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Alterations in Ultrasound Scattering Following Thermal Ablation in *ex vivo* Bovine Liver

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Abstract

Thermal ablation is a minimally invasive cancer treatment which has been rapidly gaining clinical acceptance. It is well known that thermal ablation increases the acoustic attenuation and shear modulus of tissue. In this work, we examine changes to the spatial distribution of scatterers in liver tissue following thermal ablation. Acoustic scatterers within liver tissue have frequently been modeled as pseudo-periodic. The positions of pseudo-periodic scatterers have been Gamma distributed along the beam dimension, and these scatterers are characterized by their mean scatterer spacing (MSS). Prior work have demonstrated significant changes in MSS due to diffuse liver disease, such as steatosis progressing to cirrhosis. However, relatively few results have been reported regarding changes in MSS following thermal ablation. In this study, we estimated MSS in *ex vivo* bovine liver by detecting local maxima in spectral coherence functions calculated using Thomson's multi-taper method. We examined a large number of uncorrelated regions of interest recorded from five normal bovine livers (~300 images from each animal). We also examined a large number of ROI's from five bovine livers following thermal coagulation. All bovine livers were obtained from a commercial meat production facility immediately following animal sacrifice and imaged within 12 hours. Thermal coagulation was induced by heating liver in saline water baths at 80° C for 45 minutes. For normal, unheated liver an MSS of approximately 1.5 mm was estimated. Following thermal ablation, an MSS of approximately 0.5 mm in thermally coagulated tissue was obtained. Frequently, studies estimating MSS in liver tissue provide an MSS estimate regardless of the state of tissue. Authors rarely present what their MSS estimation algorithm would produce if it were applied to tissue which is better modeled as a collection of uniformly, randomly distributed scatterers lacking periodicity. In this study, we found that thermal coagulation results in a loss of periodicity. The MSS of 0.5 mm corresponds to the value that a spectral coherence-based MSS algorithm would produce if presented with a signal that was generated from uniform, randomly distributed scatterers.

Keywords

MSS; thermal ablation; spectral coherence

I. Introduction

Thermal ablation is a minimally invasive treatment for primary and metastatic liver tumors whose success is highly dependent on treating the entire tumor [1]. As such, a low-cost and reliable imaging technology capable of delineating the extent of the treated region could greatly improve the success rate of thermal ablation therapy. It has been noted that thermal ablation greatly increases the shear modulus [2] and the attenuation coefficient [3] of liver tissue. However, relatively little work has been devoted to evaluating changes in scattering in the liver due to thermal ablation.

If scatterers are uniformly and randomly distributed they may be characterized in terms of a backscatter coefficient and their number density. In the liver, a pseudo-periodic model of scattering has been proposed. In the pseudo-periodic scattering model, scatterers are arranged according to a Gamma distribution and are characterized by their mean scatterer spacing (MSS). Several methods have been developed in order to estimate the underlying MSS. In this paper we determine MSS by examining the maximum of the spectral coherence function [4]. We estimate MSS in *ex vivo* bovine liver prior to and following tissue heating in a saline bath.

II. Materials and Methods

A. Spectral Coherence and MSS

We represent the backscattered ultrasound echo signal as a random time series. A random time series may be characterized by the autocovariance function in the time domain, or by the Loève spectrum in the frequency domain. The Loève spectrum is defined according to [5]:

$$\gamma(f_1, f_2) = E[dZ(f_1)dZ^*(f_2)] \quad (1)$$

In the equation, f_1 and f_2 are two arbitrary frequencies and dZ denotes an increment process. Practically speaking, the Loève spectrum is estimated by taking a discrete Fourier transform (DFT) of radiofrequency (RF) data and computing an autocorrelation of that DFT [6]. Spectral coherence is a whitened version of the Loève spectrum. It is given by:

$$\gamma_c(f_1, f_2) = \frac{\gamma(f_1, f_2)}{|\gamma(f_1, f_2)|} \quad (2)$$

Periodic scattering results in local maxima in the spectral coherence function due to constructive interference. MSS is related to the local maximum at frequency coordinates $f_{1,max}$ and $f_{2,max}$ by:

$$MSS = \frac{c}{2 * |f_{2,max} - f_{1,max}|}$$

In the equation, c is the speed of sound in tissue.

In order to estimate spectral coherence, we utilized the multi-taper method reported by Thomson [7]. In the multi-taper method, a sequence of RF data is multiplied with multiple, orthogonal window functions prior to computing the DFT. When using the multi-taper method an estimate of the Loève spectrum is given by:

$$\hat{\gamma}(f_1, f_2) = \frac{1}{K} \sum_{k=0}^{K-1} y_k(f_1) y_k^*(f_2) \phi(f_1) \phi^*(f_2)$$

In the equation y_k is a Fourier transform of windowed ultrasound RF data, where the window is the k^{th} discrete prolate spheroidal sequence (DPSS). ϕ is a phase factor which accounts for the fact that the position of the first periodic scatterer may vary from one windowed data segment to the next. In this work, the first periodic scatterer location was estimated by the location in the envelope of an RF data segment with the maximum amplitude.

B. Simulations

Three types of scattering in tissue were simulated: diffuse, periodic, and sparse scattering. Diffuse scattering tissue consisted of uniformly distributed, randomly placed Rayleigh scatterers with a density of 32 scatterers/mm³. For pseudo-periodic scattering a diffuse background was simulated along with pseudo-periodic scatterers which were placed directly in the center of the beam in the lateral and elevational direction and whose axial positions were given by a Gamma distribution. The MSS for the periodic scatterers was 1.3 mm and the standard deviation was 12%. Additionally the scattering amplitude of the periodic scatterers was multiplied by a Gaussian random number with mean 300 and standard deviation of 50.

Sparse scattering phantoms were simulated by randomly placing 1–3 intense scatterers in the beamline. Simulated phantoms were assigned a sound speed of 1600 m/s. Two sets of phantoms were simulated representing normal and thermally coagulated liver. The simulations of normal liver were assigned a linear attenuation coefficient with a slope of 0.5 dB/cm MHz and the thermally coagulated liver simulations were assigned an attenuation slope of 1.0 dB/cm MHz. For both normal and thermally coagulated liver 12,000 independent A-lines were simulated. For the normal liver 10,000 A-lines contained periodic and diffuse scatterers and 2,000 A-lines contained sparse and diffuse scatterers. For thermally coagulated liver 10,000 A-lines contained diffuse scatterers only and 2,000 A-lines contained sparse and diffuse scatterers.

An ultrasound RF echo signal was calculated by frequency domain simulations using a linear array ultrasound transducer according to the method developed by Li and Zagzebski [8]. The transducer had a center frequency of 5.0 MHz with a –10 dB bandwidth of 2.0 MHz. The transducer was made up of 128 elements having sizes of 0.2 mm laterally and 5 mm elevationally. The lateral and elevational transmit focus of the simulated transducer was at a depth of 3 cm. Dynamic receive focusing and dynamic aperture was simulated with an F/# of 2.

C. Ex vivo bovine liver

Two groups of ten livers were obtained from a slaughterhouse and utilized in the *ex vivo* experiments. One group of ten bovine livers was used for through transmission measurements of sound speed and the other group was used for MSS estimation. From each group of ten livers, five of them were subject to heating in a saline bath maintained at 80° C for 45 minutes. When the liver was not being heated or imaged, it was stored in a refrigerator to avoid tissue decay.

For through transmission sound speed measurements, the amplitude of a signal from a single element transducer was recorded prior to and following insertion of a cylindrical sample inserted into a large water bath maintained at room temperature, 22° C. A five cycle sinusoidal burst excited the transmitting transducer. Three pairs of transmitting (Panametrics, Model No.'s V306, V382, and V309) and receiving (Aerotech Delta, Model No.'s PN2794-1, PN2794-2, PN2794-3) single element transducers were utilized. To determine the sound speed, the shift in the peak of the burst was recorded following insertion of the sample. For each liver, a measurement was made with each of the three transducers. Over the all 15 measurements (5 samples by 3 frequencies), the average sound speed was 1598 ± 6.4 in the unheated liver and was 1592 ± 5.6 in the heated liver.

The remaining ten bovine livers were utilized for MSS estimation. For MSS estimation, RF data was recorded from approximately 300 planes in each liver. A linear array transducer, the VFX 9L4 operating at a center frequency of 6 MHz, was used with the Siemens S2000 ultrasound scanner (Siemens Ultrasound, Mountain View, CA, USA). Prior to any imaging tissue was immersed in saline and was degassed in a low pressure vacuum chamber (25 mm Hg). For the heated tissue, approximately a half an hour was given so that imaging could be performed with the thermally coagulated tissue at room temperature. For imaging, the assumed sound speed of the ultrasound transducer was set to 1590 m/s for the thermally coagulated tissue and 1600 m/s for the unheated tissue. An offset was placed between the transducer and the tissue in the form of a plastic bag filled with ethylene and glycol solution, such that the sound speed matched the tissue. The focal depth was set between 3 and 5 cm depending on the depth of tissue.

III. Results

A. Simulations

Estimates of MSS were obtained by averaging spectral coherence calculations over 10 independent A-lines for two different gate lengths, 12 mm and 16 mm, respectively. The gated data segments were centered at a depth of 40 mm. Local maxima were detected in the frequency range of 2.8 to 7.0 MHz. At each gate length a total of 1,200 MSS estimates were obtained for both simulated tissue types. Note that the maximum MSS that may be estimated is equal to half the gate length. This is logical as a minimum of 2 periodic scatterers must be present in the gated data segment to determine an MSS. These results of the MSS estimation are plotted as histograms in Figs. 1 and 2. The histograms reveal that the distribution of MSS estimates shift towards larger spacings as the gate length increased.

The mean, standard deviation, and mode of the MSS estimates are shown in Table 1. We note that the mean MSS estimate depends upon the gate length. Therefore for simulated liver tissue, the mode of the MSS estimates is what corresponds to a physical quantity. We computed values of the mode of 1.27 and 1.3 mm, corresponding to the true MSS of 1.3 mm. Meanwhile, the mean MSS estimate increases from 1.49 to 1.62 mm for the same data set. In the case of the simulated thermally coagulated tissue there was no true MSS. However, the MSS estimates obtained indicate that most of the probability mass was concentrated at small scatterer spacings, one mm or less. This is likely because of the inverse relationship between frequency and scatterer spacing. At high frequency differences, nearby peaks correspond to small, closely spaced MSS. At low frequency differences, nearby peaks correspond to greater differences in larger MSS. Hence, the long tail in the histograms from MSS of approximately 2 mm up to 6 or 8 mm.

B. Ex Vivo Bovine Liver

For the *ex vivo* data, spectral coherence was calculated for ROI's with a fixed lateral extent of 12 mm and a variable axial extent of 12, 14, 16 or 18 mm. An example ROI and spectral coherence calculation are shown in Fig. 3. As in the previous section, we display histograms of all ~1500 MSS estimates in Figs. 4 and 5. As the gate length increases, we achieve a stable mode in the MSS estimates in the liver. As shown in Table 2, the mode of the MSS estimates in the liver fluctuates between 1.25 and 1.37 mm. As in the simulations, the mean of the MSS estimates steadily increases from 2.45 up to 3.06 mm.

Meanwhile, for MSS estimates in the thermally coagulated *ex vivo* bovine liver the mode in the MSS estimates exhibits large fluctuations between 0.45 and 1.00 mm. A large probability mass can also be seen at spacings between 0.4 and 1.0 mm in the histogram plotted in Figs. 4 and 5. This result agrees with simulated data where no pseudo-periodic scattering was present. According to the simulations, an apparent peak in the MSS distributions at small spacings is simply an algorithmic artifact and doesn't likely correspond to any characteristic spacing in the tissue.

IV. Discussion

In prior work, changes in MSS have been shown to indicate pathological changes to the liver, such as cirrhosis [9]. A fundamental assumption often made is that scattering in liver tissue under investigation remains pseudo-periodic. In this way, MSS is a meaningful parameter for both healthy, normal tissue and tissue in a pathological state. In this work, we showed that structural changes in liver tissue resulting from thermal coagulation disrupt pseudo-periodic scattering in the liver. We found that an MSS of 1.3 mm could be associated with scattering in normal liver. This is in close agreement with what prior authors have measured in human liver, who have estimated an MSS of approximately 1.0 mm. However, an MSS of 0.5 to 1.0 mm found in thermally coagulated tissue was strictly an algorithmic artifact. These results don't imply that an MSS image would not be useful for delineating the extent of the thermally coagulated region. Rather, different MSS estimation algorithms may yield different results in thermally coagulated tissue because there is no true

MSS to associate with this tissue. In light of this, future work on MSS estimation should consider both periodic and aperiodic tissue.

Acknowledgments

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References

1. Goldberg SN, Dupuy DE. Image-guided radiofrequency tumor ablation: challenges and opportunities—part I. *J. Vasc. Interv. Radiol.* 2001; 12(9):1021–1032. [PubMed: 11535764]
2. Bharat S, Techavipoo U, Kiss MZ, Liu W, Varghese T. Monitoring stiffness changes in lesions after radiofrequency ablation at different temperatures and durations of ablation. *Ultrasound Med. Biol.* 2005; 31(3):415–422. [PubMed: 15749565]
3. Gertner MR, Wilson BC, Sherar MD. Ultrasound properties of liver tissue during heating. *Ultrasound Med. Biol.* 1997; 23(9):1395–1403. [PubMed: 9428138]
4. Rubert N, Varghese T. Mean scatterer spacing estimation using multi-taper coherence. *IEEE Trans. Ultrason. Ferroelectr. Freq. Control.* 2013; 60(6):1061–1073. [PubMed: 25004470]
5. Haykin S, Thomson DJ. Signal detection in a nonstationary environment reformulated as an adaptive pattern classification problem. *Proc. IEEE.* 1998; 86(11):2325–2344.
6. Varghese T, Donohue KD. Characterization of tissue microstructure scatterer distribution with spectral correlation. *Ultrason. Imaging.* 1993; 15(3):238–254. [PubMed: 8879094]
7. Thomson DJ. Spectrum estimation and harmonic analysis. *Proc. IEEE.* 1982; 70(9):1055–1096.
8. Li Y, Zagzebski JA. A frequency domain model for generating B-mode images with array transducers. *IEEE Trans. Ultrason. Ferroelectr. Freq. Control.* 1999; 46(3):690–699. [PubMed: 18238469]
9. Fellingham LL, Sommer FG. Ultrasonic characterization of tissue structure in the in vivo human liver and spleen. *IEEE Trans. Ultrason. Ferroelectr. Freq. Control.* 1984; 31(4):418–428.

Fig. 1.

Histogram of MSS estimates in simulated data at a 12 mm gate length. Y-axis is given as probability density such that the sum of all bins equals 1. L. = unheated Liver. T.C. = Thermally Coagulated liver.

Fig. 2.

Histogram of MSS estimates in simulated data at a 16 mm gate length. L. = unheated Liver.
T.C. = Thermally Coagulated liver.

Fig. 3.

(A) B-mode image of unheated *ex vivo* bovine liver with 18 mm ROI outlined in red. (B) Corresponding spectral coherence function with maximum indicated by arrow.

Fig. 4.
Histogram of MSS estimates in *ex vivo* bovine liver with a 12 mm gate length. L. = unheated Liver. T.C. = Thermally Coagulated liver.

Fig. 5.
Histogram of MSS estimates in *ex vivo* bovine liver with a 16 mm gate length. L. = unheated Liver. T.C. = Thermally Coagulated liver.

Table 1

Mean, mode, and standard deviation of MSS estimates in simulated tissue.

Gate Length (mm)	Mean $\pm$ σ , unheated liver	Mean $\pm$ σ , heated liver	Mode, unheated liver	Mode, heated liver
12	1.49 $\pm$ 1.19	1.25 $\pm$ 1.12	1.27	0.45
16	1.62 $\pm$ 1.51	1.47 $\pm$ 1.55	1.30	0.43

Table 2

Mean, median, and standard deviation of MSS estimates in *ex vivo* bovine liver.

Gate Length (mm)	Mean $\pm$ σ , unheated liver	Mean $\pm$ σ , heated liver	Mode, unheated liver	Mode, heated liver
12	2.45 $\pm$ 1.51	2.31 $\pm$ 1.63	1.25	0.84
14	2.78 $\pm$ 1.75	2.48 $\pm$ 1.86	1.35	0.45
16	3.00 $\pm$ 2.01	2.74 $\pm$ 2.11	1.37	1.00
18	3.06 $\pm$ 2.15	3.01 $\pm$ 2.50	1.27	0.53