OPTICAL OBSERVATION OF DESTRUCTION OF MICROCAPSULES USING A HIGH-SPEED VIDEO CAMERA

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Abstract
The destruction of the microcapsules having an elastic thin shell is discussed. The optical observation of the capsule destruction using a high-speed video camera is carried out. As the driving pressure is increased, the microcapsules trapped at the anti-node of acoustic standing wave show circling movements, and then the microcapsules eventually collapse. At the moment of destruction, it is found that the microcapsules change in shape and the internal gas jets out of the capsule rapidly. The capsule destruction also depends on the existence of the free bubbles in the surrounding media. It is found that the mechanism of capsule destruction can be categorized two types: one is due to the increasing driving sound pressure and the other is due to the existence of the free bubbles in the surrounding media. It is considered that the destructions of multi-capsules depend on some parameters; however, these two types of capsule destruction are dominant factors.

Introduction
In the ultrasonic diagnosis field, there are a large number of reports on diagnosis techniques using capsule destruction, for example flash echo imaging (FEI) and drug delivery system (DDS).[1] These ultrasonic medical techniques are used because of its safety to human body. Especially, DDS has advantages such as low side effects following local drug administration and non-incision. On the other hand, since it is reported that adverse effects on human body by shock wave and micro-jet by capsule destruction,[2] clarification of the mechanism of capsule destruction and establishment of safety standard to human body are very important. In this paper, the optical observation of the capsule destruction in an acoustic standing wave using a high-speed video camera is carried out, and the mechanism of capsule destruction are discussed.

Methods
Most types of clinical microcapsules have an elastic thin shell and contain gases or liquids such as drug solution. In our experiments, microcapsules (F-80ED, Matsumotoyushi, Japan) made of PVC (polyvinylden chloride–acrylonitrile) and whose average radius is 50 μm are used. The percentage of the hollow part of the microcapsule is approximately 98%, while Young's modulus and the Poisson ratio of the shell material are unknown. This microcapsule is categorized as "hard shell", it, however, expands and contracts slightly by driving sound pressure.[3][4] The imaging system is shown in figure 1. A bolt-clamped Langevin transducer with a diameter of 30 mm is excited with a continuous sinusoidal signal at the frequency of 115 kHz. Since an acoustic standing wave is generated in the observational cell filled with degassed water, the microcapsule is trapped in the center of the cell. When the microcapsule is contracted by positive pressure, it is forced toward the node of the acoustic standing wave. Similarly, when the microcapsule is expanded by negative pressure, it is forced toward the anti-node. Since the force caused by the acoustic standing wave is proportional to the volume of the microcapsule, it is finally trapped at the anti-node of the acoustic standing wave. The light from the xenon lamp is directed to the observational cell and received by the high-speed video camera (FASTCAM, Photoron, Japan) whose maximum recording rate is 40.5 kHz equipped with a long-distance microscope, so that the microcapsule can be observed in shadow graphs. This method is widely applied to the observations of single bubble sono-luminescence (SBSL).[5] Some microcapsules are attracted to each other due to secondary Bjerknes forces, so that trapping only a single microcapsule is difficult. In our experiments, only a single microcapsule can be trapped from a low-concentration solution of microcapsules.

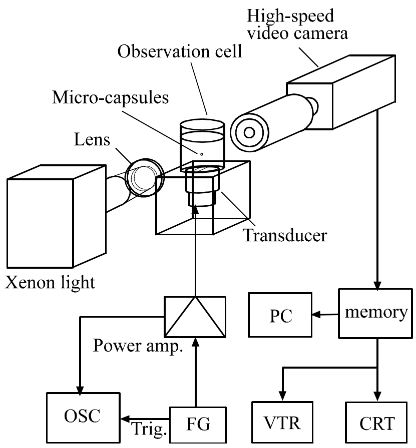

Figure 1 : Measurement system with a high-speed video camera.

Results

Destruction due to increasing sound pressure

As the driving pressure is increased, the microcapsules trapped at the anti-node of acoustic standing wave eventually collapse. In ascending order of driving pressure until the destruction, the following behaviors can be observed on the microcapsules regardless of the radius.

a) Since the binding force by the standing wave is smaller than the buoyancy of microcapsules, the microcapsules can not be trapped.
b) The microcapsules are trapped at the anti-node of standing wave.
c) The microcapsules show circling movements around the anti-node.
d) The cycle of circling movements is getting shorter and shorter.
e) The microcapsules eventually collapse.

Figure 2 shows the image of the circling microcapsule with a radius of 63 μm driven at the frequency of 115 kHz and a sound pressure of 33.75 kPa. Since the backlight is not refracted, the center of microcapsule looks bright. The microcapsule circles around the anti-node of standing wave. The turning radii are approximately 1 to 3 times larger than the capsule radii, and the cycles of circling movements depend on the driving pressure, i.e., the cycles are getting shorter and shorter with the increasing driving pressure.

Figure 3 shows the images of the collapsing microcapsule with a radius of 25 μm driven at the frequency of 115 kHz and a sound pressure of 100 kPa. The video sampling rate is 27 kHz. The microcapsule retains its spherical shape in image a), and it expands rapidly and changes in shape in image b). In image c), the internal gas jets out of the capsule rapidly. After the emission of gas in image d), it is seen that the shape of microcapsule isn't spherical any more and the capsule shell has evidently collapsed. The emitted internal gas unites with the broken shell again in image e) ~ h), and moves to out of the camera view.

The threshold sound pressure for capsule destruction depends on the radii of microcapsules. Figure 4 shows the relationship between the capsule radius and the threshold sound pressure for capsule destruction for the 20 samples whose radii are from 10 to 80 μm. In Fig.4, when the driving sound pressure is increased, it is found that the microcapsule with larger radius has the lower threshold sound pressure, i.e., the larger microcapsule collapse easily. Above-mentioned process from trapping to destruction can be observed on most of all observations in our experiments. Since the circling movements are appeared at several tens kPa lower than the threshold sound pressure, it is considered the circling movements are the foretaste of the destruction.

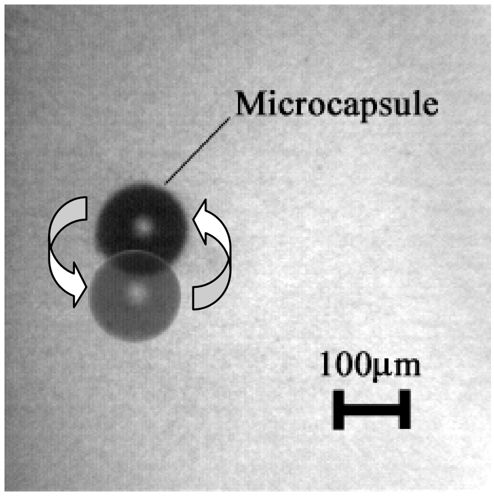

Figure 2 : Image of a circling microcapsule. (f=115[kHz], P=33.75[kPa], R_0=63[μm])

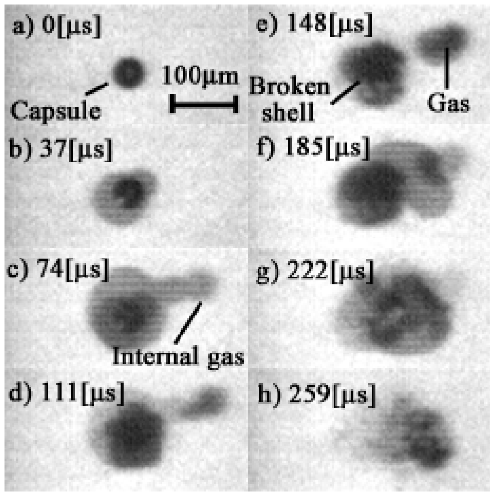

Figure 3 : Images of destruction of a single microcapsule. (f=115[kPa], P=100[kPa], R_0=25[μm], 27000[frames/sec])

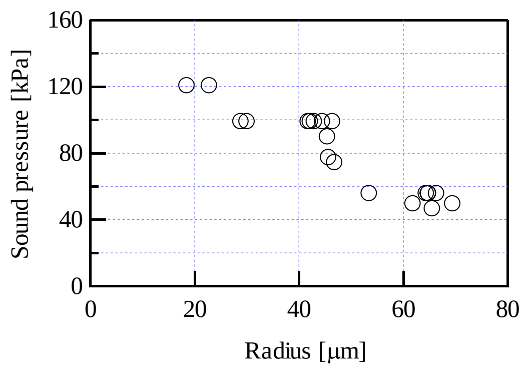

Figure 4 : Relationship between capsule radius and threshold sound pressure for capsule destruction.(f=115[kHz])

Destruction due to existence of free bubble

Micrometer size bubbles which do not have a shell under water are well known as ultrahigh pressure generator, for example SBSL and micro-jet. It is reported that the sono-luminescing gas bubble generates the shock wave at the moments of rebound by Kaji et al.. (Figure 5) [5] Therefore, it is considered that the capsule destructions also occur due to the existence of the free bubbles in surrounding media. Figure 6 shows the motion of the collapsing microcapsule due to the free bubble. The video sampling rate is 13.5 kHz. Since the capsule is spherical and the internal gas is enclosed perfectly, the image of capsule looks dark due to the refraction of light. The image of free bubble also looks dark. On the other hand, since the broken shell is flooded, the light can transmit and the image of broken shell looks bright. The microcapsule and the free bubble are attracted to each other slowly due to secondary Bjerknes forces. In spite of the relatively low driving pressure, the microcapsule is destroyed as in Fig.3. It is considered that the microcapsule is destroyed due to the cavitation effects of the free bubble with the shock wave or the micro- jet, and this phenomenon is homotype of cavitation erosion found in water screw. [6][7]

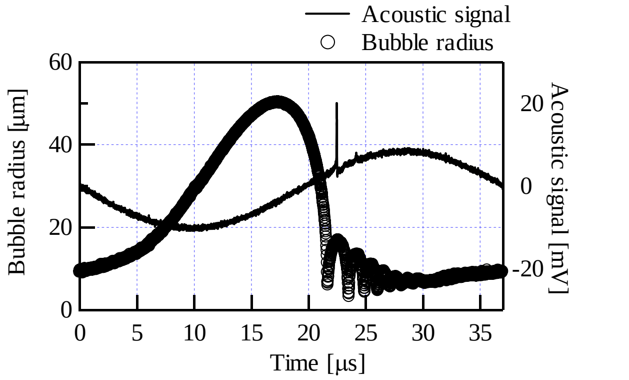

Figure 5 : Radius versus time curve for the sonoluminiscing bubble and received acoustic signal at 2[mm] from the bubble. (M. Kaji et al., Jpn. J. Appl. Phys., 2002)

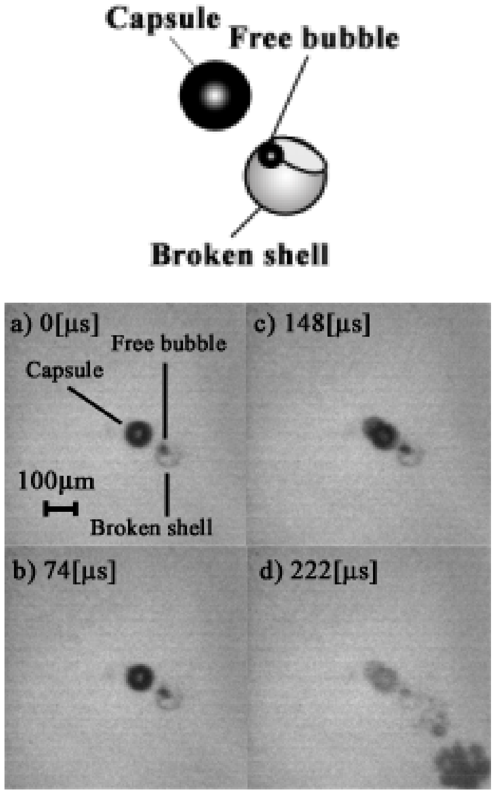

Figure 6 : Images of destruction of a capsule caused by a free bubble. (f=115[kHz], 13500[frames/sec])

Destruction of multi-capsules

Considering in clinical use, the most of the capsule destructions occur with multi-capsules. Figure 7 shows the images of destruction of the multi-capsules. Three microcapsules are trapped at the anti-node of standing wave in image a). In image b), one of three microcapsules changes in shape slightly, and then it collapses rapidly in image c). At the moment of destruction, other two microcapsules are separated,

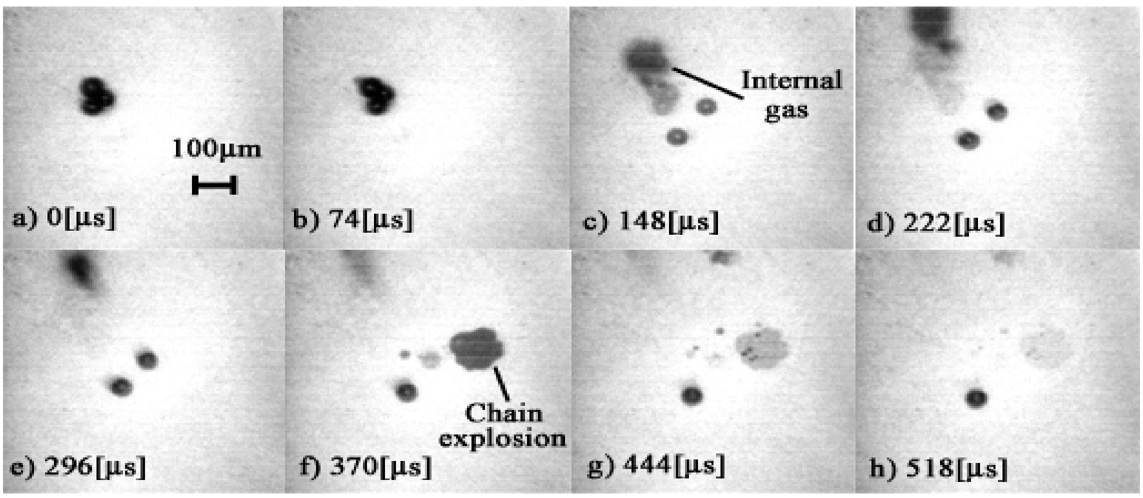

Figure 7 : Images of destruction of multi-capsules.(f=115[kHz], 13500[frames/sec])

and one of them collapses after some delay as the chain explosion. It is considered that these results are the combination of the destruction due to the increasing sound pressure in Fig.3 and the destruction due to the existence of free bubbles in Fig.5; the mechanism of multi-capsules destructions is mentioned below.

a) Since the binding force by standing wave is smaller than the buoyancy of microcapsules, the microcapsules can not be trapped.
b) The multi-capsules are trapped at the anti-node of standing wave.
c) The aggregation of microcapsules shows circling movements.
d) The largest microcapsule in the aggregation collapses first, and the internal gas jets out.
e) Some other microcapsules collapse as the chain explosion due to the cavitaion effects of the free bubbles (the scattered internal gas).

The destructions of multi-capsules are greatly influenced from the internal gases scattered by the microcapsule which collapses first. It is considered that the destructions of multi-capsules depend on some parameters; however, above mentioned two types of the single capsule destructions are dominant factors.

Conclusion

The destructions of microcapsules having an elastic thin shell are observed using a high-speed video camera. Two types of the single capsule destruction are observed: one is due to the increasing sound pressure and the other is due to the cavitation effects of the free bubble in surrounding media. In the case of the destruction due to the increasing sound pressure, it is found that the microcapsule with larger radius has lower threshold sound pressure for its destruction and the circling movement is the foretaste of the destruction. In the case of the destruction due to the cavitation effects of free bubbles, the microcapsule collapses in spite of low driving pressure. It is considered that these two types of capsule destructions are dominant factor compared with some other parameters. The destruction of multi-capsules is due to the combination of these two types, i.e., the largest microcapsule collapses first, and then the other capsules collapse as the chain explosion due to the internal gases scattered by the microcapsule which collapses first. In our experiments, the experimental conditions, the capsule material and the transmitted waveform, etc., are different from clinical use; however, it is considered that these experimental results are very important for DDS.

References

[1] W. M. Saltzman, “Drug Delivery,” University Press, Oxford, 2001.

[2] K. Tachibana, T. Uchida, K. Ogawa, K. Yamashita, N. Tamura, “Induction of cell membrane porosity by ultrasound” Lancet, 353, pp. 1409 1999

[3] D. Koyama, A. Sakai and Y. Watanabe, “Basic study on sub-harmonic imaging by using microcapsules,” in Proceedings of the 17th International Congress on Acoustics, 2001 p. 6C-02-04.

[4] D. Koyama, N. Barbier and Y. Watanabe, “Shell effects on vibration behavior of a microcapsule in an acoustic field,” Jpn. J. Appl. Phys., (submitted).

[5] M. Kaji, N. Bergeal, T. Asase and Y. Watanabe, “Observation of sonoluminescing bubble motion at the rebounding phase,” Jpn. J. Appl. Phys., vol. 41 No.5B, pp. 3250 2002.

[6] T. G. Leighton, “The Acoustic Bubble,” Academic Press, London, 1994.

[7] F. R. Young, “Cavitation,” Mcgraw-hill Book Company, London, 1989.