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Observation of Micro Hollows Produced by Bubble Cloud Cavitation

気泡クラウドキャビテーションにより形成される微小窪みの観察

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1. Introduction

Ultrasonic wave mediated drug delivery system has several features because bubble cavitation, when a high intensity ultrasonic wave irradiates, assists drug injection into cells. Especially, micro pores, which are produced on the cell membrane by bubble cavitation (Sonoporation), might be a powerful tool to improve efficacy of drug delivery system. However, mechanisms of the bubble cavitation is too complex and it is difficult to optimize the ultrasonic wave irradiation sequence for the bubble cavitation. Moreover, the microbubbles aggregate and make a bubble cloud under ultrasonic wave irradiation, optimization of the ultrasonic wave irradiation sequence becomes a difficult task because the bubble cavitation also depends on the condition of the bubble cloud. [1)]

In this paper, bubble cloud cavitation is evaluated using a blood vessel phantom made by NIPA (N-isopropylacrylamide) gel. Levovist (Bayer, Germany) is adopted as micro bubbles.

2. Methods

Fig. 1 shows the experimental set-up. Micro-bubbles flow into a flow channel having the diameter of 2 mm. The flow channel is molded by NIPA gel which has several features as a phantom of flow channel. The first feature is that its acoustic properties are almost the same with those of soft tissues. For example, the sound velocity for NIPA gel (APS 0.2 mol%) is 1540 m/s. The second feature is optical transparent. Dynamics of micro bubbles inside the flow channel can be directly observed by a microscope. Acoustic contrast agent “Levovist” is used as microbubbles. After ultrasonic wave irradiation described below, micro hollows produced inside the flow channel are observed by a confocal laser scanning microscope.

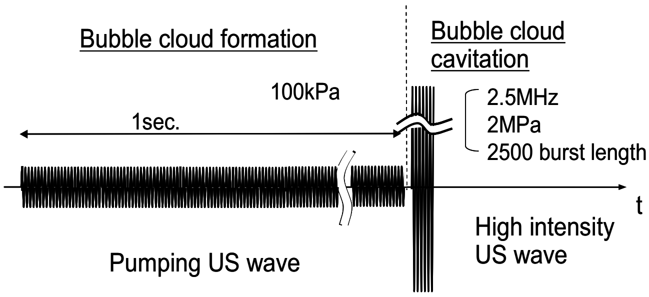

Fig.2 Ultrasonic wave irradiation sequence

Ultrasonic wave irradiation sequence is shown in **Fig.2**. First, a pumping ultrasonic wave is introduced. The microbubbles aggregate by an acoustic radiation force between microbubbles and they make a bubble cloud. The bubble cloud are trapped at the wall of flow channel due to an acoustic radiation force. The sound pressure of the pumping ultrasonic wave is set to 100 kPa, which is lower than the threshold level of bubble destruction and the irradiation time is long enough in order to produce bubble cloud. In this experiment, the frequency of the pumping ultrasonic wave is fixed to 2.5 MHz. The total irradiation time is 1 s. After irradiation of the pumping ultrasonic wave, a high intensity ultrasonic wave is introduced to

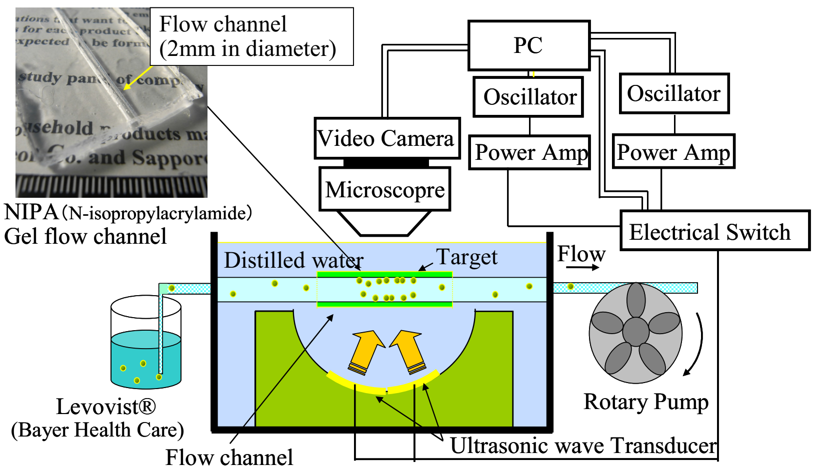

Fig. 1 Schematic diagram of the experimental set-up.

produce micro hollows due to bubble cloud cavitation. Frequency, sound pressure and the burst length of the high intensity ultrasonic wave are 2.5 MHz, 2 MPa and 2,500 wavelength, respectively.

3. Results

Dynamics of bubble cloud cavitation is observed by using short-pulse high-brightness LED light sources. The exposure time is set to 0.5 ms. **Fig.3** shows the observation results of bubble cloud in cavitation. Fig. 3(a) is bubble cloud produced by pumping ultrasonic wave. Fig. 3(b) and (c) are the photographs which are taken for the same region just after and 0.5 ms after high intensity ultrasonic wave irradiation. From the results, we found that low density bubble cloud is produced when the bubble cloud cavitation starts. We call this bubble cloud as bubble mist in the following discussion. And we also found that the life-time of the bubble mist is shorter than 0.5 ms.

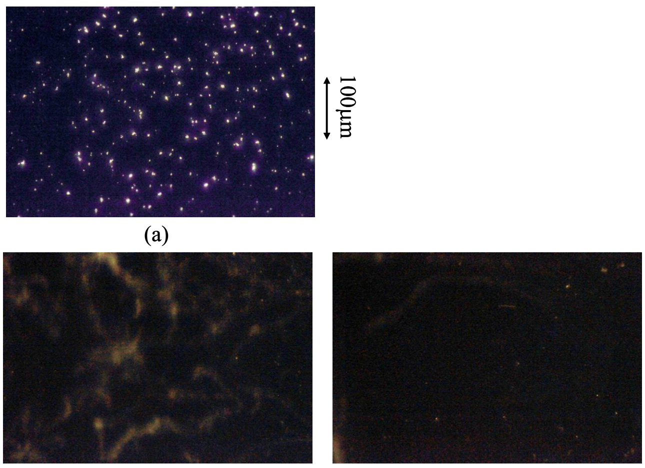

Fig. 3 Observation of bubble cloud cavitation. (a): Bubble cloud. (b): Just after starting bubble cloud cavitation. (c): 0.5 ms after starting bubble cloud cavitation.

Fig.4 shows the bubble cloud and the bubble mist produced on the same region. Fig. 4(a) is the bubble cloud which is observed by an optical microscope. Fig. 4(b) is the bubble mist which are taken just after starting the bubble cloud cavitation. In order to clear the bubble mist, brightness of the image is set to 7.5 times higher than that of the bubble cloud image. Fig. 4(c) is the photograph which is taken at 10 s after the bubble cavitation. A part of bubble cloud is not destructed in this experiment. Fig. 4(d) shows micro hollows produced by bubble cloud cavitation. It is observed for the same region by a confocal laser microscope. By comparing the bubble cloud and bubble mist images with the micro hollow image, it is understood that a lot of micro hollows are formed in the surroundings of the bubble mist. The arrows shown in Fig. 4(d) shows such micro hollows. This result shows that bubble mist formation is important mechanism to produce the micro hollows.

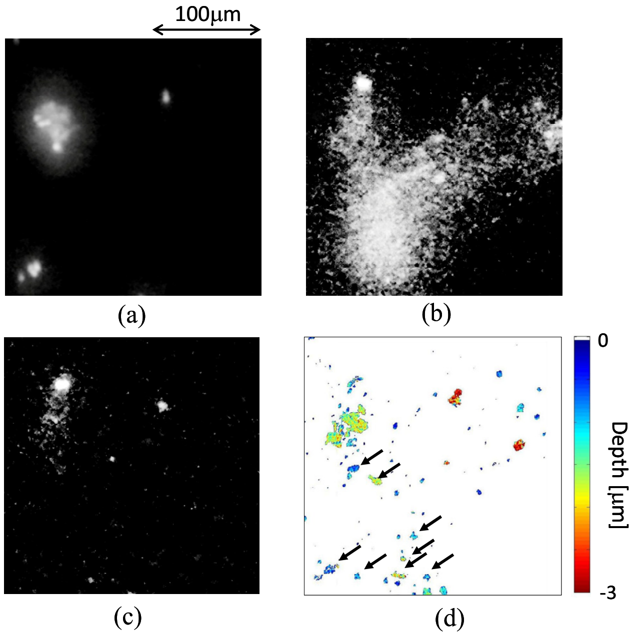

Fig.4 Comparison of bubble cloud image with micro hollow image observed by a confocal laser microscope. (a) : Bubble cloud, (b): Bubble mist (7.5 times brightness for emphasis), (c): Bubble cloud remained after bubble cloud cavitation. (d): Micro hollows produced by bubble cloud cavitation.

4. Conclusion

A lot of effects appear in microbubble cavitation and it is considered that these effects relate with each to produce micro pores in sonoporation. Mechanism of cavitation for a single bubble is studied both theoretically and experimentally, however, cavitation which is caused by bubble cloud is not clear yet. In this paper, microbubble cloud and the micro hollows produced by bubble cloud cavitation are observed for the same region. From the results, it is found that bubble mist is low density bubble cloud with very short life time, which is produced by bubble cloud cavitation and promotes the micro hollows in bubble cloud cavitation. This result implies that the ultrasonic wave irradiation sequence which produces adequate bubble cloud is important for production of micro hollows on the surface of flow channel.

Acknowledgment

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Reference

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