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A traveling wave mode ultrasonic transducer for low-frequency sonophoresis

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1. Introduction

Ultrasonic cavitation is described as the formation and accompanying oscillations of vapor microbubbles caused by instantaneous negative pressures in a liquid due to ultrasonic irradiation. When cavitation bubbles oscillate and subsequently collapse, hydrodynamic phenomena such as microjets, shockwaves, and microstreaming are induced, which act as mechanical stresses on surrounding boundaries[1)].

Sonophoresis is a minimally invasive transdermal drug delivery method using ultrasonic waves. Mechanical stimuli on the skin surface induced by ultrasonic cavitation bubbles temporarily modify the outermost layer (stratum corneum), allowing the penetration of high molecular weight drugs through the skin[2)]. In conventional ultrasonic irradiation, cavitation bubbles do not uniformly form on the skin, resulting in creating high permeability regions that are both localized and inhomogeneous.

This research aims to achieve short-term and highly efficient transdermal drug delivery by uniformly generating ultrasonic cavitation on the skin surface, thereby forming extensive and uniform transport regions. In this paper, we developed a multimode ultrasonic transducer with multipolar electrodes. By exciting the traveling wave mode, we demonstrate that cavitation effects can be uniformized on the target material surface.

2. Proposed ultrasonic transducer

2.1 Prototype model

Fig. 1 shows the design and dimensions of the multimode ultrasonic transducer. The proposed transducer has an outer diameter of 24 mm and a height of 8.5 mm. A Ti-6Al-4V titanium alloy bowl-shaped acoustic resonator is bonded with epoxy resin to a ring-shaped piezoelectric element (C-201, Fuji Ceramics) whose positive electrode is divided into four segments.

2.2 Driving method

We proposed two driving methods for the in-phase driving method applies in-phase sinusoidal voltage to the four-segment electrodes of the piezoelectric element, exciting the axisymmetric vibration mode. The traveling wave method applies sinusoidal voltages with phase differences of $\pi/2$ between adjacent electrodes, exciting the traveling wave vibration mode. **Fig. 2** shows the deformation of the piezoelectric element for both the in-phase and traveling wave driving methods.

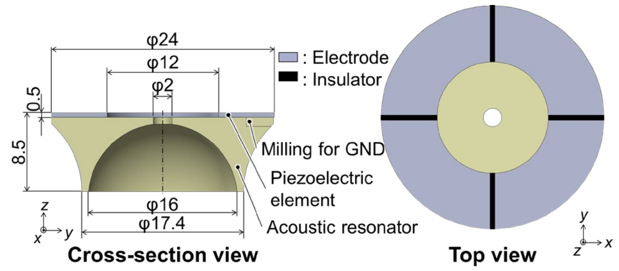

Fig. 1 Design and dimensions of the multimode ultrasonic transducer prototype.

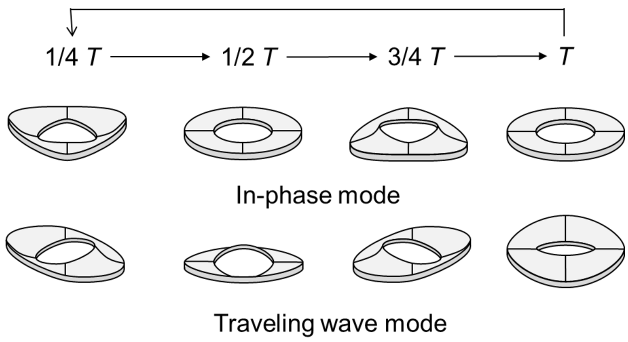

Fig. 2 Deformation of the piezoelectric element for the in-phase and traveling wave driving method.

3. Cavitation observation

A transducer was positioned on polyurethane gel phantom, which mimics biological tissue, within a chamber filled with pure water. Cavitation bubbles on the cavity aperture surface were captured using a high-speed camera at a frame rate of 2000 fps and an exposure time of 1/2000 s. In the driving experiments, the input frequencies were 102 kHz and 78 kHz for in-phase and traveling wave driving, respectively. The applied voltage amplitude was 120 V_{pp}.

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Figs. 3(a) and **(b)** present the positions of cavitation bubbles, by red dots, for the in-phase and traveling wave driving methods, respectively. The bubble positions were extracted from the recorded 10000 images corresponding to 5 s ultrasonic irradiation and cumulatively displayed in the image. In the in-phase driving method, the distribution of cavitation bubbles was observed in the center and near the outer edge of the aperture. In contrast, with the traveling wave driving method, cavitation bubbles were distributed in the middle of the radial direction.

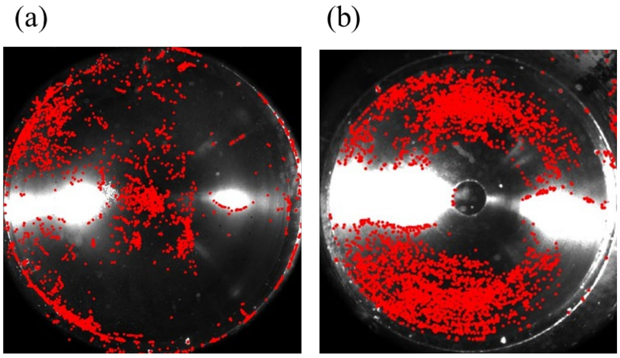

Fig. 3 Experimental results of cavitation observation driven by (a) in-phase and (b) traveling wave driving method. The red dots indicate the positions of the cavitation bubble generated.

4. Artificial membrane stain

We treated a polymer-made artificial membrane (Strat-M, Merck) using the proposed transducer to demonstrate the cavitation effect on the target surface. The top surface of the membrane is coated by synthetic lipids that mimic the outermost layer of the skin (stratum corneum). The lipid layer can be partly removed by hydrodynamic stresses arising from the oscillation of cavitation bubbles. A membrane sample was placed on an urethan gel phantom immersed in PBS solution and insonified with the in-phase or traveling wave driving method. The applied voltage signal was a sinusoidal burst wave with the peak-to-peak amplitude of 120 V_{pp}, the input frequencies were 102 kHz and 79 kHz for the in-phase and traveling wave methods, respectively.

The treated membrane was stained with 0.5% w/v food color red solution for 15 min. **Figs. 4(a-c)** shows the staining results, and **Figs. 4(d-f)** are processed images in grayscale with contrast adjusted. Because the stain material is water-solvable, a portion of the membrane surface where lipid coating was removed by cavitation effect was stained red. The traveling wave driving method exhibited more uniform and enhanced cavitation effect.

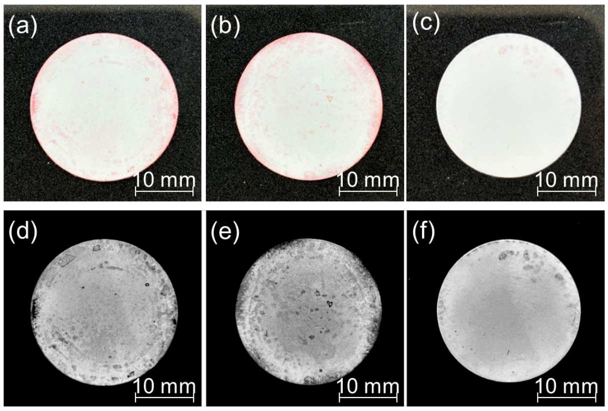

Fig. 4 (a-c) show the staining results of the artificial membrane in in-phase drive, traveling wave drive, and control (no ultrasonic treatment), respectively. (d-f) show the photographic contrast of the staining results.

5. Conclusion

An ultrasonic transducer was developed to generate ultrasonic cavitation uniformly over a wide area on the skin surface. The electrodes of the piezoelectric element were divided into four parts which were driven by voltage signals with phase differences, enabling to excite circumferential traveling wave vibration. Cavitation bubbles were generated at the middle area that cannot be generated by the conventional in-phase driving. Ultrasonic irradiation of the artificial membrane was performed, confirming that ultrasonic cavitation was able to remove lipids from the membrane surface.

In the future, we will fabricate a transducer that can improve the acoustic pressure generated by traveling wave driving. In future work, we will confirm that ultrasonic irradiation using a combination of in-phase and traveling wave driving will make the range of cavitation generation uniform on the skin surface.

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