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Effect of PRF on efficiency of tissue erosion in histotripsy with ultrasonic focus scanning in the direction of 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 sonication 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. Our previous study[1)] has shown that HIFU focus scanning, described below, can expand the treatment region and increase treatment efficiency for the input acoustic energy.

Here, in histotripsy, it is common to repeat several cycles of HIFU sonication to the same spot to complete the treatment. In clinical practice, it is desired that cycle duration will be reduced to increase throughput. Therefore, in this study, we examined how the cycle duration affects the treatment efficiency when focus scanning is performed.

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 sonication. 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 shows 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 HIFU pulses were delivered for 200 cycles at a repetition frequency of 1 and 2.5 Hz. Acoustic intensity in all sonications was constant at 70 kW/cm^2. The ultrasound sequence with scanning the focus toward the transducer was designed to utilize the mechanism of "shock scattering", [2)], in which a cavitation bubble cloud is formed by reflected waves from individual bubbles.

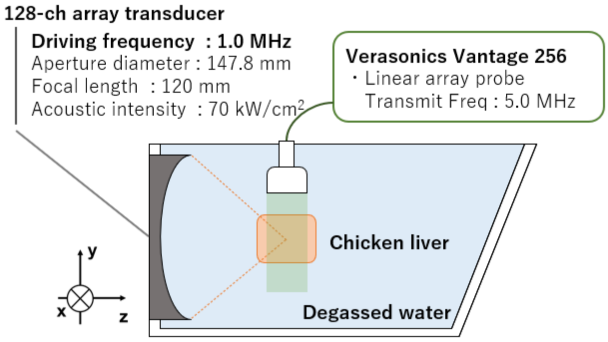

Fig. 1 Experiment setup

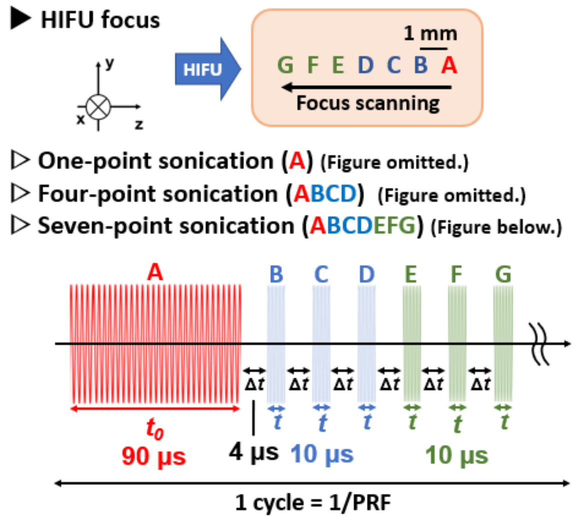

Fig. 2 HIFU focuses and exposure sequence

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“Shock scattering” is phenomenon in which a single bubble generated by the negative pressure of ultrasound plays the role of free-end 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. 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

Fig. 3 shows the change in echo intensity after 200 cycles of sonication compared to before the sonication. The ROI was set to a 10×15 mm^2 area, including the treated region. Regions indicated with negative values represent a decrease in echo intensity due to tissue erosion. When the PRF was 1 Hz, the eroded area expanded with the increase in the number of focal points. However, when the PRF was 2.5 Hz, the shape of the eroded area was distorted and the expansion of the eroded area with the increase in the number of focal points was smaller.

Fig. 4 shows the energy efficiency of the treatment after 200 cycles of sonication. Energy efficiency was calculated by dividing the treatment area in the ROI by the input acoustic energy. In this case, the area where the echo intensity decreased by more than 3 dB after 200 cycles of sonication compared to before the sonication was considered as the treatment area, assuming that the area was sufficiently eroded. Values are averages of n = 5 for 1 Hz and n = 2 for 2.5 Hz, normalized by the one-point sonication value at each PRF.

At PRF of 1 Hz, the efficiency improved as the number of focal points in the sequence increased. This is thought to be due to the efficient generation of bubble clouds with less energy by the focus scanning method considering the shock scattering. On the other hand, at a PRF of 2.5 Hz, the efficiency decreased as the number of focal points increased. As suggested in Fig. 3, the treatment area did not expand significantly with increasing number of focal points at 2.5 Hz. In sequences with a larger number of focal points, the total sonication duration is longer and more acoustic energy is input. Thus, the reason for the decrease in energy efficiency was that the expansion of the treatment area was less than the increase in input energy. The reason the treatment area did not expand much is thought to be that some cavitation bubbles remained until the next cycle, scattering the ultrasound and preventing bubble clouds formation at the next cycle. This effect is called cavitation memory and is reported to be larger at higher PRF,[3]. Since more bubbles were generated in sequences with a larger number of focal points, the effect of cavitation memory would have been greater, and the tissue erosion did not progress sufficiently.

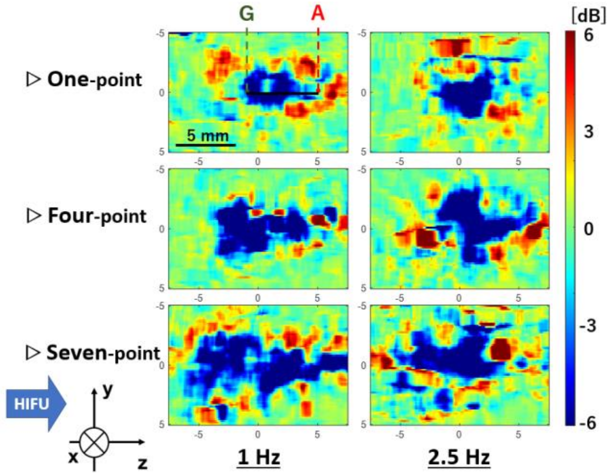

Fig. 3 Echo intensity change after 200 cycles of sonication compared to before the sonication

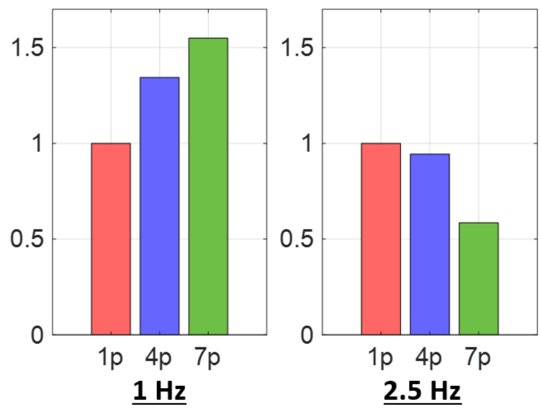

Fig. 4 Energy efficiency of the treatment after 200 cycles of sonication

4. Conclusion

In this study, we experimentally investigated the effect of PRF on treatment efficiency in histotripsy using HIFU focused scanning. The results showed that at sufficiently low PRF, the treatment efficiency improves with focus scanning, but at higher PRF, the efficiency conversely decreases with focus scanning. Further experiments are required to investigate the cause of the efficiency decrease in detail and to improve the sequence by reducing the cavitation memory effect.

References

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