

## Production and validation of acoustic field to enhance trapping efficiency of microbubbles by using a matrix array transducer

超音波 2次元アレイを用いた微小気泡の捕捉効率向上のための音場形成とその検証

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### 1. Introduction

We have ever reported our attempts to control microbubbles using the primary and secondary acoustic forces to elucidate the conditions in sound pressure, central frequency of ultrasound, and flow velocity for active path selection [1,2] and trapping in blood flow [3] of microbubbles using artificial blood vessels. In those experiments we have examined with single element transducers to produce focused or plane acoustic fields, by using concave or flat transducers, respectively. However, considering an *in vivo* application, there is a limitation to place a transducer on the body surface because focal area of the acoustic field is fixed. Furthermore, it is difficult to change focal area dynamically to produce acoustic force at a desired position using a single element transducer. If a 2D array transducer is applied to control the behavior of microbubbles, not only the shape of acoustic field can be designed, but also multiple focal area can be produced and steered simultaneously, which is realized by changing delay time in sound elements.

Since nowadays the 2D array transducers are widely used for the HIFU therapy [4], where a continuous wave is required to shorten treatment time, there is a concern of overload in each element to produce high temperature gain. However, though a continuous wave is also necessary to guarantee acoustic force for active control of microbubbles in blood flow, the maximum sound pressure is required at least several hundred kPa, which is much less than that of HIFU. In this paper, we report our challenge to design and to produce a continuous acoustic field to trap higher amount of microbubbles in flow using a 2D array transducer.

### 2. Method

We have used a square flat array transducer, which has air-backed 64 PZT elements with the

aperture of  $23.9 \times 23.9 \text{ mm}^2$ , the size of each element of  $2.9 \times 2.9 \text{ mm}^2$ , and the pitch of the elements of 3.0 mm, respectively. The resonance frequency of the element is 1 MHz, where the drive unit was required to produce continuous square wave with minimum delay pitch of 5 ns. **Fig. 1** shows the experimental setup. A thin channel, which was made of poly(ethylene glycol) (PEG) [3] with the gap of 2 mm, was fixedly floated from the bottom of a water tank with filled water. The observation area was focused and adjusted in the center of the channel by an optical microscope (Omron KH-7700) from the bottom of the tank. The axis of 2D array transducer was set to cross the center of the observation area with the angle  $\theta = 40^\circ$  and the distance  $d = 50 \text{ mm}$ , where the array surface was entirely soaked below water. Also we prepared the suspension of microbubbles, which are F-04E microcapsules (Matsumoto Oil) [2] with a shell made of poly(vinyl chloride) (PVC), a specific gravity of 0.0225, and an average diameter of 4  $\mu\text{m}$ .

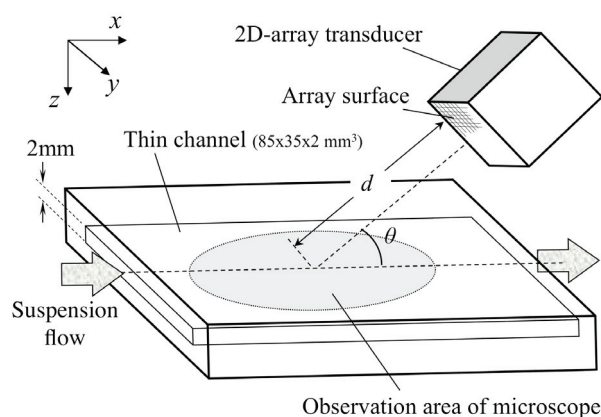


Fig. 1 Experimental setup to trap microbubbles by using a 2D array transducer.

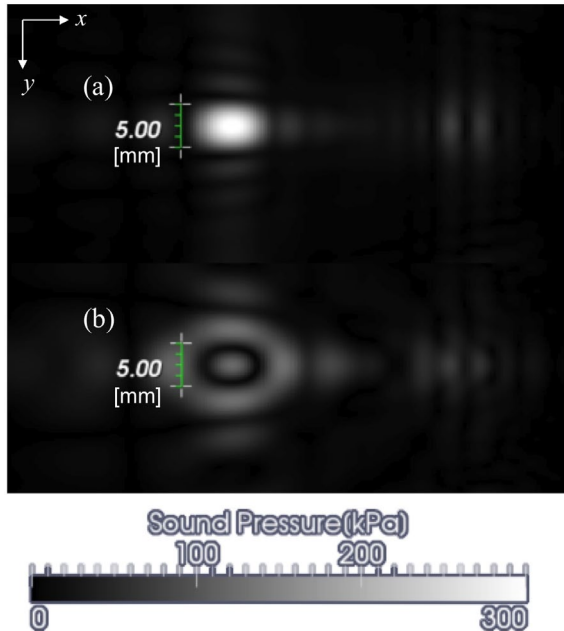
Then we prepared two types of acoustic fields, which were produced by setting delay time in 64 elements individually. The focused acoustic field was produced to make a focal point in 50 mm on the axis from the array surface. On the other

hand, the defocused acoustic field was produced by shifting phases in the central 16 elements from the focused one. **Fig. 2** shows the delay times to produce both of the acoustic fields, where the phases in the darkened elements were reversed.

| ch | 1    | 2    | 3    | 4    | 5    | 6    | 7    | 8    | ch | 1    | 2    | 3    | 4    | 5    | 6    | 7    | 8    |
|----|------|------|------|------|------|------|------|------|----|------|------|------|------|------|------|------|------|
| 8  | 0    | 0.33 | 0.58 | 0.68 | 0.68 | 0.58 | 0.33 | 0    | 8  | 0    | 0.33 | 0.58 | 0.68 | 0.68 | 0.58 | 0.33 | 0    |
| 7  | 0.33 | 0.68 | 0.93 | 1.05 | 1.05 | 0.93 | 0.68 | 0.33 | 7  | 0.33 | 0.68 | 0.93 | 1.05 | 1.05 | 0.93 | 0.68 | 0.33 |
| 6  | 0.58 | 0.93 | 1.15 | 1.28 | 1.28 | 1.15 | 0.93 | 0.58 | 6  | 0.58 | 0.93 | 0.65 | 0.78 | 0.78 | 0.65 | 0.93 | 0.58 |
| 5  | 0.68 | 1.05 | 1.28 | 1.40 | 1.40 | 1.28 | 1.05 | 0.68 | 5  | 0.68 | 1.05 | 0.78 | 0.90 | 0.90 | 0.78 | 1.05 | 0.68 |
| 4  | 0.68 | 1.05 | 1.28 | 1.40 | 1.40 | 1.28 | 1.05 | 0.68 | 4  | 0.68 | 1.05 | 0.78 | 0.90 | 0.90 | 0.78 | 1.05 | 0.68 |
| 3  | 0.58 | 0.93 | 1.15 | 1.28 | 1.28 | 1.15 | 0.93 | 0.58 | 3  | 0.58 | 0.93 | 0.65 | 0.78 | 0.78 | 0.65 | 0.93 | 0.58 |
| 2  | 0.33 | 0.68 | 0.93 | 1.05 | 1.05 | 0.93 | 0.68 | 0.33 | 2  | 0.33 | 0.68 | 0.93 | 1.05 | 1.05 | 0.93 | 0.68 | 0.33 |
| 1  | 0    | 0.33 | 0.58 | 0.68 | 0.68 | 0.58 | 0.33 | 0    | 1  | 0    | 0.33 | 0.58 | 0.68 | 0.68 | 0.58 | 0.33 | 0    |

**Fig. 2** Map of delay times [ $\mu\text{s}$ ] in 64 elements to produce a focused acoustic field (left), and an intentionally defocused acoustic field (right).

We have confirmed by calculating the shape of two acoustic fields on the observation area. **Fig. 3(a)** shows the distributions of sound pressure, where maximum sound pressure in the focused field was normalized to be 300 kPa. Meanwhile, the defocused one was calculated as shown in **Fig. 3(b)**, where the distribution of sound pressure seemed to be spread by exchanging the maximum intensity.

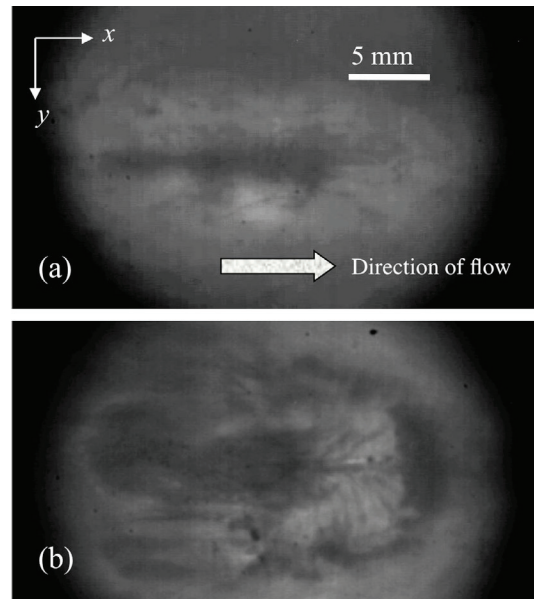


**Fig. 3** Calculated distributions of sound pressure of (a) focused and (b) defocused acoustic field, respectively.

### 3. Results

We have confirmed the behavior of microbubbles when the suspension (volume density: 2.35 [ $\mu\text{l/ml}$ ]) was injected under the two types of acoustic fields. **Fig. 4** shows the microscopic images, where suspension flows from

left to right with a flow velocity of 1 mm/s. In both of results, microbubbles were propelled by primary acoustic force and trapped in the middle of the channel. In **Fig. 4(a)**, trapped microbubbles were confirmed near the focal area, which is similar to our previous results using a single element transducer [3]. On the other hand, in **Fig. 4(b)**, more amount of trapped microbubbles were confirmed than that in **Fig. 4(a)**, which indicates that the defocused acoustic field has an advantage to be able to control the behavior of microbubbles in multiple areas of blood vessel network.



**Fig. 4** Microscopic images with suspension flow of microbubbles under (a) focused and (b) defocused acoustic field, respectively.

### 4. Conclusions

We have designed a defocused acoustic field by phase-reversing a part of elements in a focused one to apply to trap more microbubbles. In the next step we are going to measure quantitatively for precise evaluation of various acoustic fields.

### Acknowledgment

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### References

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