Dynamics and control of cavitation during HIFU application

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Abstract: In this paper the results of two studies related to high-intensity focused ultrasound (HIFU) and cavitation are reported. The first study described used polyacrylamide phantoms to gain insight into the behavior of cavitation activity in the focal region of the HIFU transducer. Results indicate that cavitation is the source of the previously-observed enhanced heating effect in HIFU. The second study discussed used agar-graphite phantoms to see if changing the duty cycle of the driving could affect some amount of control over the cavitation activity; the results indicate that it can.

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1. Introduction

Above a certain critical acoustic pressure threshold, the temperature rise measured near the focus of a high-intensity focused ultrasound (HIFU) source in a tissue-mimicking phantom behaves much differently than below this threshold. It has been shown that the change in behavior can be attributed to cavitation activity[1,2,3] - the bubbles act as an additional heating source[2] in two ways: (1) they re-radiate the incident HIFU at higher frequencies which is absorbed and (2) they allow viscous heating to occur at the bubble wall. This 'enhanced heating' effect has also been observed *in vivo*[4].

In addition, cavitation bubbles have recently proven useful in a number of different ways: creating larger and deeper lesions[5], as tissue ablators[6,7], and as image enhancers during HIFU application[8]. Although cavitation has been shown to be beneficial, if it is directed to the wrong region or allowed to continue out of control, it can cause irreversible damage to healthy tissue. In light of this fact, it is essential that the cavitation behavior should be well understood, and if possible, controlled. In this paper, we present results from experiments designed to observe cavitation in optically-transparent tissue phantoms with video imaging and experiments designed to gain a degree of control over the cavitation field.

2. Experimental Methods

Two independent experimental setups were used to collect the data presented in this paper. One was used for the video imaging (VI) experiments, and the other for the cavitation control (CC) experiments. The two apparati were built similarly enough so that a single schematic (Fig. 1) can be used to represent both.

The HIFU source (Sonic Concepts, H201, H102)[15] was driven by an amplifier (ENI 150, ENI A-500), whose input signal (2.0 MHz for the VI study, and 1.1 MHz for the CC study) was provided by a function generator (HP8116A, HP33120A). The amplifier output impedance was matched to the HIFU source via a matchbox provided by the manufacturer of the HIFU source transducers. The PCD transducer (Panametrics, V313) was a 15 MHz, single element focused piezo-electric receiver. The signal from the PCD transducer was high-pass filtered (cut off frequency 5 MHz; Allen Avionics, F508-5PO-B) and input to a peak detector (Panametrics, PDM-2, 5052UA) whose output was recorded by a data acquisition (DAQ) computer. The temperature near the focus of the HIFU was measured by an E-type thermocouple (Omega Engineering, 0.13 mm wire diameter). The tip of the thermocouple was positioned off axis (at a pressure null) so as to minimize any thermocouple artifacts. The DAQ computer both collected data and controlled the function generator (via GPIB) so that precise insonation times could be achieved. The lens (Navitar 18-108 mm zoom), camera (Pulnix 9701-TM), VCR (Sony DSR-11) and light source (Stocker + Yale, Lite Mite) were only used in the VI experiments.

In a general sense, the experimental protocol for each study was the same: after confocally aligning the PCD and HIFU transducers, the phantom was insonified for a set amount of time (from 7 s to in some cases 55 s) while simultaneously recording both the PCD and thermocouple voltages as a function of time. For the CC experiments, both CW and pulsed insonation were employed; for the VI experiments, only CW insonation was used. The main difference between the two studies was the type of tissue phantom used. In the CC study, agar-graphite phantoms were used[1,2,9], while in the VI study, optically-transparent acrylamide phantoms with BSA (Bovine serum albumin) were employed[9,10].

All of the pressures reported in this paper are pressure amplitudes and were found using a

calibration performed by the authors which relates the voltage amplitude applied to the HIFU transducer to the focal pressure amplitude in water. The measurements were made using a calibrated membrane hydrophone. (Precision Acoustics, 0.2mm element 15 μm membrane hydrophone).

3. Results and Discussion - VI Experiments

An image of the acrylamide phantom prior to insonation is shown in Fig. 2a. Visible in the image are the front face of the PCD transducer (the out-of-focus circle) and the tip of the thermocouple. The HIFU focal zone (defined by the half-maximum intensity contour) is indicated with a black oval. The HIFU transducer (not shown) is situated to the left of this field of view, so the HIFU beam propagates from left to right. Figure 2b shows the lesion that develops after a 10 s exposure (CW, 3.0 MPa, 2.0 MHz). The shape and size of this lesion are comparable to ones created in the absence of a thermocouple. Figure 3a shows the temperature near the focus as a function of time for three different focal pressures. The peak PCD voltage as a function of time is shown in Fig. 3b. The insonation time was 7 s at both 0.5 and 1.9 MPa, and 10 s at 3.0 MPa. At 0.5 MPa, there is no measurable heating, and likewise no detectable cavitation. The grouping of red data points around 0.4 V (the minimum non-zero output of the peak detector) is the result of increased scattering by the phantom (due to the higher insonation pressure amplitude) - it should not be interpreted as evidence of cavitation. The data points that fall between 0V and .4V are attributed to noise which is picked up by the system between the peak detector and the digitizer in the computer.

The data taken at 3.0 MPa indicates that the cavitation threshold has been exceeded. Note that for this pressure, the temperature rise is not smooth - rather it possesses a complicated structure. From the beginning of the time series to 5 s, the temperature rises quickly and erratically,

and then from 5 s to 10 s (when the HIFU was turned off) the temperature decreases, despite a constant acoustic intensity from the HIFU source. Following Refs. 2 and 3, we call these two behaviors enhanced heating and bubble field shielding respectively. Enhanced heating has been described above. Shielding can be attributed to cavitation bubbles being formed in front of the HIFU focus which shield the position of the thermocouple from acoustic energy, thus causing a decline in temperature.

Acoustic shielding by the HIFU-induced bubble field is also reflected in the peak PCD voltage as a function of time - note the decrease in PCD voltage from 5 to 10 s. Further evidence that the HIFU energy is being shielded from the focal region is evident in the final frame of video from the highest pressure run, Fig. 2b. A lesion was formed with dimensions roughly equivalent to that of the HIFU focus. The optically-apparent lesion forms because the BSA in the acrylamide denatures (and hence loses transparency) above a certain temperature threshold[10]. Note that the lesion is thicker (in the photo's up/down direction) to the left of the thermocouple; this is can be attributed to the cavitation activity that occurs pre-focally - the temperature rise is greater and thus more BSA denatures. This is very similar to the *in vivo* cavitation lesions shown by Watkins *et al.*[11] The development of this lesion as a function of time can be seen in Mm. 1. The movie begins before the HIFU is turned on, and concludes after it is turned off. When the HIFU is turned on, the words "HIFU ON" appear in the lower middle portion of the field of view. It is compelling to see that when the thick part of the lesion begins to develop, the focal temperature begins to decrease (i.e. at roughly 5 s after the HIFU is turned on). In the movie it is clear that the lesion "grows" towards the source (which is to the left of the field of view), in agreement with other studies[12].

Mm1. This is where the movie file link should be placed.

4. Results and Discussion - CC Experiments

As a reminder, the phantoms used in the CC study were agar-graphite based, thus there are no images showing the behavior of the focal zone during insonation. Furthermore since the phantoms and instrumentation employed for this setup were different, a quantitative comparison of the PCD signals from the VI and CC experiments should not be made.

The goal of the CC experiments was to see if using pulsed insonation could change the character of the cavitation noise as a function of time - more specifically, we wanted to see if shielding could be avoided entirely. In figure 4 we show the results of two experimental runs, each performed at the same pressure amplitude (2.93 MPa). The red line shows the PCD signal resulting from a 20 second CW insonation. The blue line shows the PCD signal during a 5 second CW insonation followed immediately by a 60 second pulsed insonation (here the duty cycle was 20%). Note the dramatic decline in PCD signal during the CW insonation. As before this decline can be attributed to cavitation bubbles forming in the pre-focal region which shield the focal region from acoustic energy, thus inhibiting cavitation there. There is also a dramatic decline (with approximately the same negative slope as the red line) in the blue line for the first 5 seconds of the data run, which is not surprising since the insonation parameters for this time span were the same as for the red line. There is a drastic difference in the PCD signal after the insontion is switched from CW to pulsed. The signal first increases and then remains constant for the remainder of the experimental run. We maintain that this is evidence that pulsing the HIFU can control the cavitation activity prefocally, allowing ulrasound energy to reach the focus (i.e. it eliminates shielding).

5. Conclusions and Future Work

Evidence has been provided that supports the claim that enhanced heating and shielding during HIFU insonation can be attrubuted to cavitation activity near and in front of the focus of the HIFU transducer. In addition, we showed that some degree of control over the cavitation field can be gained by driving the sound source in a pulsed manner, rather than with CW insonation. A qualitative explanation of how the control is achieved is as follows. Assume a priori that there are sufficient cavitation nuclei in the focus to foster the development of a cavitation field. When those nuclei are driven in a CW manner, they can grow via rectified diffusion to a size limited by the shape instability threshold (see Yang *et al.*[14] for a detailed discussion of HIFU-relevant bubble dynamics). When the bubbles become shape unstable they break up into many smaller bubbles; these smaller bubbles subsequently grow via rectified diffusion and the growth-breakup cycle is repeated, multiplying bubble densities and physical effects (including shielding) until the HIFU is turned off.

Bubble growth during pulsed insonation is not limited by the shape instability threshold because the bubble cannot reach this critical size during the brief on-time of the ultrasound. Instead, the bubbles grow (again via rectified diffusion) until the end of the on-time, and then dissolve (but not completely) during the off time. Since they do not dissolve completely they make up a population of pre-existing bubbles, poised to serve as cavitation nuclei for the next on-time of the ultrasound. Note that this explanation suggests the existence of an optimum duty cycle (ratio of HIFU-on time to total time) at which the HIFU source should be driven.

An obvious next step to this work is to perform cavitation control experiments with acylamide phantoms. Doing so will allow the development of the lesion to be monitored optically.

If shielding is truly absent while operating above the cavitation threshold, the shape of the lesion would coincide with the focal zone of the HIFU transducer, as opposed to the tadpole shape seen in Fig. 2b and Mm. 1. Furthermore, the optimal duty cycle for heating should be determined. Since the optimum duty cycle depends on the rate at which bubbles grow and dissolve with HIFU-on and HIFU-off times respectively, we expect it to be a function of the dissolved gas concentration and effective viscosity in the phantom.

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Captions

Figure 1: Schematic showing the experimental set up used for the two studies described in the text. The light source, VCR, camera and lens were only used in the VI study.

Figure 2: Images from video, showing the focal region prior to (a) and following (b) insonation (3.0 MPa, 2.0 MHz, CW for 10 seconds).

Figure 3: Plots showing temperature (a) and peak PCD signal (b) as a function of time during and following insonation for three different focal pressures: 0.5 MPa (red), 1.9 MPa (blue) and 3.0 MPa (black). Insonation time for the two lower pressures was 7 seconds, and 10 sections for the highest pressure, all at 2.0 MHz.

Figure 4: Plots of the peak-detected PCD signal acquired for two different types of intonations. Red: 20 seconds of CW insonation; blue: 5 seconds CW insonation followed by 55 seconds of pulsed (20% duty cycle) insonation.

Figures

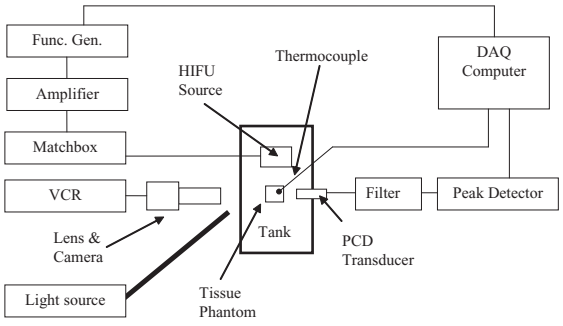
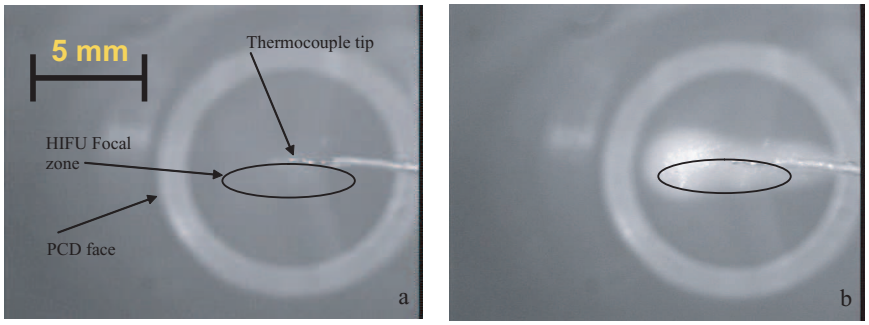


Fig. 1: .



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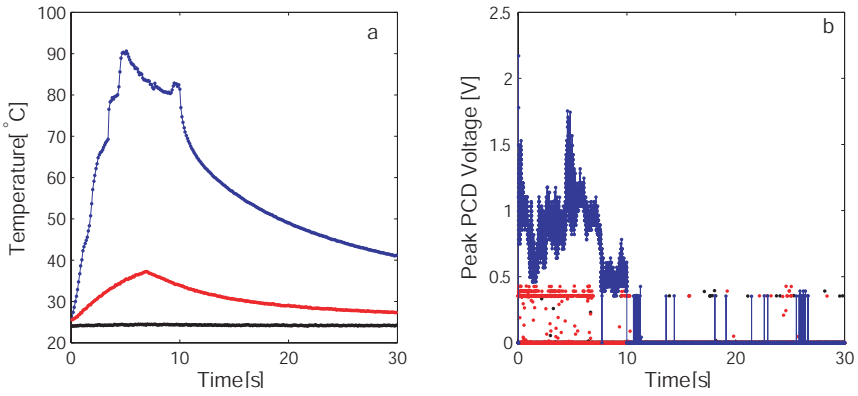

Fig. 3:

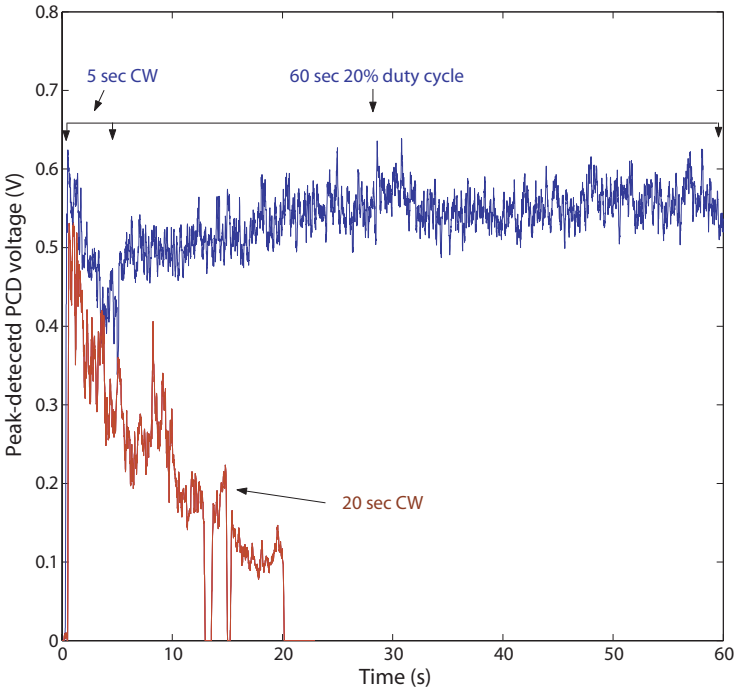
5 sec CW
60 sec 20% duty cycle
20 sec CW
Peak-detecetd PCD voltage (V)
Time (s)
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0
10
20
30
40
50
60

Fig. 4: