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Effects of Rose Bengal on Cavitation Generation in Gel Phantom Investigated using High-Speed Camera

高速度撮影を用いたローズベンガルのキャビテーション気泡の成長における効果の解析

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Introduction

HIFU (High Intensity Focused Ultrasound) is clinically used as a noninvasive method of cancer treatment. It is generated outside the body and focused at the cancerous tissue and induces irreversible changes to the tissue. The thermal bioeffect of ultrasound has been cosidered to be the primary mechanism for such changes.

Other than the use of the thermal bioeffect, sonodynamic treatment using the sonochemical bioeffect of ultrasound has been proposed. In sonodynamic treatment, a sonosensitizer is activated through the collapses of cavitation bubbles. Typically, the activated sonosensitizer generates active oxygen which induces irreversible changes to the tissue.

Rose bengal (RB) is such a sonosensitizer. It has been found not only to be sonochemically active but also to reduce cavitation threshold.[1-3)]

Highly efficient as well as controlled generation of cavitation bubbles is crucial for realizing effective as well as safe sonodynamic treatment. In this study, the inception threshold and lifetime of cavitation bubbles are investigated using a high-speed camera.

Material and Method

Experimental Setup

Fig.1 shows the experimental setup. A focused ultrasound array transducer (Imasonic) and a gel phantom were placed in a PMMA water tank. The phantom consisted of a polyacrylamide (PAA) gel containing either 0, 0.5, 1, or 10 mg/l of RB. The focus was located in the gel. The transducer had 128 elements with an equal area and outer and inner diameters of 100 and 36 mm. Its center and maximum-efficiency frequency was 1.0 and 1.2 MHz, respectively. The water tank was filled with deionized water, whose DO level and temperature were maintained 20-25 %, and 36 °C, respectively.

A high-speed camera was set to observe the behavior of the ultrasonically generated cavitation bubbles. Its frame rate and exposure time was set to 500 kfps and 0.25 µs, respectively.

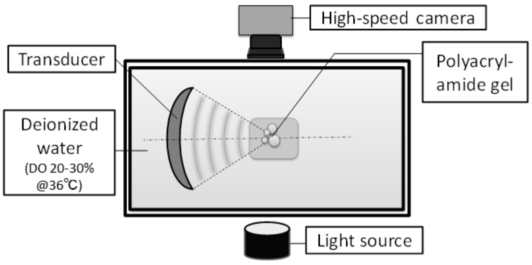

Fig.1 Experimental setup

Experiments

In this study two types of experiments were performed.

A. Threshold of cavitation bubble cloud generation

The aim of this experiment was to estimate the effect on the threshold of cavitation cloud formation.

Dual-frequency ultrasound exposure, proposed in our previous study, was employed for effcient generation of cavitation clouds.[4,5)]

In this method of exposure, waveforms emphasizing either the positive or negative peak pressure are synthesized by superimposing the second-harmonic onto the fundamental. These waves are called “P and N waves”, respectively. The exposure sequence, started with N waves immediately followed by P waves, which can generate cavitation at high efficiency, was employed.

Waves at the fundamental and second-harmonic frequency of 0.8 and 1.6 MHz, respectively, with the same amplitude were superimposed to each other. The total ultrasound intensity was varied from 7 to 40 kW/cm^2. Five experiments were performed for each condition.

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B. Lifetime of cavitation bubbles.

The aim of this experiment was to estimate the effect on the lifetime of cavitation bubbles. The exposure sequence, started with “trigger” waves at an extremely high intensity (40 kW/cm^2) with a short duration (250 μs) followed by “sustaining” waves at a relatively low intensity with a long duration (500 ms) both at 1.2 MHz, was employed. The trigger waves are considered to genenrate cavitation bubbles, and the sustaining waves are to sustain them by oscillating them.

The lifetime of cavitaiton bubbles was estimated by observing them by high-speed camera 10 and 100 ms after the trigger exposure in the duration of sustain waves. The concentrations of RB in the PAA gel were the same as the experiment *A*. Ten experiments were performed for each condition.

Results and Discussion

A. Threshold of cavitation bubble cloud generation

Fig.2 shows the probability of the cavitation cloud generation. The tendency is seen to increase as the RB concentration increases.

B. Lifetime of cavitation bubbles.

Fig.3 shows high-speed camera images of the cavitation cloud during the trigger exposure and the cavitation bubbles at 10 ms and 100 ms after the trigger exposure. Dependence on RB concentration is hardly seen. Effect of RB on the lifetime of cavitation bubbles was not detected.

Kawabata et.al[3)] reported that RB reduced both *in vitro* and *in vivo* cavitation thresholds by more than an order of magnitude. However, in this study, such a dramatic effect of RB was not observed either in the bobble cloud generation or in the lifetime of cavitation bubbles.

The biggest difference between the previous study and this study is the exposure time. It was more than two orders of magnitude longer in the previous study. These suggest that the effect of RB on cavitation threshold and lifetime does not depend on only the RB concentration but also on the exposure time. This should be examined in future work.

Conclusion

In this study, the effects of RB on cavitation threshold and lifetime were investigated. As the result, RB reduced the cavitation cloud generation threshold. However, the reduction of threshold was not as great as the previous report. Furthermore, no effect of RB on the lifetime of cavitation bubbles was observed.

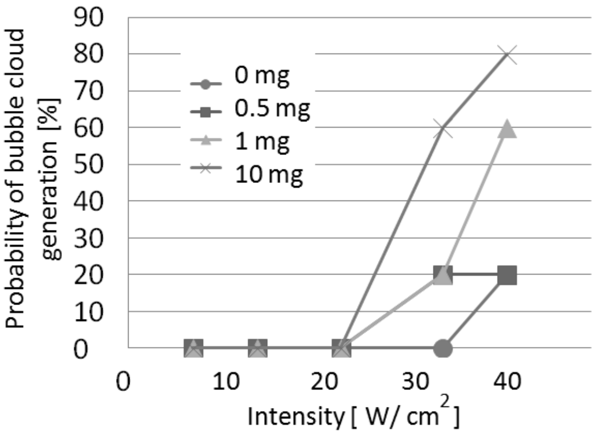

Fig.2 Probability of bubble cloud generation

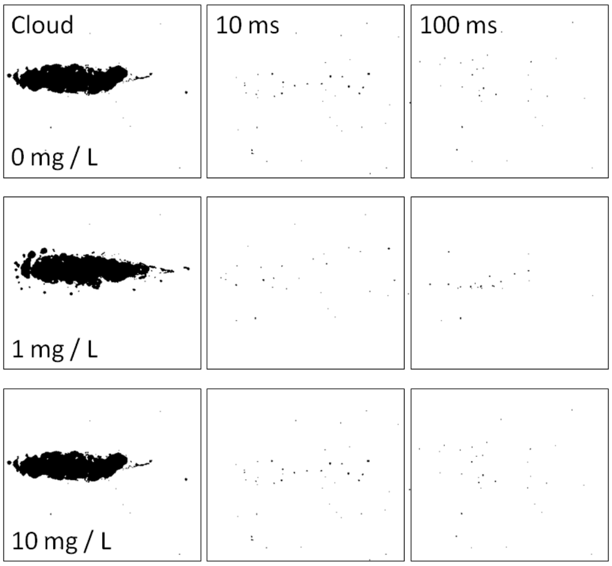

Fig.3 High-speed images of experiment B
(Binarized images,black pixel : cavitation bubbles)

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