Development of efficient method of histotripsy by expanding cavitation region using ultrasound focus scanning in the direction of ultrasound propagation

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1. Introduction

HIFU (high-intensity focused ultrasound) is one of the non-invasive modalities for cancer treatments. In this treatment, ultrasound generated outside a body is focused on a target tissue in the body. Cavitation bubbles generated by the strong negative pressure during HIFU exposure oscillate in volume, causing heating, chemical, and mechanical effects on the surrounding region. Histotripsy is a treatment technique that utilizes this mechanical effect, in which the irradiation of HIFU pulses with a low duty ratio and extremely high acoustic pressure mechanically destroys tissue through shock waves, hydrodynamic fluctuations, and shear stress generated by the collapse of cavitation bubbles. The size of the region treated by Histotripsy in a single HIFU exposure is small, typically in the order of mm. This provides a good spatial selectivity of the treatment, but at the same time results in a long treatment time when the tissue to be treated is much larger than it. Therefore it is important to expand the treatment region to reduce the treatment time. In this study, we experimentally investigated a HIFU exposure sequence for an efficient method of histotripsy, which is expected to increase the treatment throughput.

2. Experimental setup

Fig. 1 shows the 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 chicken liver was placed in a water tank and used as a HIFU exposure target. It is known that region treated by histotripsy show lower brightness in ultrasound images. Therefore, we performed ultrasound imaging of the HIFU focal area in the plane including the direction of HIFU propagation.

The HIFU focal points and exposure sequence are shown in **Fig. 2**. The sonication time for the first focal point A was 90 μs to increase the probability of cavitation bubble cloud generation, and the sonication time for the second and subsequent sonications was 10 μs. The sequence shown in **Fig. 2** was used as 1 cycle, and 400 cycles were irradiated at a repetition period of 300 ms. Acoustic intensity in all sonications was constant at 71 kW/cm2. The ultrasound sequence with scanning the focus toward the transducer was created to utilize the mechanism of 'shock scattering', [1)], in which a cavitation bubble cloud is formed by reflected waves from individual bubbles.

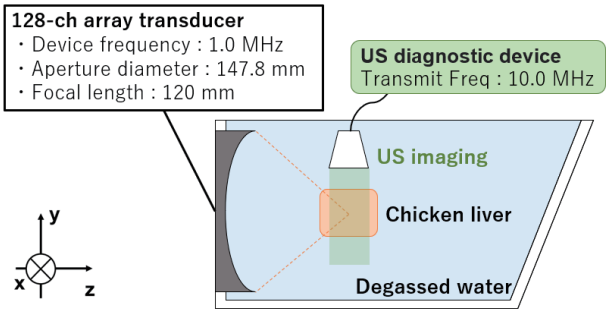

Fig. 1 Experiment setup

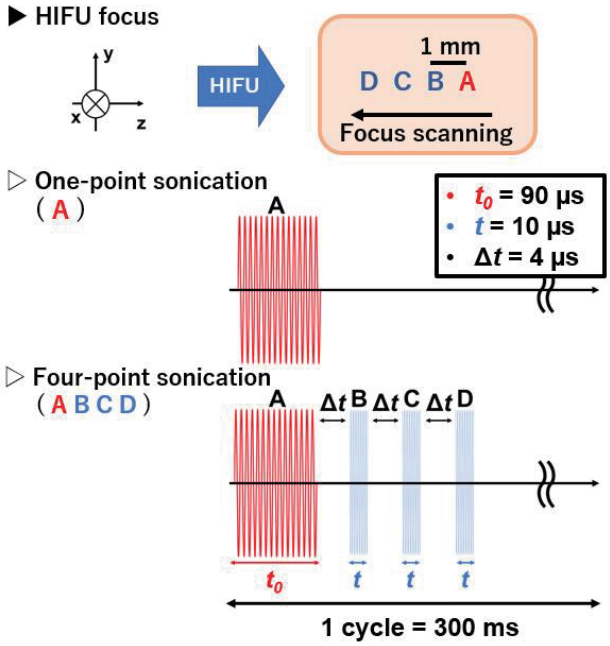

Fig. 2 HIFU focuses and exposure sequence

'Shock scattering' is based on the mechanism that a single bubble generated by the negative pressure of ultrasound plays the role of free-end

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reflection, and that the nonlinearly distorted incident wave with highly positive pressure is at the free end, generating a strong negative pressure, which in turn generates additional bubbles to form a cloud. [1] By setting the focal points as described above, it is thought that the cloud generated immediately before can be used as a reflector to generate further clouds more efficiently with shorter time sonication.

3. Results and Discussion

Experimental results are shown for the cases with the one-point and the four-point sonication. **Fig. 3** shows high-speed camera images of 0.8% agarose gel exposed to HIFU. Cavitation bubble clouds were further generated even after a short sonication time at the second and later points in the four-point sonication, and the bubble cloud region was enlarged compared to the one-point sonication. Therefore, it was confirmed that focus scanning is effective in expanding the bubble cloud generation region.

We assumed that a cavitation bubble cloud would grow in the chicken liver as shown in Fig. 3, and sonicated with the same sequence.

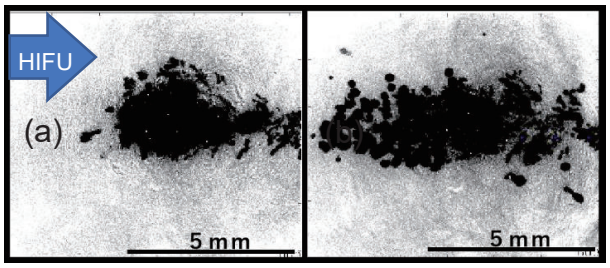

Fig. 3: Cavitation region in the gel by one-point (a) and four-point sonication (b)

Fig. 4 shows the brightness change in B-mode images after 400 cycles of sonication compared to the brightness before the sonication. The brightness of B-mood images is displayed in 256 gradations from 0 to 255. The ROI was set to a 5× 15 mm^2 area, including the treatment region. Regions indicated with negative values represent a decrease in brightness due to tissue disruption. Similar to the bubble regions shown in Fig. 3, the four-point sonication demonstrated in Fig. 4(b) resulted in a larger area of tissue disruption compared to the one-point sonication shown in Fig. 4(a). **Fig. 5** shows the average brightness change plotted every 50 cycles in the ROI up to 400 cycles, averaged for n = 9 each. The vertical axis shows the brightness change from that before the sonication. After 400 cycles sonication, the brightness change increased by a factor of about 1.67 in the case with the four-point sonication, compared to the case with the one-point sonication. This means improved time efficiency of treatment. Moreover, the treated region per acoustic energy increased by a factor of about 1.25.

Further studies are needed to determine the possibility of expanding the cloud region and Histotripsy more efficiently by further increasing the number of focal points and optimizing the sequence.

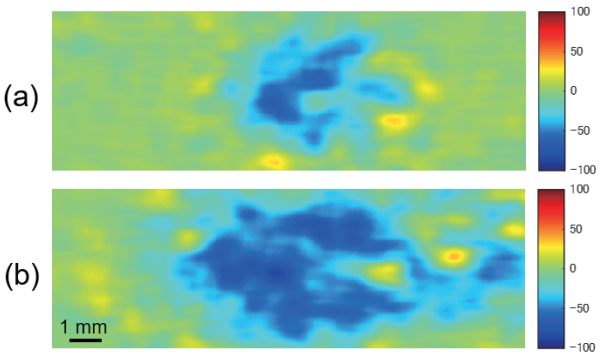

Fig. 4 Brightness change after 400 cycles by one-point (a) and four-point sonication (b)

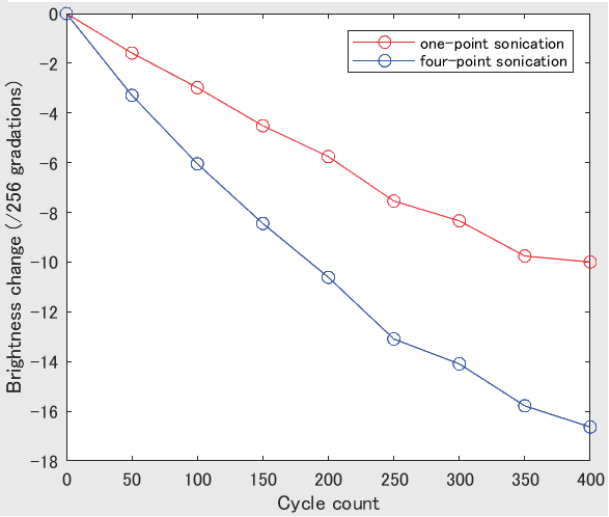

Fig. 5 Brightness change

4. Conclusion

In this study, we experimentally investigated a method to efficiently destroy a tissue in Histotripsy by setting multiple focal points in the direction of ultrasound propagation and expanding the region of cavitation cloud generation. The four-point irradiation was more efficient than the one-point irradiation in Histotripsy. However, further studies are needed to improve the treatment efficiency and to investigate the relationship between the cavitation bubble cloud region and the treatment region in the tissue, such as improving the HIFU sequence and identifying the cavitation bubble cloud region by ultrasound imaging.

References

1) A. D. Maxwell et al.: J Acoust. Soc. Am., 130, (2011).