

Quantitative evaluation of the amount of phospholipid desorbed from a microbubble by pulsed ultrasound

Reina Kobayashi, Daisuke Koyama, Hiraku Tabata (Doshisha Univ.), Marie Pierre Krafft, (Univ. of Strasbourg)

Abstract— Microbubbles have potential applications as drug and gene carriers, and the drug release can be triggered by ultrasound irradiation in blood vessels. In this paper, the molecular desorption from a single microbubble under ultrasound irradiation was observed, and the amount of molecules desorbed from the bubble surface was estimated quantitatively. Microbubbles with a radius of 20 to 100 μm were fabricated, and DMPC was used as the shell material. The amount of molecules desorbed from a single microbubble was estimated from the contact angle between the bubble and a glass plate. The contact angle of the bubble decreased gradually in the cell after the DMPC molecules in the solution were adsorbed on the bubble surface. When a microbubble was exposed to a 50-cycle pulsed ultrasound with an amplitude of 20 kPa at 38.8 kHz, the contact angle increased dramatically; 70% of the DMPC molecules were desorbed from the bubble surface.

I. INTRODUCTION

Microbubbles have potential for applications as drug and gene carriers, and the drug release can be triggered by ultrasound irradiation in blood vessels. The acoustic response of microbubbles coated by surfactants have been investigated by several groups, indicating the viscoelasticity of the surrounding molecular shell and the internal gas affect the behavior of the bubble under ultrasound irradiation. Considering the practical drug delivery system, the molecular concentration on the bubble surface is one of the important factors for the quantitative drug administration. In this paper, the molecular desorption from a single microbubble under ultrasound irradiation was observed, and the amount of molecules desorbed from the bubble surface was estimated quantitatively.

II. METHODS

1,2-dimyristoyl-sn-glycero-3-phosphocholine (DMPC) was used as the surfactant, and tens-micrometer-sized microbubbles coated with DMPC were fabricated using DMPC solution (0.3 mM) and fluorocarbon gas. The optical observation system consists of a high-speed camera and an ultrasound cell. The microbubbles were attached on a glass plate placed in the cell. A bolt-clamped Langevin transducer was attached to the bottom of the cell, and the bubble was irradiated once with 50-cycle pulsed ultrasound with 20 kPa at 39 kHz. The desorption of the DMPC molecules from the surface of the bubble was evaluated by measuring the contact angle between the bubble and the glass plate; a decrease of the contact angle indicates desorption of the DMPC molecules from the bubble surface.

Reina KOBAYASHI, Doshisha Univ. Japan, phone: 080-1497-7866; e-mail: rena98109@gmail.com

III. RESULTS

Time change of the contact angle of the bubble was measured before and after ultrasound irradiation (Fig. 1). The molecular concentration on the bubble surface was estimated from the contact angle. The molecular concentration was decreased significantly by ultrasound irradiation at $t = 120$ s. The average values of the molecular concentration before and after ultrasound irradiation were 0.23 and 0.07 mM, respectively; 70% of the molecules adsorbed on the bubble surface were desorbed by pulsed ultrasound. Larger sound pressure amplitude gave larger amount of the molecular desorption, implying that larger vibration amplitude of the bubble induced larger amount of the molecular desorption.

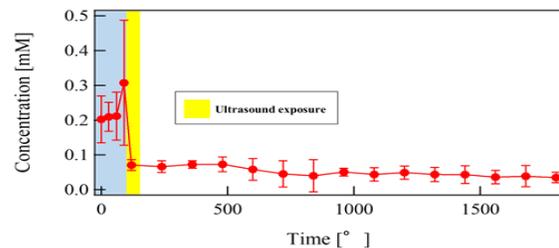


Figure 1. the change in the DMPC concentration on the bubble surface with respect to time in the case of 0.3 mM.

IV. DISCUSSION & CONCLUSION

This report discusses the quantitative evaluation of the amount of molecular desorption from a single microbubble by ultrasonic irradiation. The relationship between the concentration of the surrounding DMPC solution and the contact angle of the bubbles on the glass plate was investigated in advance, and it became possible to estimate the molecular density on the bubble surface during ultrasound irradiation. When the bubbles were irradiated with ultrasound in a simulated intravascular environment, the respiratory vibration of the bubbles caused about 70% of the molecules to desorb from the surface of the bubbles, which is expected to lead to the control of drug release in clinical practice.

REFERENCES

- [1] Y. Ando, H. Tabata, M. Sanchez, A. Cagna, D. Koyama, M. P. Krafft, "Microbubbles with a self-assembled poloxamer shell and a fluorocarbon inner gas," *Langmuir*, 32, 12461–12467,

2016