Controlled Cryogenic Ablation Using Ultrasonic Sensing

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***Abstract*—The Cryoablation process is one of the methods for treating various tissue abnormities. Cryoablation devices are mostly minimally invasive and are used in open loop control, monitored by additional imaging devices. In this study, we monitor the growth of the ablated area by using a miniature ultrasonic transducer that is collocated with the tip of the cryogenic device. The 20 MHz ultrasonic sensor is capable of measuring the size of the ice sphere that is created in front of the needle. In addition to real time monitoring of the ablation process, the ultrasonic sensor will be able to determine the local thickness of the tissue prior to the treatment (thus enabling the setting of the power of the ablation treatment). The combined device will shorten the ablation treatment and will eliminate the need for additional ablation treatments or monitoring devices. The proof of concept was done in water, ultrasonic gel and muscle tissue. In the experiments we found that, in the frequency domain one can identify at 10-12 MHz the increase of the intensity of the returned echo in the ice and the decrease of the signal after the ice-tissue boundary. One can correlate the increase of the intensity with the growth of the ice sphere.**

Keywords – Cryogenic, Ablation, Control, Ultrasound, Piezo, Ice

I. INTRODUCTION

Cryosurgery, also referred to as Cryotherapy or Cryoablation, is a minimally invasive surgical technique in which freezing is used to destroy undesirable tissue. Cryoablative techniques have persistently improved over the past forty years with the development of successive generations of devices including Cryoneedles, Cryoballoons, intraoperative ultrasound and vast knowledge of the mechanisms by which cells are affected by low temperature exposure [1]. We now recognize two mechanisms causing cell death following a freezing cycle: direct mechanism adjacent to the ablating device of cell rupture due to intracellular ice crystal formation and cellular dehydration with associated osmotic damage, and indirect mechanism of ischemia and necrosis throughout the tissue/tumor peripheral zone [2, 3]. To perform a cryosurgical procedure successfully, it is important to monitor precisely and evaluate accurately the extent of freezing. Failure to do so can lead to either insufficient or excessive freezing, and consequently, to recurrence of malignancies treated by cryosurgery or to destruction of healthy tissues [4]. Most of the Cryoablation devices are used in an open loop control. The results of the treatment are inspected by additional imaging devices such as ultrasound, camera, temperature sensors and other sensors according to the relevant application [1].

In this study, we intend to add a miniature ultrasonic sensor to a cryoablation device in order to determine the treatment progress in real time, observing the ice sphere's boundary growth. This capability allows controlling directly the ablation process by closed loop control. Such a device, will be able to determine much more effectively (faster, more accurately and more precisely). The close loop controlled cryogenic device will be more efficient and safe than the current treatment. In addition to real time monitoring of the ablation process, the ultrasonic sensor will be able to determine the local thickness of the target area before treatment and will enable a more accurate setting of the device's parameters (freezing power and period). The system will shorten the ablation treatment and eliminate the need for reoccurrence treatments.

To the best of our knowledge, there is no Cryoablation device with collocated sensor that monitors in-situ the progress of the target tissue's freezing.

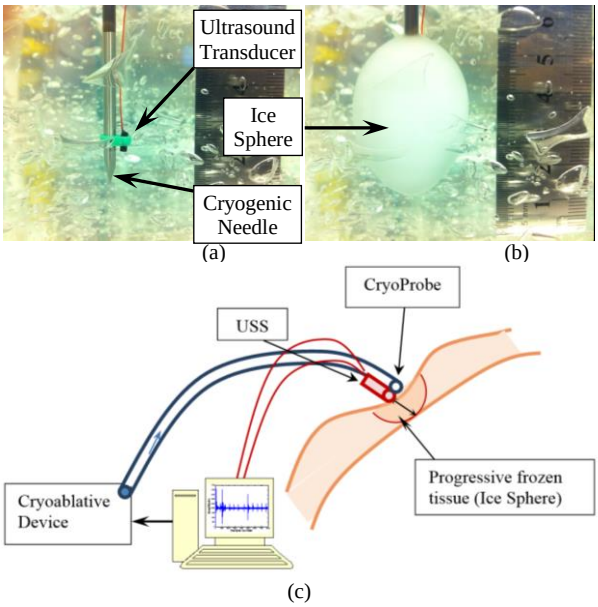

Figure 1: CryoProbe to sensor connection before (a) and after (b) freezing; Schematic overview of the system (c)

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The purpose of the present study is to show feasibility of detecting the ice sphere growth from within the ice sphere during Cryoablative therapy without using additional monitoring devices. We assume that by transducing a high frequency ultra-sound wave we will be able to determine the location of the ice sphere outer boundary due to the impedance differences between frozen and unfrozen tissue. We expect to be able to distinguish the frozen tissue's returning echo's (inside the ice sphere) from the unfrozen tissue's returning echo's (at the outer rim of the ice sphere).

In section 2 (Method), we will present an overview of the entire system with detailed description of its two main components; Ablation device and monitoring device, following with an explanation of the monitoring method and the analysis done. Section 3 (Results) will include a summary of the results of different analysis steps and our conclusions will be presented in section 4.

II. METHOD

A. System Overview

The controlled Cryoablation system, that we developed is a device for Cryoablation therapy with an ultrasound transducer attached to it as shown in Figure 1. In the future the ultrasonic sensor will be integrated into the cryogenic needle.

The main components of the system are:

1. A cryoablation device with a Cryoprobe reaching extreme low temperatures (about -170ºC) at its tip. Acronymed as CAS.
2. A forward looking ultrasonic sensor that can measure regular and frozen tissue up to 10 mm in depth. Acronymed as USS.

The detailed description of the components is described in the following sections.

B. Ablation Device

We used the Cryo-ablative device designated as IceSense3™ system (Figure 2) manufactured by IceCure Medical. IceCure Medical developed a minimally invasive Cryo-ablation therapy for the Women health market [5].

Figure 2: IceCure's IceSense3™ System (Left) and its CryoProbes with an example of Ice Sphere at their tip (Right)

The IceSense3™ system, provides a minimally invasive, in-office, definitive treatment which uses low temperatures (about -170 C°) to destroy (ablate) the targeted tissue in situ. The system uses a closed loop cryogen which reaches a Cryoprobe tip at the center of the ablate tissue and cooled to sub-zero temperatures, removing heat from the targeted tissue by conduction [6] (See Fig 1b and Figure 2). During the Cryo-ablative procedure, an ice spheroid (for convenience we regard to it as a sphere) is formed around the Cryoprobe tip. The ice sphere size varies in time and can reach a diameter of 40 mm and length of around 55 mm after 10 minutes.

C. Monitoring Device

We have used an Ultrasound transducer manufactured by Vermon, France as our monitoring (Figure 3).

Figure 3: Vermon ultrasonic sensor -Ø2X5.5 mm

The transducer is a single element transducer with outer dimensions of Ø2X5.5 mm and central frequency of 18.5 MHz as shown in the frequency response in Figure 4.

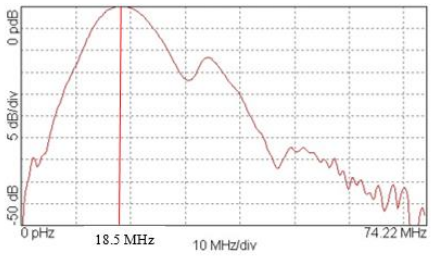

Figure 4: Vermon US sensor frequency response with central frequency of 18.5 MHz

This frequency is equivalent to 0.126 mm axial resolution [7] in water. The frequency response (Figure 4), has a central frequency of 18.5 MHz (at -3dB) bandwidth frequency of 8.7 MHz, low cut frequency 14.2 MHz and high cut frequency 22.9 MHz.

The ultrasound transducer time response in water is noted in Figure 5.

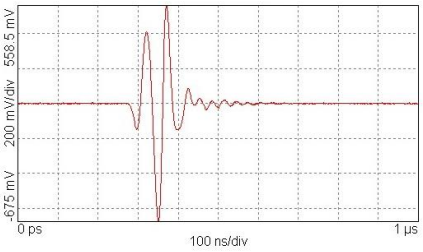

Figure 5: USS time response

The transducer is controlled by USBox system of Lecoeur Electronique Company, transmitting 230 Volts (1 volts step), square pulse. The monitoring was done in A-mode, transmitting and receiving from the same transducer. The returning Echo's were monitored by Matlab software, sampling in 80 MHz in order to observe returning Echo's of up to 40 MHz.

D. Experimental Method

Our main objective, was to recognize the outer contour of the ice sphere in real time (during treatment) when our monitoring device is located at the center of the freezing zone hence allowing us to have both treating and monitoring elements in a single device. The transducer was chosen to be minimally in size to allow in the future positioning inside the ablating element (less than ø3 mm). In this experiment, we connected it to the center of the CryoProbe freezing zone with additional connector placing the transducer adjacent to the CryoProbe outer surface (Figure 1). We have used US Parker gel inside a Standard 1000 ml beaker as our tissue model (ablated medium) and compared it to water and chicken breast tissue.

Several cryogenic treatment simulations were done. The freezing process duration was up to 10 minutes. The ice sphere size was measured using an external camera in time periods of 30 seconds as a reference to the transducer measurements. All returning echoes were received in a time to voltage raw data manner and several analyses were done in order to observe the ice sphere growth as detailed below.

E. Data Analysis

Looking at the time response of the echo (Figure 6), one can observe the large attenuation of the signal in the ice.

The ice-water boundary, cannot be distinguished from direct A-mode inspection of the ice sphere's outer contour.

In order to detect the boundary we transferred the signal to the frequency domain using Matlab software's signal analysis toolbox. We are using the following steps to estimate accurately the ice sphere's contour's distance:

1. The sound velocity in ice is estimated by correlating the signal response near the exit of the transducer (called ringing in the US jargon) in water and ice.
2. Using the sound velocity, the time response is converted into distance and an A-mode US image is derived (Figure 6).

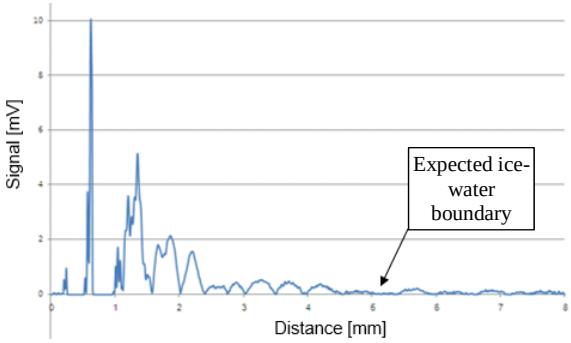

Figure 6: Returning US Echo of 5 mm thick frozen meat slice

3. The time response is also converted to the frequency domain using the short time Fourier transformation. The representation of the data is in a spectrogram that enables identification of significant features in the image (See Figure 7).

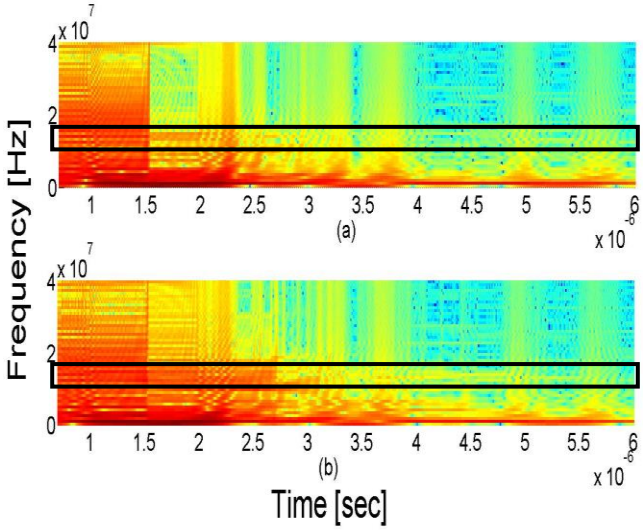

Figure 7: The spectogram at 3 mm (a) and 4 mm (b) radius Ice sphere (In Parker Gel). The area of interest of 10-12 MHz is in the black frames. The intensity of the echo is depicted by jet colormap.

4. In order to emphasize the growth of the ice sphere we used a binary conversion. This calculation is based on the reduction of the spectrogram according to the derivative of the intensity in the spectrogram (growing intensity black, and vice versa).
5. We also calculated, the sum of the total intensity at the targeted frequency range and found that it is a good indicator of the growth of the ice sphere.

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III. RESULTS

Using the correlation analysis, we were able to determine that the frozen gel used has a sound velocity of 2520 m/s (the literature value of ice sound velocity is 3600 m/s and water 1430 m/s) with this property determine we were able to match the returning Echo's with their correct location.

The dynamic process of the growing ice sphere is characterized by the increase of the intensity from the ice layer and the reduction of the intensity of the echo from the water or tissue layer beyond the ice sphere. Figure 7 demonstrates that this process is the most apparent in the bandwidth of 10-12 MHz.

Focusing on the bandwidth we identified in Figure 7 we are able to show a consistence advancing increase of intensity of the echo in time as shown in Figure 8 (red and yellow in the jet colormap).

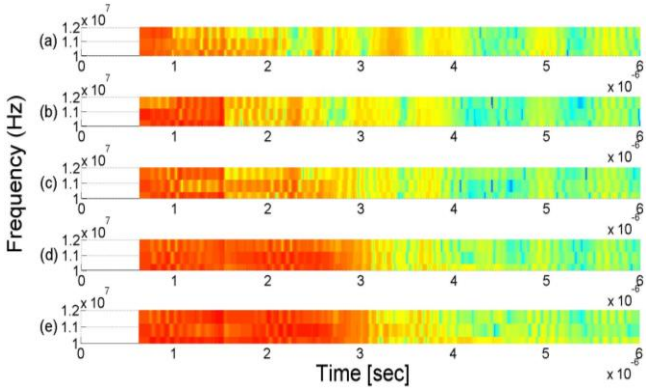

Figure 8: 10-12 MHz Range at different ice sphere sizes: radius of – 0 mm (a), 2 mm (b), 3 mm (c), 4 mm (d) and 5 mm (e) - (In Parker Gel The intensity of the echo is depicted by jet colormap

This dynamic process can be correlated to the growth of the ice sphere. The increase in the echo from the ice is more emphasized than the decrease in the gel.

To better distinguish the intensity increments, we did additional binary analysis (Figure 9).

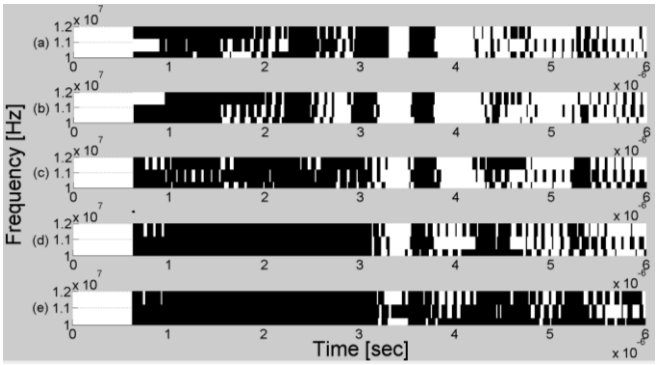

Figure 9: 10-12 MHz Range Binary differences analysis between the base line (0 Sec) and different ice sphere sizes: radius of – 1 mm (a), 2 mm (b), 3 mm (c), 4 mm (d) and 5 mm (e) - (In Parker Gel)

Each signal received at different ice sphere size was compared to the base signal (prior to the freezing cycle) – areas with increased intensity than the base signal are shown in black and areas with lower intensity than the base intensity are shown in white. The advance of the boundary can be detected by the increase of the black area with the growth of the ice sphere. This binary intensity contrast is easier to detect using computerized models in real time.

Finally, we calculated the total intensity of the returning Echo's of different ice sphere sizes during its growth and received an increasing graph for each experiment. We compared all experiments in gel and water in a single graph

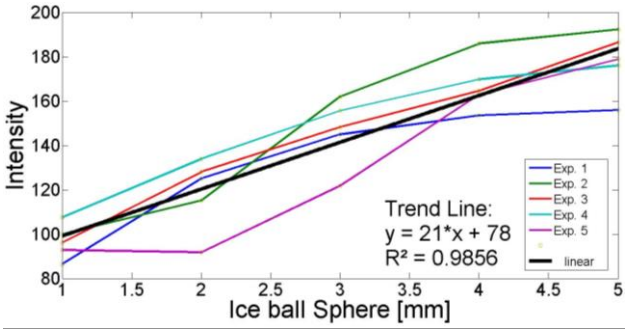

Figure 10: Retrieved signal Total Intensity Vs. different ice sphere sizes – 10-12 MHz Range (All Experiments in water or Parker Gel) with additional combined Linear Trendline (in black).

and receive a linear trend line with R-squared value of 0.9656 (Figure 10).

One can see that the total intensity is a good quantitative measure for the increase of the ice sphere.

The results in the chicken breast tissue show similar results to the gel. There were visible increments with time of

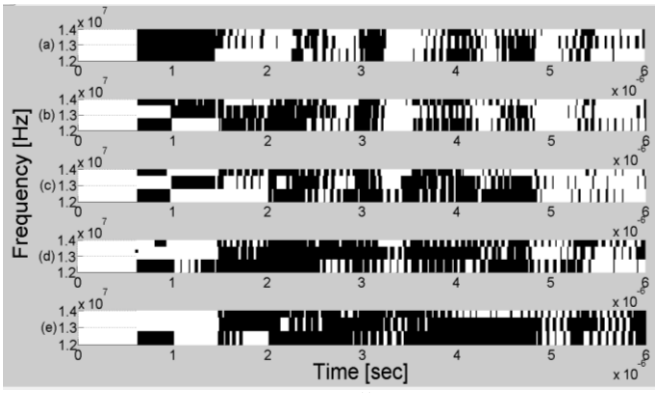

Figure 11: 10-12 MHz Range Binary differences analysis between the base line (0 Sec) and different ice sphere sizes: radius of – 1 mm (a), 2 mm (b), 3 mm (c), 4 mm (d) and 5 mm (e) - (In chicken breast)

the returning Echo's at 10-12 MHz frequency range, better observed when looking at the binary analysis (Figure 11).

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We also repeated the returning Echo's total intensity calculation of different ice sphere sizes during its growth and received an increasing graph similar in values to all other experiments (Figure 12).

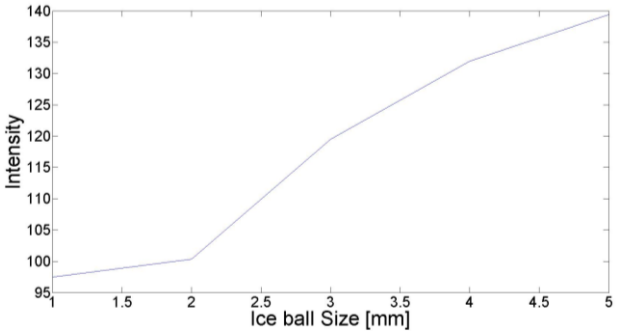

Figure 12: Retrieved signal Total Intensity Vs. different ice sphere sizes – 10-12 MHz Range (In chicken breast)

Combining all the information gathered from the results, we receive a very good indication that measuring the ice ball growth from inside the ice ball is possible even in real time.

IV. CONCLUSIONS

Examining our results, we can clearly distinguish a growing intensity of the signal with the ice sphere growth. We also noticed, that our finding are similar when using ultrasound gel and breast tissue as our ablate model.

With further experiments (using improved ultrasound sensor), we will be able to determine the exact correlation between the intensity growth to the ice sphere real size with high accuracy and precision.

This capability will allow us to monitor the Cryoablation treatment from within the Cryo-ablative device and in the future have a closed loop combined device both treating and monitoring in real time.

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