1P5-5

Enhancement of Efficiency in Ultrasonic Generation of Reactive Oxygen Species by Scanning Focus
超音波焦点走査を用いた超音波による活性酸素生成の効率向上

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1. Introduction

Cavitation bubbles generated by High-intensity focused ultrasound (HIFU), are used for sonodynamic treatment method, in which cancer cells are destroyed due to Reactive Oxygen Species (ROS) induced by oscillations and collapse of ultrasonically generated cavitation bubbles. The acoustic pressure needed for generating cavitation is higher than that for utilizing it by an order of magnitude. Our previous study demonstrated that Trigger HIFU sequence[1)] consisting of an extremely high intensity and short pulse (Trigger pulse) to generate cavitation bubbles followed by a relatively low intensity and long burst (Sustaining burst) to oscillate them was effective to generate ROS efficiently in [2)].

To increase the efficiency of ROS generation for efficient sonodynamic treatment, scanning HIFU foci is examined in this study, considering the diffusion of precursors of ROS.

2. Material and method

2.1 Experimental setup

The experimental setup is shown as **Fig. 1**. A focused ultrasound transducer and a sealed chamber filled with 1 mol/L of potassium iodide (KI) solution were laid in degassed water. The transducer with an outer diameter of 147 mm and a focal length of 120 mm was driven at 1 MHz. A high-speed camera was operated at 250 kfps to observe the distribution of cavitation bubbles.

2.2 ROS measurement

A KI method was used to measure the amount of ROS, where the generated ROS oxidize iodine ions producing triiodide ions with an absorbance peak at 355 nm. The amount of ROS, measured as the absorbance, was compared between before and after HIFU exposure.

2.3 Exposed sequences

Four different exposure sequences as shown in **Fig. 2** were compared. One was exposure at a single

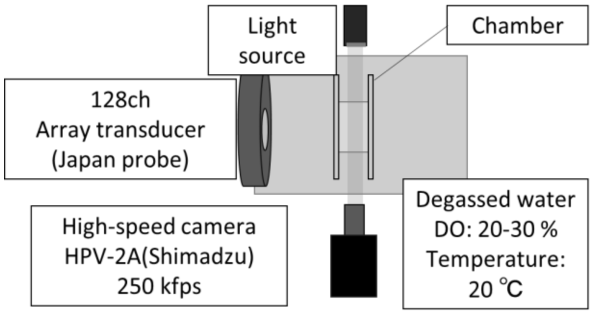
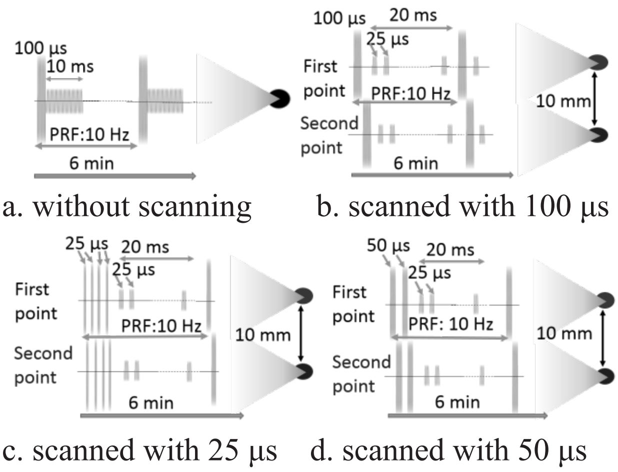


Fig. 1 Schematic of experimental setup

focal point without scanning and the others were at two focal points scanned with intervals of 25, 50 and 100 μs. The intensities of Trigger pulse and Sustaining burst were 100 kW/ cm^2 and 500 W/cm^2, respectively. Each sequence was continued for 6 minutes at a PRF of 10 Hz.

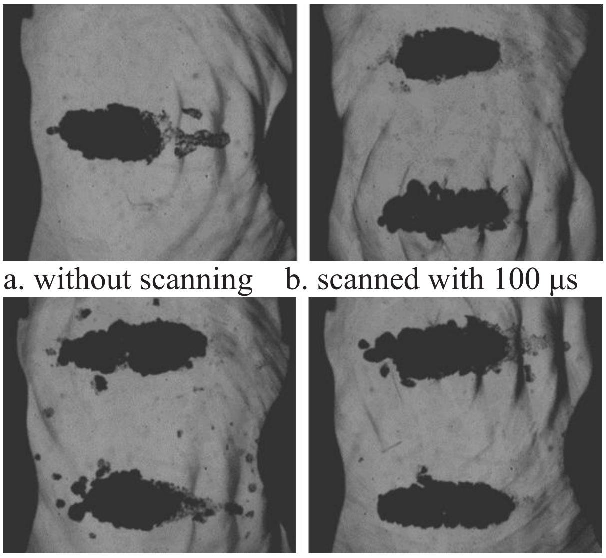
3. Result

Optical images of cavitation bubbles during Trigger pulse taken by high-speed camera are shown in **Figs. 3a**, **3b**, **3c** and **3d**. In both sequences with and without scanning, cavitation bubbles were generated as a form of cloud[3)]. **Figs. 4a**, **4b**, **4c** and **4d** are the pictures during Sustaining burst, i.e. 300 μs after the end of Trigger Pulse, showing



a. without scanning b. scanned with 100 μs
c. scanned with 25 μs d. scanned with 50 μs

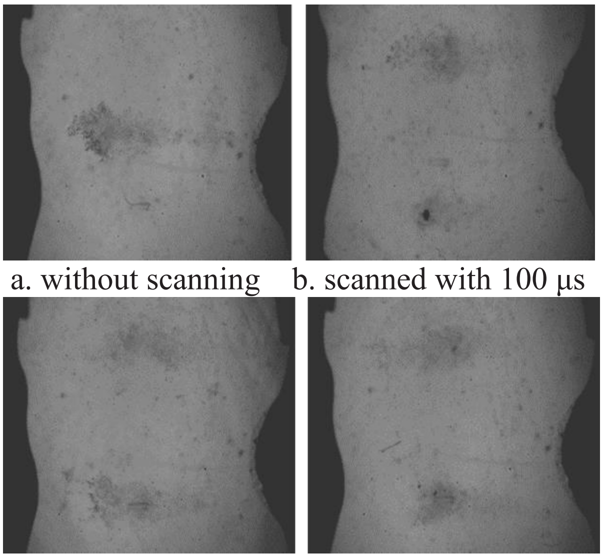
Fig. 2 Exposed sequences



a. without scanning   b. scanned with 100 µs

c. scanned with 25 µs   d. scanned with 50 µs

Fig.3 Cavitation bubbles during Trigger pulse



a. without scanning   b. scanned with 100 µs

c. scanned with 25 µs   d. scanned with 50 µs

Fig.4 Cavitation bubbles during Sustaining burst

remaining clouds.

Table. I shows the differences in absorbance at 355 nm between before and after HIFU exposure and the efficiencies of ROS generation, which were calculated by dividing the absorbance by the input acoustic energy and normalized by that of the sequence without scanning. Among the scanning sequences, the 25 µs scanning produced the largest amount of ROS, but it was less than the sequence without scanning.

4. Discussion

Table. I Difference of measured absorbance at 355 nm and ROS generation efficiency

	w/o scanning	w/ 25 µs scanning	w/ 50 µs scanning	w/ 100 µs scanning
Absorbance [abs.]	0.0023	0.0043	0.0020	0.0020
Efficiency [arb.unit]	1.00	0.87	0.43	0.43

The difference of sequences between with and without scanning is whether there is intermittency after irradiating Trigger pulse. In case of scanning at 100 µs, there is a intermittency of 100 µs at each focus while there is no intermittency in the sequence without scanning.

The results suggest that it is important for efficient ROS generation to irradiate Sustaining burst as soon as possible after Trigger pulse at the same focus. When the foci are scanned, the cavitation cloud generated at the first focal point could disappear too quickly during the intermission time.

To analyze the relationship between cavitation bubbles and intermission time, the area of cavitation bubbles at the start of Sustaining burst is listed in **Table. II**, showing that shorter intermission time led a larger area of cavitation bubbles and a higher efficiency of ROS generation .

5. Conclusion

In this study, the efficiency of ROS generation was measured for several sequences. Scanning foci had been thought to improve the efficiency, however it was less than the sequence without scanning. The results suggest that it is the most important for ROS generation to irradiate Trigger pulse immediately after Sustaining burst.

Table. II Area of bubbles in each sequence

	w/o scanning	w/ 25 µs scanning	w/ 50 µs scanning	w/ 100µs scanning
Area of bubbles [mm^2]	12.8	11.7	10.9	8.5

References

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