1-1-2007

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Transmission Ultrasound to guide Minimally Invasive Thermal Therapy

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Abstract—**Minimally Invasive Thermal Therapy (MITT) is an effective way to destroy diseased tissue and could replace surgery, chemotherapy or radiation. During MITT, temperatures in the range of 55-95 °C are produced locally, resulting in tissue coagulation. A real-time imaging method is required to prevent damage to the nearby normal tissue during heating and to visualize the changes in size and shape of the diseased tissue. It is known that acoustic attenuation is sensitive to both the tissue temperature and the structural changes during thermal therapy. This work examines the potential of ultrasound attenuation imaging during MITT to quantitatively monitor lesion formation dynamics. A transmission ultrasound camera (AcoustoCam, Imperium Inc., Silver Spring, MD) was used to collect acoustic images. The AcoustoCam was initially calibrated using a set of 10 PVCP (Polyvinyl Chloride Plastisol) tissue-mimicking phantoms. The attenuation values were measured by an insertion technique and found to be in the range of 2.18-26.46 dB at a frequency of 4.76 MHz. The 8 bit mean pixel intensity displayed on the screen, and 14 bit mean pixel intensity from the camera's sensor were extracted. A laser fiber (2 cm long cylindrical diffuser, Photoglow, Yarmouth, MA) was used to locally heat albumen temperature-sensitive phantoms and bovine liver tissue. The 8 bit mean pixel intensity as well as temperature were recorded for the heating and cooling periods every two seconds in a region close to the laser fiber. The relationship between the AcoustoCam mean pixel intensity and acoustic attenuation was established. Heating the agar-albumen phantoms and bovine liver tissue increased the local temperature and resulted in an ellipsoidal lesion. In all heating experiments an initial rapid attenuation decrease at low temperatures was followed by a gradual increase in attenuation as temperature increased. During the cooling procedure, attenuation increased rapidly until it reached a steady state, and remained at an attenuation value greater than the value when no thermal lesion was present within the sample. The initial attenuation decrease and the final attenuation increase are reversible and are hypothesized to be a temperature effect, while the gradual change in attenuation at higher temperatures is assumed to be due to protein coagulation. In summary, it was shown that the acoustic camera could monitor in real time the dynamics of lesion formation and that the attenuation profile during heating follows a reproducible pattern.**

I. Introduction

Minimally Invasive Thermal Therapy (MITT) is an effective way to destroy localized diseased tissue and could be used as a replacement to conventional surgery, systematic chemotherapy, or radiation. Comparing to other cancer treatment methods, MITT is less risky and less invasive as it causes minimal damage to the overlying or surrounding tissue. It also requires shorter recovery times and results in a decrease in treatment costs due to its decreased complexity and short treatment duration [4]. During MITT, high temperatures in the range of 55 °C to 95 °C are produced locally in the target tissue or tumour, resulting in irreversible protein coagulation in a target volume of tissue. Thermal ablation procedures use energy sources that destroy a tumour by using thermal energy. The volume of damaged tissue is conventionally called a "lesion" [14]. Several thermal ablation techniques to destroy cancerous tissue have been investigated. These include High Intensity Focused Ultrasound (HIFU) [5, 16, 10], laser ablation [12, 1], microwave ablation [13] and radiofrequency ablation [3].

In MITT a real-time imaging method is desired to prevent the nearby normal tissue from damage during heating and by visualizing the changes in size and shape of the heated tissue throughout the treatment. Several imaging modalities have been investigated in the context of image-guided thermal therapy. Some of these include MRI [6], CT [8] and ultrasound. Ultrasound is non-invasive and less expensive than other imaging modalities, and could be used for the majority of the patient population. Ultrasound attenuation is known to strongly change with temperature with reversible changes mainly due to the temperature effect and irreversible changes assumed to be a result of the coagulation effect [15, 2].

This study involves the investigation of using a transmission ultrasound camera (AcoustoCam, Imperium Inc., Silver Spring, MD) to estimate the acoustic attenuation change during thermal therapy. The AcoustoCam system has previously been used to assess the effects of tissue heating in a few studies [9], [11]. The present study is different from the previous works done, in that: **a.** The attenuation coefficients of the tissue-mimicking phantoms used to calibrate the AcoustoCam are measured, instead of assuming such values based on phantom composition. **b.** Attenuation changes as a function of thermal dose will be investigated. **c.** The AcoustoCam array used has a better SNR compared to previous studies.

II. Methods

The AcoustoCam ultrasonic camera is an attenuation-based ultrasound system which is developed by Imperium Inc. (Silver
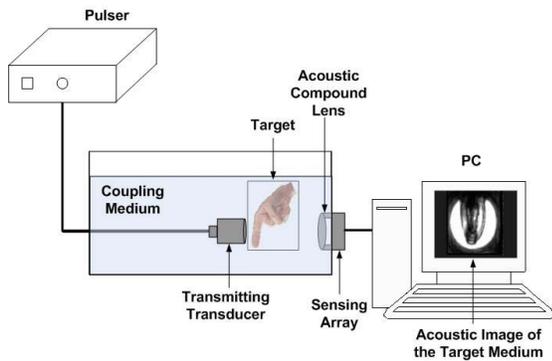
Fig. 1.   A schematic diagram of the AcoustoCam system

Spring, MD) and employs a patented technique that allows collection of ultrasonic images of an object in a similar way that a digital camera captures light images. This transmission ultrasound camera as illustrated in Figure 1 consists of three major parts:

1. The transmitting transducer is a non-focused planar transducer (2.54 cm diameter) which is operated at 3.5 MHz - 7 MHz frequency and produces unfocused planar ultrasound waves that is attenuated by the sample.

2. The acoustic compound lens consists of two acoustic lenses and focuses the ultrasound beam onto a small region of the receiving array.

3. The ultrasound sensing system (Receiving array) consists of a silicon readout array and a PE-CMOS array which is responsive over a wide frequency range. It has 128 by 128 pixel elements and an active size of 1 cm^2.   The ultrasonic burst pulser sends pulses to the unfocused transmitting transducer to produce highly uniform plane ultrasound waves. The plane ultrasound wave travels through the target, gets attenuated and after striking the acoustic lens system is focused onto the sensor array. The focused ultrasound exerts a pressure upon the piezoelectric coating of the sensor array which will be converted to a time-varying signal. The ReadOut Integrated Circuit (ROIC) that is attached to the centre of the of the array is a patented, custom-designed circuit that contains 120×120 cells or pixels. Each pixel contains the necessary circuitry to detect and capture the electrical signals that are generated by the piezoelectric elements. Each datum is then rescaled to a 14-bit value. This process results in the formation of the image data, and repeats 30 times/second to produce a gray scale image on a circular shaped background which corresponds to the diameter of the illuminating beam. The whole setup should be placed in degassed and deionized water. Two types of data could be extracted from the AcoustoCam system: the 8-bit data is the mean pixel intensity of the displayed acoustic image which ranges from 0 to 255. The 14-bit data is the uncompressed sensor's output and is acquired by using the AcoustoVision software which is a software that allows the user to operate the system through a Graphical User Interface

(GUI). Automated access to the 14-bit data is however limited.

A. AcoustoCam Calibration

To obtain quantitative data, the AcoustoCam must first be calibrated with samples of known attenuation called Tissue-Mimicking (TM) phantoms. PVCP (Polyvinyl Chloride Plastisol, MF Manufacturing Co., Fort Worth, Texas, USA) is a non-toxic white opaque plastic solution which was used for TM phantom construction in this study. A set of 10 PVCP phantoms of different thicknesses were constructed. A method called *the insertion technique* was employed to measure the acoustic attenuation of each phantom independently. The insertion technique for attenuation measurement consisted of two similar transducers each having a focal length of 10 cm (Figure 2). One of these transducers acted as a transmitter and sends out ultrasonic pressure wave (P_1) while the other transducer received the attenuated pressure wave (P_2).

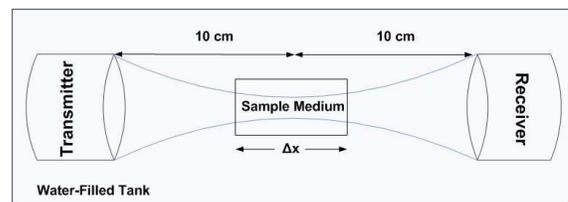These measurements were performed at 4.76 MHz (the

Fig. 2.   Schematic of acoustic attenuation measurement setup

center frequency of the transducer used in the AcoustoCam setup). The sample attenuation was calculated using $\alpha = -20 LOG_{10} \frac{P_2}{P_1}$, to estimate the attenuation of each phantom, known as α in the equation. The measurements were repeated five times to determine the experiment reproducibility. The phantoms were then imaged with the AcoustoCam system and the corresponding 8-bit and 14-bit mean pixel intensities were extracted. Both the 8-bit and 14-bit mean pixel intensities were graphed against their corresponding attenuation values obtained by the insertion technique to establish the relationship between mean pixel intensity and attenuation.

B. Laser Heating Experiments

A 2-cm cylindrical diffuser (Photoglow, Yarmouth, MA) was used to locally heat samples of temperature-sensitive albumen phantoms constructed according to a recipe developed by Iizuka et al (1999). The albumen-based phantom was chosen due to its demonstrated utility as a tissue-mimicking material for laser irradiation [7]. The laser fiber was operated at a power of 7 Watts to conduct three similar laser heating experiments with the albumen phantom for heating periods of approximately 20 minutes. Changes in temperature and mean pixel intensity were measured in a region of interest close to the laser fiber and recorded every two seconds for heating and cooling periods. The mean pixel intensities in the region of interest were converted to their corresponding acoustic attenuations using the developed mean pixel intensity-attenuation

calibration curves. The obtained acoustic attenuation values as well as the temperature profile were plotted as a function of time on the same graph.

The same laser fiber was used to locally heat samples of bovine liver tissue. The laser heating procedure was repeated in four experiments with the laser fiber operated at 4 watts.

III. RESULTS

A. AcoustoCam calibration

The calibration procedure of the AcoustoCam system involves two stages: 1. Independent attenuation measurement of the PVCP phantom set, 2. Image acquisition of the PVCP phantom set and extracting the corresponding mean pixel intensities. As a result, each phantom is characterized by two parameters: Mean pixel intensity and acoustic attenuation. The objective of the first part of the present study was to establish a relationship between the two. Consequently, having one of these parameters will result in obtaining the other one. The following paragraphs discuss the result of the calibration procedure.

1) Attenuation Measurement: Table I lists the attenuation values of the set of PVCP phantoms according to the insertion technique measurements. The uncertainties of the attenuation values for each phantom are the result of repeating the experiment five times.

TABLE I
ATTENUATION OF THE PVCP PHANTOMS AT 4.76 MHz

Phantom	Thickness (cm)	Acoustic Attenuation (dB@4.76MHz)
Phantom A	0.52 ±0.05	2.18 ±0.03
Phantom B	1.17 ±0.05	4.91 ±0.04
Phantom C	1.71 ±0.05	7.18 ±0.20
Phantom D	2.42 ±0.05	10.16 ±0.05
Phantom E	3.17 ±0.05	13.31 ±0.06
Phantom F	3.72 ±0.05	15.62 ±0.06
Phantom G	4.30 ±0.05	18.06 ±0.06
Phantom H	4.93 ±0.05	20.70 ±0.09
Phantom I	5.45 ±0.05	22.90 ±0.13
Phantom J	6.30 ±0.05	26.46 ±0.09

2) Ultrasonic Image Acquisition: The phantoms were scanned by the AcoustoCam system and the 8-bit mean pixel intensities were extracted from the acquired acoustic images. The mean pixel intensities were then graphed versus their corresponding attenuation values as shown in Figure 3. The error bars show the calculated standard deviation of performing the experiment five times.

B. Laser Heating Experiments

Laser heating experiments were conducted with samples of albumen and bovine liver tissue to assess the change in attenuation during heating and after a lesion is created within the sample.

1) Albumen Laser Heating: Albumen phantoms (2 cm thick) were locally heated for approximately 20 minutes using a laser fiber and the AcoustoCam was used to image the phantom during the experiment. Figure 4 shows the changes
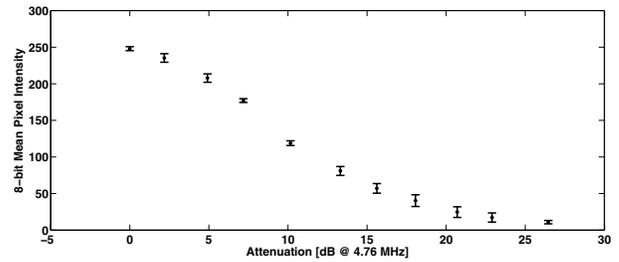

Fig. 3. 8-bit mean pixel intensity obtained from the AcoustoCam setup graphed versus acoustic attenuation

in acoustic attenuation during heating and after the heat source has been deactivated. The attenuation of a region of interest close to the laser fiber was obtained using the mean pixel intensity - attenuation relationship. The temperature profile has also been graphed along with attenuation to specify the temperature ranges at which the significant changes in attenuation occur. The thermocouple measured temperatures
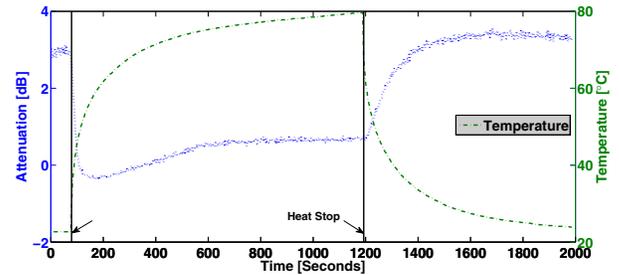

Fig. 4. Attenuation coefficient and temperature profiles for an albumen laser heating experiment

in the range of 23 °C to 80 °C.

The albumen laser heating was conducted in three separate experiments. After each experiment, the phantom was cut open and the diameter of the lesion was measured. An ellipsoidal white lesion could be seen in each case with an average lesion diameter of 0.72±0.02 cm.

2) Bovine Liver Laser Heating: Slices of bovine liver tissue were locally heated by a laser fiber while placed in the AcoustoCam system for imaging. The experiment was repeated four times. After the sample was heated for 20 minutes and cooled down to room temperature, it was cut opened and the diameter of the ellipsoidal lesion was measured to be 0.71±0.02 cm on average. Figure 5 shows the change in attenuation during the procedures of heating and cooling for bovine liver tissue. The temperature change recorded by the thermocouple showed that the temperature close to the laser fiber reached temperatures of 73 °C.

IV. CONCLUSION

The AcoustoCam proved sensitive enough to attenuation changes for a wide range of attenuation values. The proposed
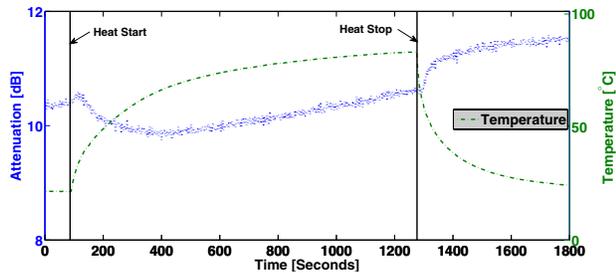
Fig. 5. Changes in attenuation and temperature during laser heating for a slice of bovine liver tissue.

methodology characterized a set of PVCP tissue mimicking phantoms by two parameters. The two parameters were the acoustic attenuation obtained by an independent insertion technique and the mean pixel intensity acquired by the AcoustoCam utility. Graphing the mean pixel intensities against their corresponding attenuation values, a relationship could be established between the two which helps to interpret the mean pixel intensity of a given sample medium in terms of acoustic attenuation.

The mean pixel intensity - attenuation calibration curve was used to assess the dynamic change in ultrasound attenuation during laser heating experiments with samples of albumen and bovine liver tissue. In all experiments, an ellipsoidal lesion was made within the sample around the light emitting portion of the laser fiber with an average diameter of 0.70 cm. The average increase in attenuation was detected to be 0.54 dB for albumen was 0.54 dB and 1.27 dB for bovine liver. Given that the lesion diameter is 0.72 cm, if we assume that the attenuation is constant in the lesion, the change in attenuation is 0.54/0.72=0.75 dB and 1.27/0.71=1.78 dB for albumen and bovine liver, respectively.

In both albumen and liver heating experiments the behaviour of attenuation during heating and cooling could be divided into three major stages:

1. The initial rapid decrease in attenuation upon the laser fiber activation.

2. The gradual small increase in attenuation after the local temperature reached 50 °C.

3. The final rapid increase in attenuation right after the heat source was deactivated.

Two significant factors are assumed to be responsible for these changes. The initial and final changes in attenuation are temperature effects and reversible. The negative effect of temperature on acoustic attenuation of water (especially at temperatures above 50 °C) could explain the reversible temperature effect. The small attenuation increase at stage 2 is hypothesized to be due to the structural changes which happen due to local heating and protein denaturation.

After the local temperature reached the room temperature, the attenuation remained at a value higher than the initial attenuation before a thermal lesion was made within the sample. The irreversibility of the total attenuation increase

suggests that the attenuation changes are not temperature dependent and that these changes are the result of the structural changes that occur due to protein coagulation.

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