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Generation and Control of Ultrasonic Cavitation on Soft Material by Dual-frequency Acoustic Resonances

二周波駆動の音響共振を用いた軟質材料上へのキャビテーション生成と制御

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1. Introduction

The administration method of insulin is mostly limited to hypodermic injection due to the clinical safety and convenience of the modality. The use of a needle gives rise to a decrease in the efficacy of care and QOL of patients and the risk of infection. To avoid this, transdermal insulin administration has been addressed. However, the applicability of the transdermal route is limited in the molecule size of the drug because large weight molecules like insulin cannot penetrate the skin barrier of the stratum corneum.

To extend the ability of transdermal drug delivery, the activities of ultrasonic cavitation bubbles have been employed as mechanical stimuli to the skin surface. Soto et al. proposed a tattoo-type flexible transdermal patch with a large number of drug-loaded small pores[1)]. Ultrasound-induced explosive cavitation of emulsifying agents enabled drug particles to penetrate the skin, though the efficacy of this method was limited to large drug particles. Schoellhammer et al. used dual-frequency sound irradiation to enhance generation and motion control of cavitation activities on a skin phantom[2)]. Nonetheless, ultrasound-assisted drug administration has not been implemented in portable devices because of difficulties in downsizing the high-power electric system for sound irradiation.

In the present study, we proposed a design of an acoustic resonator to realize both generation and motion control of ultrasonic cavitation on soft materials by using mechanical resonances of the resonator in a small volume of the sound field.

2. Materials and Methods

2.1 Pressure measurement

Our proof-of-concept prototype is shown in **Fig. 1**. The resonator was designed to resonate at around 109 kHz in water which corresponds to the primary resonance of the ultrasound transducer used in the experiment and made by cutting machining of glass. The sound pressure induced by the vibration of the resonator was measured by a needle hydrophone (HNR-1000, Onda, Sunnyvale, CA) as seen in **Fig. 2(a)**. The resonator was inserted into a cubic water container with an inner dimension of 90 mm. A Langevin ultrasound transducer was connected with the resonator through glycerin-based acoustic couplant. The measured points were scanned along the *z* axis from *z*=-4 mm to *z*=10 mm using an automatically controlled XYZ stage. A 15-cycles sinusoidal burst

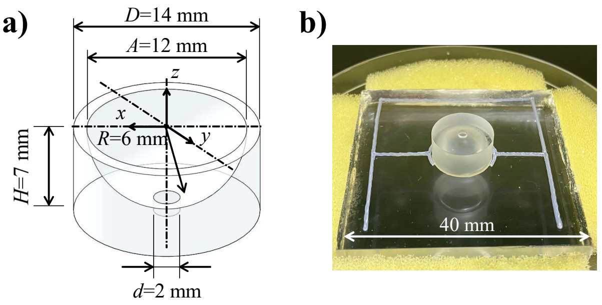

Fig. 1 (a) Schematic of the acoustic resonator design and (b) photograph of the glass-made resonator fixed by an elastic support on a urethane gel.

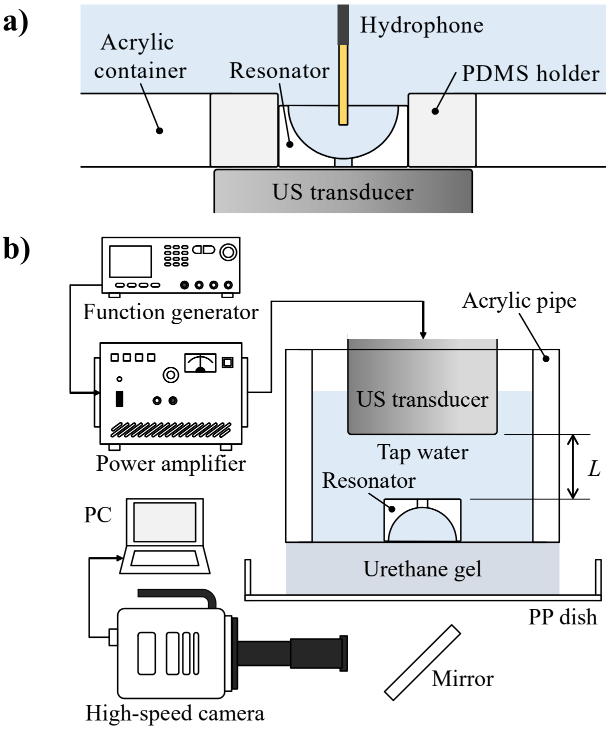

Fig. 2 Schematics of the experimental setup for (a) pressure measurement, and (b) high-speed imaging under sound irradiation.

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wave was input to the transducer at 50 V peak to peak voltage. The received signal of the hydrophone was acquired by a digital oscilloscope.

2.2 Cavitation observation

Generation and motion of cavitation bubbles were photographed by a high-speed video camera (Fastcam NOVA S12, Photoron, Japan). The experimental apparatus is shown in **Fig. 2(b)**. The resonator was placed on a urethane gel (IP-10, Exseal, Japan) and filled with tap water confined by a rectangular acrylic pipe. The Langevin ultrasonic transducer immersed in the chamber irradiated a frequency-modulated wave sequence in which burst waves with two different frequencies were alternatively excited. In the present study, the first frequency for cavitation generation is f_1=164 kHz, and the second frequency for cavitation collapse is f_2=109 kHz. The two frequencies are the lowest two resonance frequencies of the ultrasonic transducer.

3. Results

The sound pressure induced by the vibration of the resonator was measured to verify the pressure focusing effect of the resonator. In **Fig. 3**, the measured peak negative pressure induced by the resonator was normalized and compared to the direct sound propagation. It was found that the peak negative pressure is amplified inside the resonator, and rapidly attenuates toward the direction of sound wave compared to that in the absence of the resonator. Outside the resonator (z>0), the pressure amplitude was reduced approximately by 50% at the presence of the resonator.

Fig. 4 shows the side view of the cavitation structure generated inside the resonator. Cavitation bubbles were generated and trapped at the internal space of the cylindrical hole because a standing-wave field is formed there at the higher sound frequency (164 kHz). When the sound frequency was switched to the second lower frequency (109 kHz), the cavitation bubbles spread out inside the resonator and collapse on the surface of the urethane gel. The bottom views presented in **Fig. 5** show the in-plane radial distribution of the cavitation bubbles. A filament-shaped cavitation structure is seen around the center of the resonator at 164 kHz. Cavitation bubble collapse on the material surface is obvious at 109 kHz.

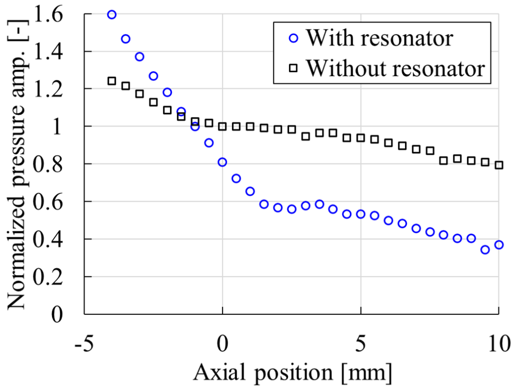
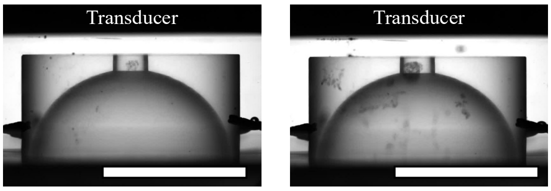
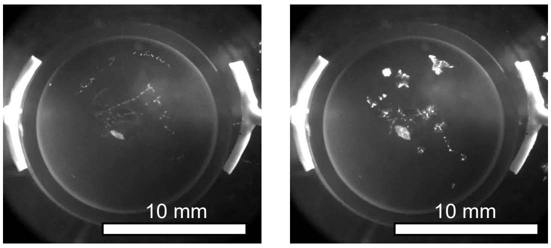


Fig. 3 Comparison of the experimental results of the peak negative pressure measured along the z axis with (circles) and without (square) the acoustic resonator. The sound frequency is 109 kHz.



f=164 kHz f=109 kHz

Fig. 4 Representative side view of cavitation structures induced in the acoustic resonator at the modulated sound frequencies f_1=164 kHz (left) and f_2=109 kHz (right). The bar presents 10 mm.



f=164 kHz f=109 kHz

Fig. 5 Representative bottom view of cavitation structures induced in the acoustic resonator at the modulated sound frequencies f_1=164 kHz (left) and f_2=109 kHz (right).

4. Conclusion

An acoustic resonator was designed and driven at two acoustic resonance conditions to induce cavitation activities on skin-mimicking soft material. It was found from the pressure measurement that the sound pressure induced by the resonator was amplified inside the resonator and rapidly attenuated. A dual-frequency wave sequence was successfully used to generate and control ultrasonic cavitation. Cavitation generation was enhanced in a standing wave field at the higher sound frequency, and cavitation bubble collapse was promoted on the soft material surface at the lower sound frequency. This implies that cavitation activity on the skin surface can be enhanced while reducing adverse skin damages caused by the primary sound wave field.

Acknowledgment

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References

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2. C. M. Schoellhammer et al.: J. Control Release **163** (2012) 154.