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Simultaneous observation of bubble cloud and micro hollows produced by bubble cloud cavitation

気泡クラウドと気泡クラウドキャビテーションにより形成される微小孔の同時観察

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1. Introduction

Ultrasonic wave mediated drug delivery system has several features because bubble cavitation which is caused by irradiation of high intensity ultrasonic wave makes micro pores on the cell membrane (Sonoporation). Efficiency of drug delivery to the target cell increases effectively by sonpolation because drug which is released from drug carrier (micro bubble) is injected directly through the pores. When an ultrasonic wave whose sound pressure is much lower than the threshold level of bubble destruction, neighboring bubbles aggregate and they make bubble clouds by an acoustic radiation force between bubbles (the Bjerknes force). Formation of bubble clouds might be a useful mechanism in drug delivery system because the control of bubble clouds motion, such as adhesion to the target wall and increase of bubble density around the target, is performed by ultrasonic waves[1,2]. However, bubble cloud cavitation shows complicated mechanisms and optimization of ultrasonic wave irradiation sequence becomes difficult tasks.

In this paper, bubble cloud cavitation is evaluated using high speed camera and 3-D observation by double cameras with different focal length. Comparison between the bubble clouds dynamics and micro hollows which are produced by bubble cloud cavitation is also carried out. It is found that bubble cloud cavitation is classified into 3 stages. Among them, first and second stages, whose duration time is about 70 µs, play important role in formation of micro hollows by bubble cloud cavitation.

2. Methods

Fig.1 shows the experimental set-up. Micro bubbles (Levovist, Bayer Helthcare, Germany) are introducced into the flow channel made by NIPA gel. Ultrasonic wave irradiates by concave ultrasonic transducer and it is focused at the flow channel. Two different king of ultrasonic waves irradiate by the same transducer. First wave is a pumping ultrasonic wave. Sound pressure of the wave is smaller than the threshold value of bubble destruction (100kPa, 2.5MHz), micro bubbles receive an acoustic radiation force (the Bjerknes force) and they aggregate and make bubble clouds. The bubble clouds are attached to the upper part of flow channel by the primary Bjerknes force. Then the second wave (High intensity ultrasonic wave) (2MPa, 2.5MHz) irradiates in order to destruct the bubbkle clouds.

Three methods are adopted in order to observe the bubble cloud dynamics in bubble cloud cavitation. First method is a digital camera observation with short time LED exposure. This method is utilized in obsrvation of micro bubble dynamics when pumping wave irradiates. It is also adopted in order to observe loci of bubble clouds when high intensity ultrasonic wave irradiates. Second method is the observation by high speed video camera (Phantom V711, Vision research, NJ. USA). Third method is 3-D bubble dynamics observation by double cameras with different focal length, which is developed in our laboratory. This methods consists of two digital cameras which have different focuses as is shown in Fig.1. When the same bubble cloud is taken by two cameras, z direction of bubble cloud can be evaluated by comparing the ratio of intensities of two images.

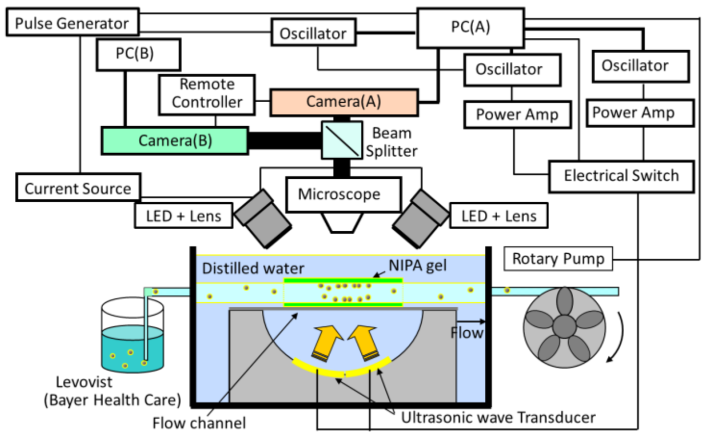

Fig.1 Experimental set-up

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Micro hollows which are produced by bubble cloud cavitation on the inner wall are observed by laser confocal microscope with water immersion objective (OLS 4000, OLYMPUS, Tokyo, Japan).

An ultrasonic contrast agent Levovist (Bayer Helthcae) is adopted as micro bubbles.

3. Results

Fig.2 shows the photograps of bubble clouds which are taken by high speed video camera when high intensity ultrasonic wave irradiates. 4 successive photographs are shown. White parts in the figure are bubble clouds. When high intensity ultrasonic wave irradiates, neighboring bubbles aggregate and they make big bubble clouds in 10 μs. Then, these bubble clouds move slowly and aggregation and segmentation between bubble clouds are sometimes performed. Lastly (after about 70 μs), the bubble clouds shown in the photograph are in almost stable state and stay at almost fixed positions. From the results, dynamics of bubble clouds in bubble cloud cavitation is classified into 3 stages. First stage is upto 10 μs, in which the bubbles form large bubble clouds by fast motion. In the second stage (up to about 70 μs), the aggregated bubbles move slowly. Lastly, bubbles in the ROI show almost stable state (third stage).

Bubble cloud posion in Z direction (Normal to the target wall) is estimated by 3-D position measurement. Fig.3 shows the distribution of z position of bubble clouds. Two experiments are carried out by changing the LED exposure time. The bubble clouds tend to be in the vicinity of target wall until 100 μs, but they move from the wall after that.

Fig.4 shows the total area of micro hollows which is measured by laser confocal microscope for different irradiation time of high intensity ultrasonic wave. Though the measurement cannot be performed for short irradiation time, because un-ruptured bubble clouds make an artifact on the image, most of micro hollows are formed until 70 μs.

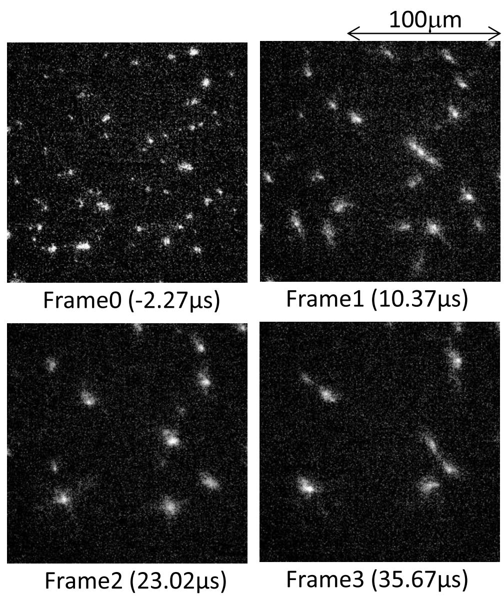

Fig2 Photographs of bubble clouds when high intensity US wave irradiates

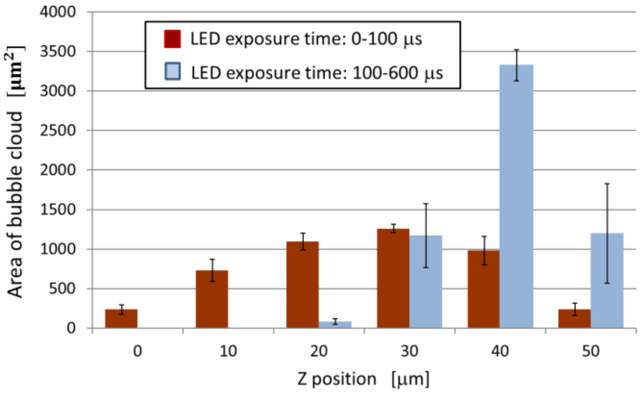

Fig.3 Measurement of Z-position of bubble clouds

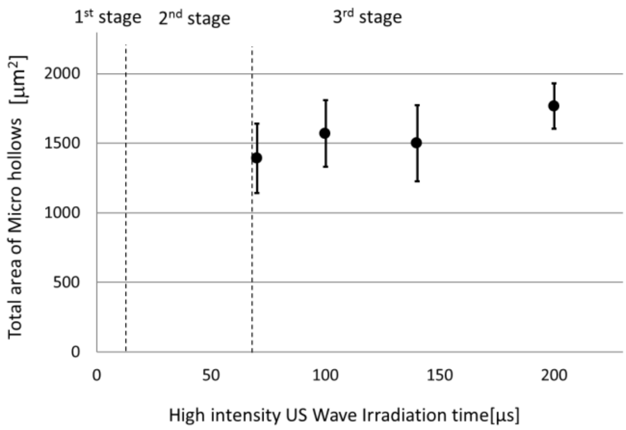

Fig.4 Total area of micro hollows for different irradiation time of ultrasonic wave

4. Conclusion

In order to evaluate the bubble clouds cavitation, three different observation methods are adopted as well as confocal laser microscope observation for micro hollows which are produced bubble cloud cavitation. Though the bubble cloud cavitation is also affected by the Bjerknes force, first and second stages which are classified from the difference of bubble clouds motion is important in production of micro hollows.

Acknowledgment

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References

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