Effect of the intended shift in the propagation direction of the cavitation generation position on the coagulation position in bubble-enhanced ultrasonic heating

Sota Kannoto[1‡], and Shin Yoshizawa[2,1,3*]
([1]Grad. School of Biomed. Eng., Tohoku Univ.; [2]Grad. School of Eng., Tohoku Univ.; [3]SONIRE Therapeutics)

1. Introduction

High-intensity focused ultrasound (HIFU) treatment is a minimally invasive cancer treatment in which high-intensity ultrasound waves are focused from outside the body on the tissue to be treated to coagulate and necrotize it. HIFU treatment has a problem of long treatment time due to the small focal region compared to the region to be treated. Therefore, methods to improve heating efficiency by using cavitation bubbles have been proposed. "Trigger HIFU sequence" has been proposed as a HIFU exposure method that efficiently utilizes the heating enhancement effect of bubbles[1)]. This method consists of a high-intensity, short-duration "trigger pulse" to generate cavitation bubbles and a medium-intensity, long-duration "heating burst" to cause sustained volumetric oscillation of the generated bubbles. In order to safely utilize bubbles for treatment, it is necessary to ensure that bubbles are generated in the region to be treated. In this study, the effects of the shift of the trigger pulse focus in the direction of ultrasonic wave propagation on the position of bubble generation and the position of coagulation were experimentally investigated by high-speed camera imaging and ultrasonic imaging.

2. Materials and Method

2.1 Experimental setup

Fig. 1 shows the experimental setup used in this study. A 128-element array transducer with a diameter of 147.8 mm and a focal length of 120 mm was used to generate HIFU at a frequency of 1 MHz. Experiments were conducted in degassed water (dissolved oxygen saturation 20~25%). A chicken breast tissue with a thickness of 2 mm embedded in 0.8% low-melting-point agarose gel (hereafter referred to as sliced tissue phantom) and a chicken breast tissue in bulk were exposed to HIFU. A linear probe was placed above the tissue and ultrasound imaging was performed at a transmission frequency of 4.63 MHz during HIFU intermission time. In the sliced tissue phantom experiment, high-speed camera images were taken at 500 fps during the HIFU exposure by backlight using a pulsed laser with a pulse duration of 200 ns.

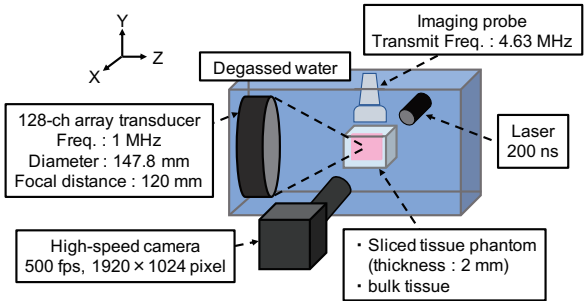

Fig. 1 Experimental setup.

2.2 HIFU sequence and image processing

Fig. 2 shows the HIFU exposure sequence. Trigger pulses with 0.025 ms at 145 kW/cm^2 and heating bursts with 43.9 ms at 5.2 kW/cm^2 (2.5 kW/cm^2 in the bulk tissue experiment) were used in the sequence. A HIFU intermission of 3.075 and 3 ms before and after the trigger pulse was provided, respectively. The cycle of 50 ms was repeated 100 times for a total of 5 s of the sonication. Ultrasound imaging was also performed during the intermission after the trigger pulse. For ultrasound imaging, the triplet pulse sequence (3P) was used, in which three pulses with phases of 0°, 120°, and 240° are transmitted in the sequence and the received waves are added together to selectively extract nonlinear echoes from bubbles[2)]. The trigger pulse was focused on the same position or 4 mm beyond the heating burst focus. The focal shift of 4 mm of the trigger pulse was set considering the phenomenon that cavitation clouds are generated in front of the focus through shock scattering (free-edge reflection of

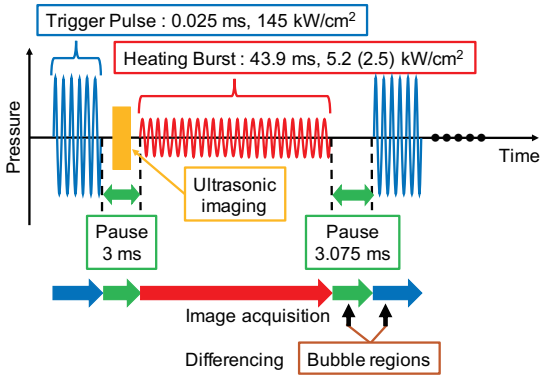

Fig. 2 HIFU exposure sequence and timing of captured image used for image processing.

ultrasound waves at the bubble surface)[3]. The processing method for high-speed camera images is also shown in Fig. 2. The images taken during the trigger pulse were differenced from those taken during the intermission immediately before the trigger pulse, and the resulting images were summed every 1 s to observe the bubble regions generated by the trigger pulse.

3. Result and Discussion

Fig. 3 shows the results with and without the focal shift of the trigger pulse for the 0-1 s, 2-3 s, and 4-5 s bubble regions. In all cases, the center of the image is the heating burst focal point, and that position is set to z = 0. Fig. 3 shows that when the focal shift was 0 mm, the position of the center of gravity of the bubble regions went back from z = -2.5 mm to -3.5 mm over time. When the focal shift was 4 mm, the bubble regions went back from z = 1.0 mm to -1.1 mm and continued to remain near the heating burst focal point compared to the case without the focal shift.

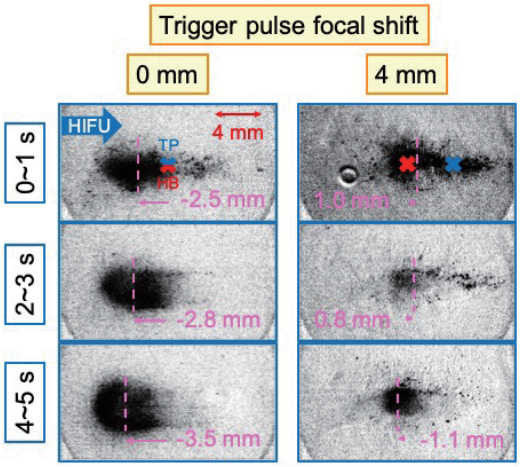

Fig. 3 Comparison of time variation of bubble regions without and with trigger pulse focal shift.

Next, the results of 3P imaging in the sliced tissue phantom and bulk tissue at 3 s from the start of HIFU exposure are shown in **Figs. 4** and **5**, respectively. In both cases, the upper row shows 3P imaging images, and the lower row shows high-speed camera images of the 2-3 s bubble regions in Fig. 4, and the coagulation regions after the sonication in Fig. 5. Fig. 4 shows that the bubble regions obtained by 3P imaging are roughly consistent with the results of high-speed camera images. Fig. 5 shows that the amount of the shift of the bubble regions obtained by 3P imaging and that of the coagulation regions are approximately the same.

Fig. 3 suggests that generated cavitation bubbles remained even before the trigger pulse in the heating burst focal region due to the temperature

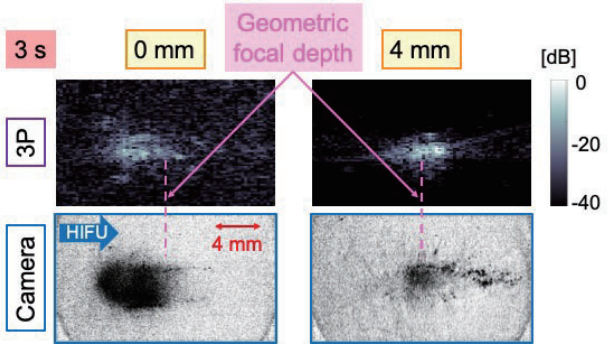

Fig. 4 Comparison of 3P imaging and high-speed camera imaging of bubble regions in the sliced tissue phantom.

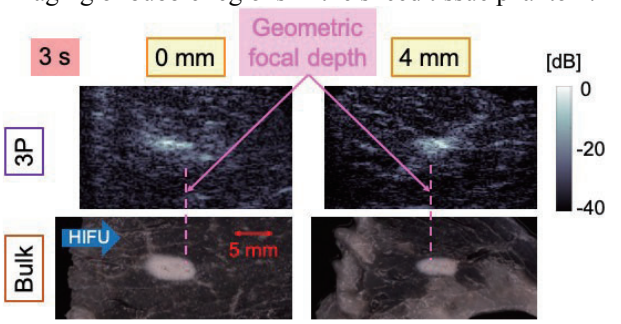

Fig. 5 Comparison of bubble and coagulation regions in the bulk tissue.

increase, and that the bubbles were generated back toward the front side by the reflection of trigger pulses from these bubbles. And it was thought that this effect could be suppressed by the focal shift of the trigger pulse. The results in Figs. 4 and 5 suggest that the amount of shift of the bubble regions can be observed with 3P imaging, which can be used as feedback to optimize the bubble regions during the cavitation-enhanced HIFU heating.

4. Conclusion

The results of this study show that the focal shift of the trigger pulse is effective in improving the reproducibility of the bubble generation position, and that 3P imaging can be used to observe bubbles, which showed the similarity to the high-speed image during the trigger pulse. Using 3P imaging as feedback, it would be possible to explore the amount of the focal shift to coagulate the intended region.

References

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E-mail: ‡sota.kannoto.p6@dc.tohoku.ac.jp, *shin.yoshizawa.e7@tohoku.ac.jp