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Development of efficient method of generating cavitation bubble clouds by scanning ultrasound focus

超音波焦点走査によるキャビテーション気泡群の効率的な生成手法の開発

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1. Introduction

High-intensity focused ultrasound (HIFU) is one of the minimally treatment techniques. Ultrasound generated outside the body is focused to a treatment region. In the focal region of HIFU, cavitation bubbles can be generated by a large negative pressure. Cavitation bubbles oscillate in a HIFU field and can enhance the heating effect of the therapeutic ultrasound. The rapid shrinkage of bubbles generate high temperature and pressure inside the bubbles, which produce reactive oxygen species for sonodynamic therapy. The collapse of bubbles induces mechanical damage to the surrounding tissue. Histotripsy on clinical trial stage employs the mechanical effect of cavitation bubbles[1]. This is a treatment method of destroying tissue mechanically by higher intensity pulses than used for thermal treatment. A treated region is absorbed in about a few months.

In this study, we experimentally investigated the effect of scanning the HIFU focus in the direction of ultrasound propagation on the generation of bubble clouds for the purpose of efficient bubble cloud generation in histotripsy and sonodynamic therapy.

2. Materials and Methods

Fig. 1 shows experimental setup. A 128-channel array transducer (Japan probe) with a diameter of 147.8 mm and a focal length of 120 mm was used for HIFU irradiation. The transducer was driven by a staircase-wave driving system (Asahi TU-TX02) at a frequency of 1 MHz. A high-speed camera (Shimadzu HPV-2A) capable of capturing images at a maximum of 1000 kfps and 102 frames was used for high-speed optical imaging. A laser light source (Cavitar CVILUX smart) was used as a backlight. A polyacrylamide gel phantom was placed in a water tank and used as a target.

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The position of HIFU focus was electronically scanned in the gel phantom. Fig. 2 shows the schematic of the focal positions and HIFU exposure sequence. The three focal positions with a spacing of 5 mm in the HIFU propagation direction were scanned, starting from the far side of the transducer. The HIFU exposure sequence consisted of only three ultrasonic pulses for bubble cloud generation at the focal points ①, ②, and ③. One of the processes of bubble cloud formation is that the cloud grows by the backward free-end reflection of ultrasonic waves from bubbles grown by the negative pressure of ultrasonic waves, which is called "shock scattering" [2]. According to the shock scattering mechanism, it would be possible to generate bubble clouds continuously by scanning the HIFU focus to the front edge of generated bubble clouds. The interval time Δt was fixed at 10 μs based on the results of preliminary experiments. The duration time of the first pulse was 100 μs in all experiments. The duration time of the second and third pulses was varied from 1 to 10 μs. The intensity of the three pulses was kept constant at 50 kW/cm^2. 102 frames were taken at 250 kfps (a frame interval of 4 μs).

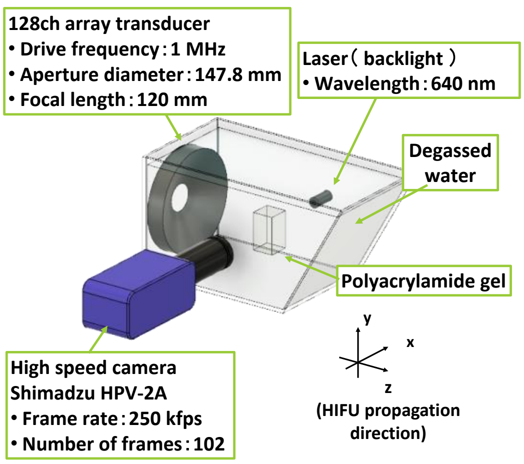

Fig. 1 Experimental setup

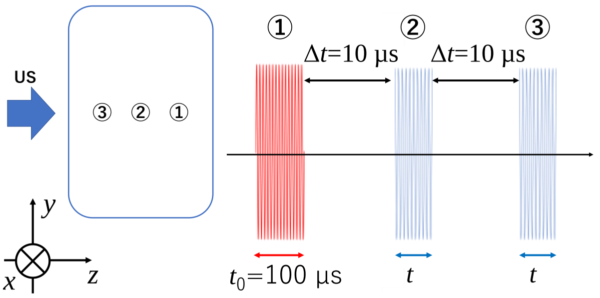

Fig. 2 Focal positions and HIFU exposure sequence

3. Results and Discussion

Fig. 3 shows the results for a duration of second and third pulses of 10 μs. It is observed that the bubble clouds are continuously generated by scanning the HIFU focus to the edge of the previously generated cloud. No bubble cloud is observed 12 μs after the start of the first pulse focused to the point ① in Fig. 3(a). On the other hand, bubble clouds were generated at focal points ② and ③ in spite of the pulse duration time of only 10 μs. This result suggests that the HIFU focus scanning according to the generated bubble cloud region can provide an efficient method of generating bubble clouds with less acoustic energy.

Table 1 shows the bubble cloud formation probability when the duration time of the second and third pulses is varied from 1 to 10 μs. The generation probability is defined in this study as a probability that a bubble cloud was generated by irradiation to the focus ③ when a cloud had been generated by irradiation to the focus ①. The results show that bubble clouds were generated with a relatively high probability with a duration of 10 μs. Bubble clouds were generated twice in three experiments even with a duration of 6 μs.

The probability did not monotonically decrease as the irradiation time decreased. This might be due to the effect of individual differences in the gels. The increase of number of experiments would reduce the effect of the individual differences. The focal spot spacing of 5 mm might have affected the results. The spacing was determined according to our preliminary experiment, and this setting may not have been optimized sufficiently. Considering the formation of bubble clouds through shock scattering mechanism, one of the important conditions is that the cloud should be generated by the first pulse irradiation at the appropriate position and region, so as to match the focal position of the second pulse. Since the position and region of a bubble cloud generated by the first pulse varies in a certain range in each experiment, the bubble cloud formation probability may be possible to be increased by setting the shorter focal spot spacing, considering the case that the size of the generated bubble cloud is relatively small.

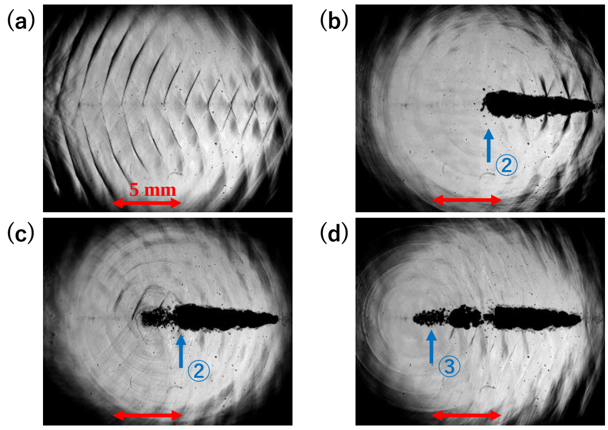

Fig. 3 High-speed images in the gel phantom. (a) about 12 μs after the start of the first pulse focused to the point ①, (b) just after the end of the first pulse, (c) during the second pulse irradiation to the focal point ②, and (d) during the third pulse irradiation to the focal point ③.

Table 1 Probability of bubble cloud generation

t (μs)	1	4	6	8	10
probability	0	0	0.67	0.50	0.83

4. Conclusion

In this paper, we investigated the effect of scanning the focus in the direction of ultrasonic wave propagation on the continuous generation of cavitation bubble clouds. Setting the focal spot spacing in consideration of the bubble cloud formation through shock scattering mechanism, bubble clouds were generated in the second and third focal regions even with a shorter pulse duration than that required for the first cloud formation. Further study is needed to evaluate the efficiency of bubble cloud generation in detail. It will be necessary to increase the number of trials with various settings of the focal position and interval time.

References

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