

# Dynamics of thermoelastic expansion for native and coagulated *ex-vivo* bovine liver tissues

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## ABSTRACT

Dynamics of the thermoelastic expansion of native and coagulated *ex-vivo* bovine liver tissues after their irradiation by short laser pulses were studied. The differences in optical and thermo-mechanical properties of the native and coagulated samples such as their Gruneisen coefficient and optical attenuation depth were quantitatively determined. It was found that for coagulated *ex-vivo* bovine liver samples, the optical attenuation depth decrease by an average of 47%. Also significant differences were observed in the dynamics of thermoelastic expansion of the tissue surface. These differences can be potentially linked to differences in thermo-mechanical properties between native and coagulated samples. The changes in these properties may be used to understand the mechanisms of contrast between coagulated and non-coagulated tissues in optoacoustic imaging.

**Keywords:** optoacoustic imaging, monitoring thermal therapy, laser interferometry, surface displacement measurement, thermoelastic expansion, Gruneisen parameter.

## 1. INTRODUCTION

Optoacoustic imaging (OA) is based on the ultrasonic detection of the stresses generated by short laser pulses in targets. By combining the high contrast associated with optical imaging and the high spatial resolution of ultrasound, optoacoustics appears to be a promising medical imaging modality. Previous studies have shown that the shape and amplitude of optoacoustic signals are sensitive to the changes in optical and thermo-mechanical properties that occur when tissues are coagulated [1-3]. Hence optoacoustics may prove to be a useful tool for monitoring the delivery of thermal therapies, which involves inducing *in situ* coagulation necrosis through elevating temperature of the targeted tissues (i.e. solid tumours) to temperatures between 50 to 100 °C. . Damage induced changes in tissue optical properties and their role in optoacoustic contrast has been investigated [4], [5]. However, damage induced changes in the thermal and mechanical properties of tissues and their influence on optoacoustic signals (i.e. contrast) is not well understood. In this paper, we report on simultaneous measurements of optical and thermo-mechanical properties of native and coagulated *ex-vivo* bovine liver using an interferometric technique.

## 2. METHODS

We examined the thermoelastic expansion of native and coagulated *ex-vivo* bovine liver tissues after their irradiation by short laser pulses. The samples were illuminated by pulses from an optical parametric oscillator (OPO) system (Vibrant B-532, Oportek Inc., Carlsbad, CA, USA) at 750 nm with a repetition rate of 10 Hz and pulse-widths of ~6.5 ns. The energy of each pulse was measured and recorded using a fast silicon photodiode (DET10A, 200-1100 nm, 1 ns rise time, Thorlabs, USA). Displacements of the target's surface were measured using a modified Michelson interferometer described previously [1], [6]. Fourteen packages of bulk liver were purchased from a local market. From each piece of liver, two identical samples were prepared, one for heating and the other unheated. The samples for heating were vacuum-sealed in polyethylene bags and placed in a 70 °C water bath for either 30 minutes (N=7) or 3 hours (N=7). The heated samples were removed and placed inside the center of an aluminum cylindrical container. The untreated liver samples were also placed in the center of another cylindrical container. The liver samples were then fixed in their place by filling the remaining container space with gelatine from porcine skin type A (SIGMA life science, St. Louis, MO, USA). After hardening of the gelatine around the samples, their exposed surface was used for interferometric measurements.

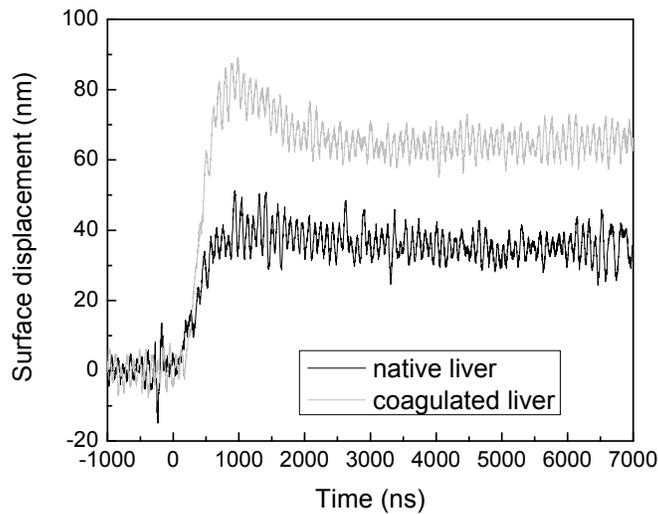


Figure 1 - Typical surface displacements for native and coagulated bovine liver samples. The laser pulse was initiated at time  $t=0$ .

### 3. RESULTS AND DISCUSSIONS

Figure 1 shows typical displacements measured from the surface of native and coagulated bovine liver samples after laser pulse irradiation. These results are in agreement with predictions obtained by solution of the time-dependent thermoelastic expansion equation for tissue-like materials [7]. Upon irradiation with a short laser pulse, the sample surface expands to reach a maximum displacement. Depending on the mechanical properties of tissue, it then may contract and reach to a new equilibrium displacement (Figure 1). We observed that this contraction is more prominent for the coagulated liver samples compared to the uncoagulated liver samples where the contractions were considerably smaller or nonexistent. The target surface remains in an initial quasi steady state equilibrium position before relaxation to a second quasi steady state position due to heat dissipation through the process of thermal diffusion. For biological tissues and tissue-like materials this thermal relaxation occurs at timescales much longer than our observation window with a characteristic time which is on the order of some hundreds of milliseconds [7]. In our analysis, we used this second quasi steady state equilibrium position as the displacement equilibrium position.

Previous studies using this interferometric technique have shown that the Grüneisen coefficient of materials can be determined by a linear fit of the equilibrium surface displacement as a function of incident laser pulse energies [6]. In addition, the slope of the initial rise due to the thermoelastic displacement of the target surface in Figure 1 can also be used to estimate the optical attenuation depth of the samples [8]. This can be done by fitting the initial rise of the target's surface displacement with an exponential growth function in which the rise time constant is dependent on the longitudinal speed of sound in the target and its optical attenuation depth. We used this technique and found an average of 49% decrease in the optical attenuation depth at the wavelength of 750 nm for agar-albumen phantoms after their coagulation. This decrease of the optical attenuation depth because of the tissue changes occurring upon coagulation is in agreement with results of previous studies [4]. Figure 2 shows the measured optical attenuation depths of the fourteen pairs of bovine liver samples, one coagulated and one unheated.

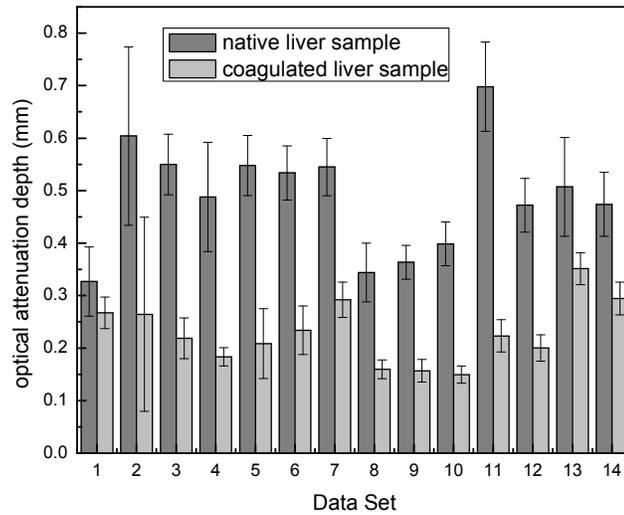


Figure 2 – The changes in the optical attenuation depth for coagulated and non-coagulated *ex-vivo* bovine tissue samples obtained from displacement of samples surface after irradiation by laser pulses. The error bar is  $\pm 1$  standard deviation.

For the *ex-vivo* bovine liver samples linear fits to the surface equilibrium displacement as a function of laser pulse energy yielded correlation coefficients between 0.76 and 0.96. An average increase of 22% in slope of the linear regression for coagulated liver samples compared to non-coagulated ones was observed. The bovine liver samples exhibited substantial variation which can be attributed to inter- and intra-organ variability of biological samples. A two sample paired t-test on slope of linear fits for the equilibrium displacement of liver sample surfaces versus laser pulse energies shows that the difference of results between coagulated and non-coagulated samples is not statistically significant ( $t = -1.90255$  and  $p = 0.08136$ ). Figure 3 shows a bar chart of the results for the pairs of bovine liver samples.

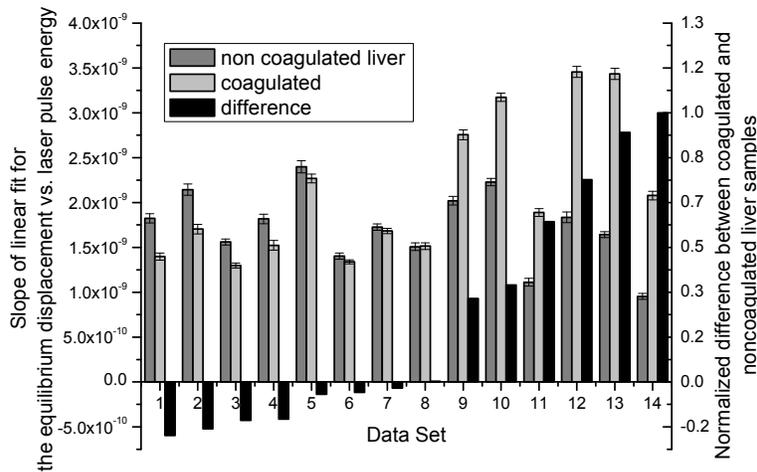


Figure 3 . Slopes of linear regression for the equilibrium displacement of sample surface versus laser pulse energy for native and coagulated liver samples and the difference of samples in each pair. The results are sorted with respect to the difference of slopes for coagulated and non-coagulated samples.

Using an approach similar to the one employed in the case of tissue-mimicking gel phantoms the optical attenuation depth of bovine liver samples were estimated. All the pairs of samples showed a smaller optical attenuation depth for the coagulated liver samples compared to the native ones. Overall an average decrease of 47% between optical attenuation depths of coagulated liver samples compared to those of non-coagulated ones was measured. A two sample paired t-test showed significant difference ( $t = 9.6153$  and  $p < 0.0001$ ) between results of coagulated liver samples and the non-coagulated samples. Figure 2 shows the optical attenuation depth of native and coagulated *ex-vivo* bovine liver tissue samples.

#### 4. CONCLUSION

The results showed a significant decrease of optical attenuation depth for the coagulated liver tissue samples compared to the native ones. This is in agreement with results of other studies using different measurement methods and also consistent with similar results obtained for tissue-mimicking gel phantoms. The slope of linear fit to the equilibrium displacement of the target surface as a function of laser pulse energy can be used to measure the Grüneisen coefficient of the sample. Our results show higher values of the slope for the coagulated samples compared to the non-coagulated ones. The natural variability of the biological samples (e.g. variations in fat and connective tissue content in the small liver areas irradiated) and sensitivity of our measurements to noise prevented us from finding a significant difference between the two groups. However significant differences in dynamics of thermoelastic expansion of native and coagulated liver tissue samples were observed. After the initial surface displacement of the tissue sample and dependent on the mechanical properties of the sample, its surface may retract. It was found that all coagulated samples had large retractions compared to the native samples. Further work is currently undertaken to relate the amplitude and time constant of this retraction behavior to differences of the mechanical properties between the native and coagulated liver tissue samples.

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