \qquad (3)$$

III. Computer Simulations

A. Simulation Parameters

The algorithm was first validated using computer simulations. In the simulations, 1000 backscattered echo waveforms were generated by randomly positioning scatterers in a homogeneous attenuating half-space. The scatterers had a Gaussian correlation function (i.e., form factor of $F_\gamma\left(f, a_{eff}\right) = \exp\left(-0.827\left(ka_{eff}\right)^2\right)$) with an a_{eff} of 6 μm and were positioned at a density of 6000/mm^3 (~ 5 scatterers/resolution cell). The attenuation and sound speed of the half-space were 2 dB/cm-MHz and 1540 m/s, respectively. The correlation length of 6 μm and attenuation of 2 dB/cm-MHz correspond to previous values measured for the cervix of pregnant rats [12]. The simulated f/3 source used to obtain the echoes had a center frequency of 33 MHz and a focal length of 9 mm. The reference amplitude spectrum returned from a plane placed at the focal plane for the source was given by

$$\left|V_{plane}\left(f\right)\right| \propto \exp\left(-2\left(\frac{f-33\ \text{MHz}}{19.2\ \text{MHz}}\right)^2\right) \qquad (4)$$

similar to the source to be used to determine the ultrasonic attenuation of the rat cervix.

After generating the echoes, the waveforms were combined into 20 sets of 50 waveforms per set. Each waveform was then windowed into five sections with each section having a corresponding length of 0.5 mm along the beam axis. There was 50% overlap between the sections resulting in a total length of 1.5 mm along the beam axis. After windowing, the Fourier Transform was obtained for each section, and the amplitude spectra from all 50 waveforms corresponding to the same window location were averaged to obtain an estimate of $E\left[\left|V_{refl}\left(\omega\right)\right|\right]$ at that tissue depth. The estimate for $E\left[\left|V_{refl}\left(\omega\right)\right|\right]$ was then multiplied by $\exp\left(2z_o^2/w_z^2\right)$ before being fit with a Gaussian function to find an estimate for $\tilde{\sigma}_\omega$ and f_{peak} , the new spectral peak frequency, of the spectrum at that window location, z_o. After finding an estimate for $\tilde{\sigma}_\omega$ and f_{peak} for all five locations along the echo, a line was fit to f_{peak} versus z_o to obtain $\partial f_{peak}/\partial z_o$ from which α can be calculated using Eq. (3). The accuracy was further improved by using the mean value of $\tilde{\sigma}_\omega$ from the five window locations.

B. Simulation Results

When validating the algorithm, two issues were of concern. First, the algorithm should correctly compensate for the effects of focusing. Second, the algorithm should be stable even if measurement noise reduces the usable bandwidth of the received echoes (i.e., the range of frequencies not corrupted by noise). Focusing compensation was validated by moving the center of 1.5 mm region used to obtain the estimates from 1.2 mm in front of the focus to 1.2 mm past the focus. Therefore, the total depth used in the simulations was from 1.95 mm in front of the focus to 1.95 mm past the focus for a total length of 3.9 mm. Likewise, the reduction of usable bandwidth was investigated by varying the bandwidth used in the Gaussian fit to find the spectral peak frequency from 10 MHz to 50 MHz centered at the approximate location for the spectral peak prior to correcting for focusing.

The results for the simulations are summarized in Fig. 1. The error in the attenuation estimate is typically smaller than 15% except for a few window locations. Therefore, reliable estimates should be obtainable even if the usable bandwidth of the signal is significantly reduced by noise.

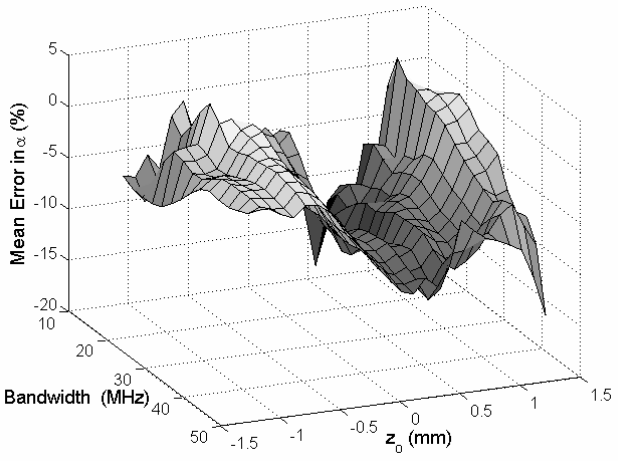

Figure 1. The value of the mean error in the attenuation for the simulations versus the usable bandwidth and the location along z_o of the 1.5-mm section used to obtain the estimates.

Although Fig. 1 indicates that the algorithm is correctly compensating for focusing for the different values of z_o, the performance is easier to evaluate if we restrict our attention to a single frequency range.

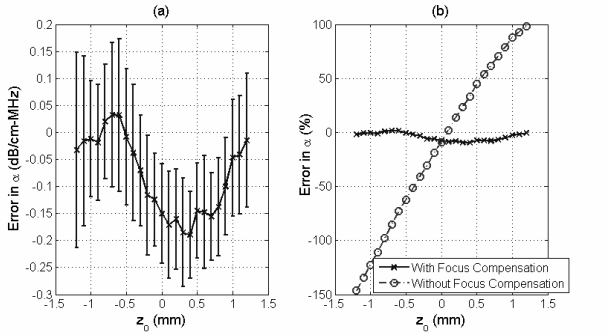

Figure 2. (a) Difference between estimated and simulated attenuation value of 2 dB/cm-MHz plotted versus location along the echo in the simulations using a bandwidth of 35 MHz. The error bars represent one standard deviation above and below the mean as calculated using the 20 independent sets of 50 waveforms. (b) Mean error in attenuation versus location along the echo in the simulations both with and without focusing compensation.

Fig. 2(a) shows the error in the attenuation estimate in dB/cm-MHz versus location along the echo using a bandwidth of 35 MHz when performing the Gaussian fit. Fig. 2(b) shows the percent error in attenuation both with and without focusing compensation. Prior to compensating for focusing, the attenuation of regions before the focus is grossly underestimated while the attenuation of regions beyond the focus is grossly overestimated. After compensating for focusing, the attenuation estimate for all of the regions is approximately the same and within ~10% of the true value for the attenuation.

IV. Ex-vivo tissue experiment

Once the algorithm had been validated using computer simulations, the next step was to validate the algorithm using an *ex vivo* tissue sample of a rat cervix. For the *ex vivo* study, we used a custom-fabricated 33-MHz lithium niobate transducer (NIH Transducer Resource Center, University of Southern California, Los Angeles, CA). In this portion of the study, a nonpregnant Sprague-Dawley rat (Harlan, Indianapolis, IN) was euthanized by exposure to CO_2 for five minutes. The experimental protocol was approved by the Institutional Animal Care and Use Committee (IACUC) at the University of Illinois at Urbana-Champaign and satisfied all campus and NIH (National Institutes of Health) rules for the humane use of laboratory animals. The rat was then weighed prior to necropsy and the cervix was dissected, trimmed, and weighed before being immediately sealed in plastic wrap (Saran Wrap). Saran Wrap was used to prevent degradation of the sample over time upon being immersed in degassed water. Because the tissue was surgically removed from the rat, the attenuation of the same rat cervix could be estimated by two separate techniques, one of which is the algorithm under evaluation.

A. *Through-transmission estimate of tissue attenuation*

The ultrasonic attenuation of the *ex vivo* cervix sample was independently estimated by essentially a through-transmission insertion loss technique. This estimate could then be used to evaluate the accuracy of our algorithm. For this measurement, the backscattered ultrasonic waveforms were recorded from a Plexiglas block placed at the focal plane both with and without the sealed cervix sample between the transducer and the block. The frequency-dependent attenuation of the cervix could then be determined by dividing the amplitude spectra and then fitting a line versus frequency to the log of the result after compensating for the passage of the ultrasound through the Saran Wrap. The attenuation measured using the insertion loss method was 2.5 ± 0.4 dB/cm-MHz.

B. *Pulse-echo estimate of attenuation using proposed algorithm*

After measuring the attenuation of the cervix tissue sample by comparing the spectrum of the received signal from the Plexiglas block both with and without the tissue along the propagation path, the attenuation of the cervix tissue sample was estimated using our developed algorithm. The cervix tissue sample was positioned slightly in front of the focus (9 mm for this transducer) in a water bath and ultrasonic echoes from the cervix were obtained along a 3-mm length of the cervix using a step size of 15 μm. The scanning was performed using a Panametrics 5900™ pulser/receiver (Panametrics™, Waltham, MA) and a computer-controlled micropositioning system (Daedal, Inc., Harrisburg, PA). The echoes were windowed into 5 sections with each section having a depth of 0.48 mm. The sections overlapped by 50%, similar to the simulations, and spanned depths between 7.8 and 9.25 mm so that only echoes from within the cervix would be used in the estimate for attenuation. The echoes were then grouped into sets of 50 waveforms with 50% overlap between the sets and an estimate for $E\left[\left|V_{refl}(\omega)\right|\right]$ at each depth was obtained by averaging the amplitude spectrum of the 50 waveforms. The

50 waveforms spanned a range of approximately 5 beam widths, which was suggested to be optimal in terms of resolution versus estimate variance for parameters estimated from the frequency dependence of ultrasonic backscatter [13]. Then, prior to finding the frequency corresponding to the spectral peak at each depth, $E\left[\left|V_{refl}(\omega)\right|\right]$ was multiplied by $\exp\left(2z_o^2/w_z^2\right)$ using $w_z = 43.8\lambda$ as was measured for our transducer while assuming a sound speed of water for the tissue.

The value for $\tilde{\sigma}_\omega$ and f_{peak} at each depth was then found by fitting the spectra to a Gaussian function using a frequency bandwidth of 40 MHz. Then, the value of $\tilde{\sigma}_\omega$ to be used in the calculation of attenuation was obtained by averaging the values of $\tilde{\sigma}_\omega$ obtained from the fit at each depth. Based on these calculations, the measured attenuation for the *ex vivo* tissue sample using our developed algorithm was 2.6±0.6 dB/cm-MHz, which is in good agreement with the attenuation value of 2.5 ± 0.4 dB/cm-MHz using the basic insertion loss technique.

V. Conclusions

The goal of this study was to modify a traditional algorithm for estimating attenuation *in vivo* by compensating for focusing without the need for a reference phantom. The algorithm was modified by compensating for focusing by assuming the field along the beam axis in the focal region could be approximated by a Gaussian function and consequently multiplying the received spectra by an appropriate term. The validity of the modified algorithm was demonstrated via computer simulations and an *ex vivo* tissue experiment. In the simulations, the accuracy of the modified algorithm was better than 15%, and the attenuation of the cervix in the *ex vivo* experiment was found to be 2.6±0.6 dB/cm-MHz, which is in good agreement with 2.5 ± 0.4 dB/cm-MHz estimated using an insertion loss technique.

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