ROLE OF COLLAGEN IN THE TEMPERATURE DEPENDENCE OF ULTRASONIC BACKSCATTER

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ABSTRACT

Purpose. The combination of hyperthermia with conventional chemotherapy or radiation has proven to be beneficial in the treatment of cancer. A major limitation for hyperthermia currently is the absence of adequate information about the temperature distribution in soft tissue to guide thermal dosimetry. We predicted a monotonic change in ultrasound backscattered energy using lipid and aqueous sub-wavelength scatterers [1]. In-vitro experiments with porcine and turkey tissue verified this prediction. Studies by others have indicated that the echo pattern in ultrasonic images is determined largely by the content, configuration, and distribution of collagen. To better understand the phenomena that cause changes in backscattered energy (CBE), we have 1) refined our theoretical model to include collagen and 2) examined the relationship between CBE and tissue structure in both simulated and measured images.

Methods. CBE images were formed from simulated B-mode images [2]. Simulated images were based on random distributions of populations of aqueous, lipid and collagen scatterers in an aqueous medium. Measured CBE was found from ultrasonic images of turkey breast in a water-bath during heating from 37ºC to 50ºC in 0.5ºC steps. Images were obtained with a Terason 2000 system (Teratech Corp., Burlington, MA) using a 7.5 MHz linear probe by placing the transducer both parallel and perpendicular to the turkey muscle fibers. For both simulated and measured images, CBE images were calculated from the squared envelopes of the B-mode images. CBE images were compared to their respective B-mode images.

Results. Correlation coefficients from CBE based on simulated images showed significant correlation between the CBE and the B-mode images. Simulated images used random placement of scatterers and therefore does not show any specific structure. For the experimental results, there was a weak correlation (r = 0.2-0.34) for both alignments of the transducer with respect to the fiber direction of the turkey muscle. Correlation was also found from regions of bright echo (r =0.39 and 0.36 for parallel and perpendicular orientations, respectively), but was strongest for regions with pure speckle texture (r = 0.8 and 0.65, respectively).

Conclusion. Examination of the statistical correlation between CBE images and their respective B-mode images indicates strong correlation between speckle texture and CBE. The effect, however, of tissue constituents and structure on CBE is not clear. Further investigation of this phenomenon is being done by comparing histological studies with CBE images to correlate fiber structure with the change in backscattered energy.

THEORETICAL PREDICTION OF CBE

$$CBE(T) = \frac{\alpha(T_R)}{\alpha(T)}\,\frac{\eta(T)}{\eta(T_R)}\,\frac{[1-e^{2\alpha(T)x}]}{[1-e^{2\alpha(T_R)x}]}$$

$$\frac{\eta(T)}{\eta(T_R)} = \frac{\left(\frac{\rho_m c(T)_m+\rho_s c(T)_s}{\rho_s c(T)_s}\right)^2+\frac{1}{3}\left(\frac{3\rho_s 3\rho_m}{2\rho_s+\rho_m}\right)^2}{\left(\frac{\rho_m c(T_R)_m+\rho_s c(T_R)_s}{\rho_s c(T_R)_s}\right)^2+\frac{1}{3}\left(\frac{3\rho_s 3\rho_m}{2\rho_s+\rho_m}\right)^2}$$

METHODS

Experimental set-up for collection of 2-D datasets

Measurements were made with the experimental configuration depicted in Figure 1. Tissue samples were heated from 37 to 50ºC in an insulated tank that was filled with deionized water. Data collection was done using Terason 2000 system (Teratech Corp., Burlington, MA) using a 7.5 MHz linear probe. The transducer was placed both parallel and perpendicular to the turkey muscle fibers.

Data Analysis in Conventional 2D Images

For a given backscattered image (Figure 2), non-rigid tissue motion was tracked for the entire tissue region over the temperature range of 37 to 50ºC in 0.5ºC steps. The motion was compensated by estimating the apparent motion of the region from one temperature measurement to the next and then transforming the second image by the measured displacement (Figure 4). Using these motion-compensated images, the change in backscattered energy (CBE) was calculated over the range of temperatures. To find CBE, the compensated images were envelope-detected. Pixel values were squared to determine the backscattered energy at that pixel. The backscattered energy image at 37ºC was used as the reference for the CBE at each 0.5ºC step.

Simulation

Our earlier theoretical model predicted that CBE from an individual scatterer will be monotonic with temperature [1]. CBE was positive for lipid-based scatterers and negative for aqueous-based scatterers. In order to investigate CBE for populations of scatterers, we developed an ultrasonic image simulation model [2], using temperature dependence for individual scatterers from our theoretical model.

MEASUREMENT OF TEMPERATURE-DEPENDENT BACKSCATTERED ENERGY

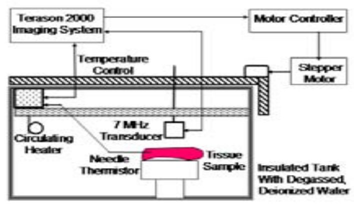


Figure 1. Experimental set-up for automatic acquisition of ultrasonic image sets from tissue at 0.5ºC intervals from 37 to 50ºC.

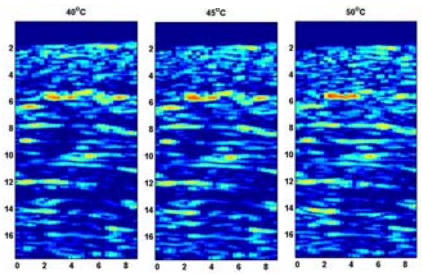


Figure 2. Log-compressed ultrasonic image at 40ºC, 45ºC, and 50ºC respectively. The transducer was placed parallel to the turkey muscle fiber direction. Backscattered energy was calculated by squaring the values at each pixel of the envelope-detected image. Figure 3(below) shows the corresponding CBE images. The backscattered energy image at 37ºC was used as the reference for the CBE at each temperature.

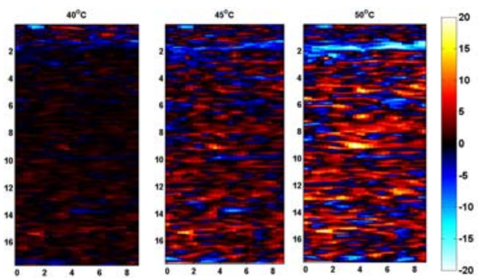


Figure 3 : The CBE images from turkey breast with the transducer placed parallel to the turkey muscle fiber. The CBE is displayed with a 20 dB scale, with red representing an increase and blue a decrease in backscatter energy.

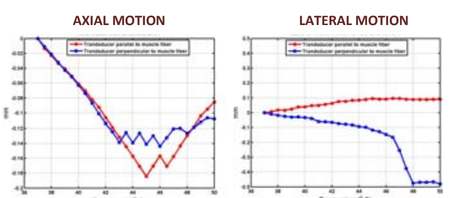


Figure 4 : The lateral and axial motion from the turkey breast experiments with the transducer parallel and perpendicular to the turkey muscle fibers. The motion is shown in mm. Maximum displacement in all specimens was about 0.2 mm in the axial and 0.5 mm in the lateral directions.

SIMULATION OF TEMPERATURE-DEPENDENT BACKSCATTERED ENERGY

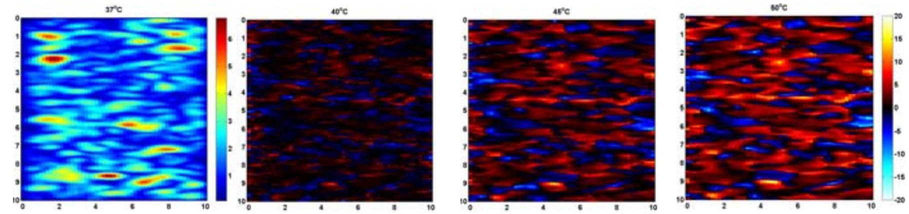


Figure 5 : (From left) Simulated log-compressed ultrasonic image with 1333 aqueous, 333 lipid and 334 collagen scatterers placed randomly in a 1x1 cm² area and the corresponding CBE images at 40ºC, 45ºC, and 50ºC, respectively. There is no distinct structure in the simulated ultrasonic images.

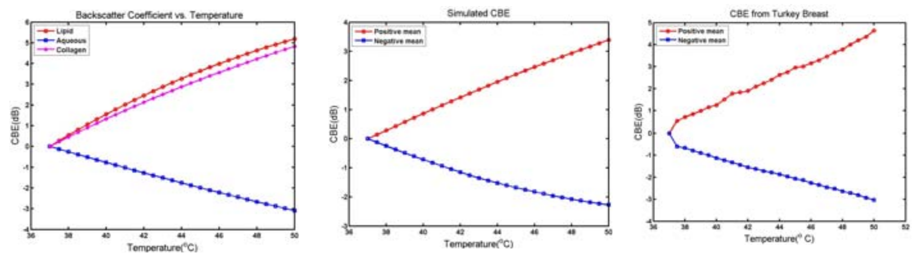
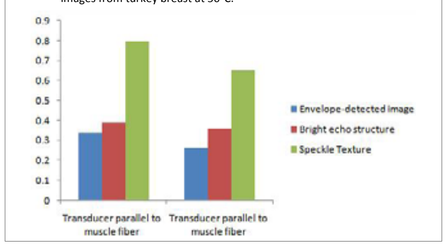


Figure 6 : (Left) The backscattered ratio for lipid, aqueous and collagen scatterers as a function of temperature. Lipid and collagen show an increase of backscatter ratio with temperature while aqueous scatterers show a decrease in backscatter ratio (calculated using the theoretical prediction equations). (Middle) CBE from simulated ultrasonic images using random placement of 1333 aqueous, 333 lipid and 334 collagen scatterers, without any additive noise. (Right) CBE from turkey breast with transducer placed parallel to the muscle fibers.

CORRELATION BETWEEN ULTRASONIC IMAGES AND CHANGE IN BACKSCATTER ENERGY WITH TEMPERATURE

Correlation Coefficients between CBE images and ultrasonic backscatter images from turkey breast at 50ºC.



Correlation coefficients, with error-bars between simulated backscatter images and CBE images for different scatterer population vs. Temperature

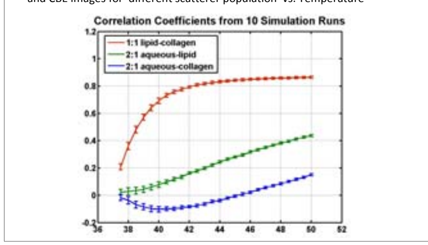


Figure 7: The statistical correlation between ultrasonic backscatter images and the corresponding CBE images. (Left) The correlation coefficients from the turkey breast images which show a strong correlation between the speckle texture and its CBE , both when the transducer is parallel and perpendicular to the muscle fibers. (Right) The correlation between the simulated backscattered images and their corresponding CBE.

CONCLUSION

A strong statistical correlation between the speckle pattern in the simulated ultrasound image and its corresponding CBE image was seen at temperatures >40ºC. For measured images, strong statistical correlation was seen at temperatures >44ºC. The exact phenomena behind CBE and how it is related to tissue structure, especially collagen, however, is still not clearly understood. Histology with collagen-staining dyes and high frequency ultrasound is being used to further establish a visual correlation between the tissue structure and the change in backscattered energy.

REFERENCE

[1] WL Straube and RM Arthur, “Theoretical estimation of the temperature dependence of backscattered ultrasonic power for noninvasive thermometry”, *Ultrasound in Med and Biol*., 20:915-922, 1994.

[2] Trobaugh, J.W., Arthur, R.M., Straube W.L., Moros E.G., “A Simulation Model For Ultrasonic Temperature Imaging using Change In Backscattered Energy ", Ultrasound in Med. & Biol., Vol. 33, No. x, pp. xxx, 2007.

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