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# Influence of bubble flow in bubble enhanced HIFU
マイクロバブル援用 HIFU における気泡流入の影響

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## 1. Introduction

High-intensity focused ultrasound (HIFU) is widely used for therapeutic applications because it is an attractive and non-invasive tool by which to provide thermal therapy [1]. The sound pressure at the focal point reaches hundreds of megapascals, resulting in an increase in temperature, which necrotizes cells. Although HIFU treatment has been applied to prostate and breast tumors, for example, it is difficult to treat targets that lie behind bone (e.g., brain tumors) or that lie deep inside the body (e.g., liver tumors), because the ultrasound beam is reflected, refracted, and attenuated by the intervening tissue and/or bone. In order to resolve this problem, microbubble-enhanced HIFU has been developed [2-3]. Microbubbles are used as contrast agents for therapeutic applications of ultrasound imaging, and in a previous study, we used microbubbles to enhance the heating effect at the focal point of HIFU treatments. This enhancement of heating is caused by the generation of thermal energy based on the volume oscillation of microbubbles under the ultrasound irradiation. However, when microbubbles exist on the ultrasound pathway, they disturb the ultrasound propagation and distort the acoustic field. Distortion of the acoustic field leads to defocus and causes unexpected damage to tissue in the body.

In the previous study, we proposed a method by which to destroy microbubbles on the pathway of ultrasound and to focus the thermal energy only at the focal point in microbubble-enhanced HIFU treatment [4-5]. Previous study we only used bubble contained gel phantom. So we neglected the effect of intravascular bubble flow.

In this study we used gel phantom with bubble flow model.

## 2. Method

The commercially available Sonazoid™ contrast agent was selected as a microbubble contrast agent. The average diameter of Levovist™ is 1.3 micrometer. An experiment was conducted with a polyacrylamide gel phantom with bubble flow model. In the phantom experiment we decided the blood vessel diameter (3 mm) and flow speed (21 mm/sec) by ultrasound image of a liver with the contrast agent. **Fig. 1** shows the experimental setup, which can measure the temperature distribution of the heating area. The piezoelectric (PZT) transducer generates ultrasound waves. The diameter and focal length of the PZT transducer are both 40 mm. The resonance frequency of the PZT transducer is 2.2 MHz. The ultrasound waves are irradiated to a gel in the water. The water is maintained at 37 deg C. The container filled with polyacrylamide gel is a cube having sides of 50 mm. A thermal liquid crystal sheet, the color of which changes with respect to temperature in the range of 50 to 60 deg C, is placed in the gel and positioned in the plane of the ultrasound beam axis.

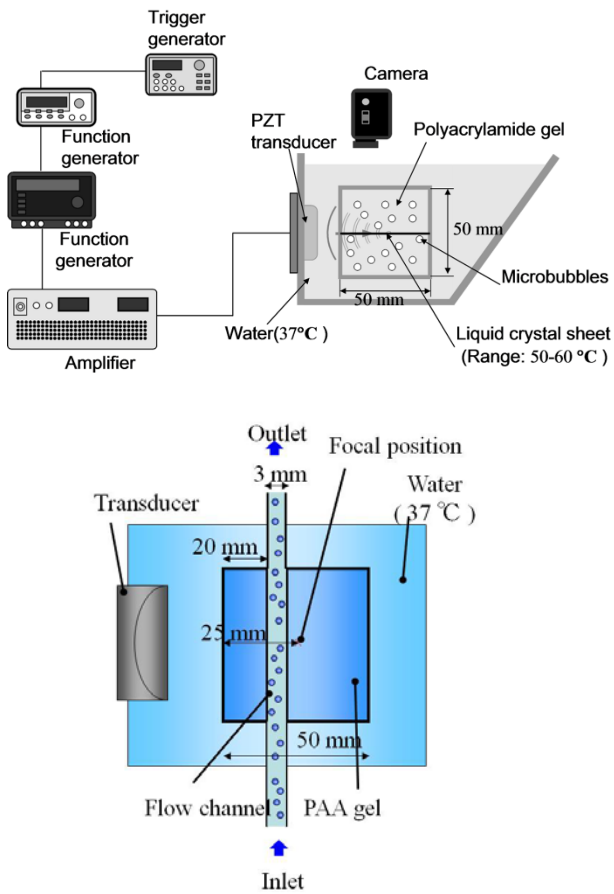


Fig. 1 Experimental apparatus.

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### 3. Microbubble enhanced HIFU with bubble flow model

Microbubble contrast agents have encapsulating shells because they are designed to be stable in order to be used in intravenous injection. We proposed an advanced method, which is irradiating high intensity burst waves and weak waves in turn. High intensity burst waves are for oscillating and fragmenting microbubbles. Fragmented bubbles are dissolved during the subsequent weak waves, which are for heating the focal point. Weak waves should be decided enough weak not to oscillate and enlarge smaller microbubbles fragmented by high intensity ultrasound.**Fig. 2** shows the sequence of this method.

"Bubble destruction ultrasound parameters"
Frequency:2.2MHz,Intensity:3000W/cm$^2$,
Exposure time: 9.12 μsec
"Heating ultrasound parameters"
Frequency:2.2MHz, Intensity 500W/cm$^2$,
Exposure time:2 msec

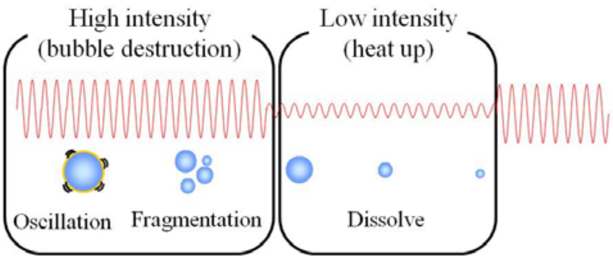


Fig. 2 Ultrasound sequence of microbubble enhanced HIFU

### 4. Result and discussion

Images of the temperature distribution for air flow, water flow and bubble flow with the advanced method of bubble enhanced HIFU are shown in **Fig. 3**. In the case of the air flow, the heat-up region occurs at the edge of the flow channel. This result suggests that ultrasound propagation was disturbed by the air flow. We observed the heat up region at the focus point as same as flow channel phantom with water flow experiment. Microbubbles in the blood vessel phantom couldn't flow into the focused ultrasound pathway. Because micorobubules collapsed by destruction burst wave or kept back the bubble by the acoustic radiation force at the edge of focused ultrasound pathway. Our bubble enhanced HIFU method have the possibility to use in the liver treatment with intravascular bubble flow.

### 5. Conclusion

We evaluated our microbubble enhanced HIFU method with intravascular bubble flow phantom model. In the result, our method can use in the liver treatment with intravascular bubble flow.

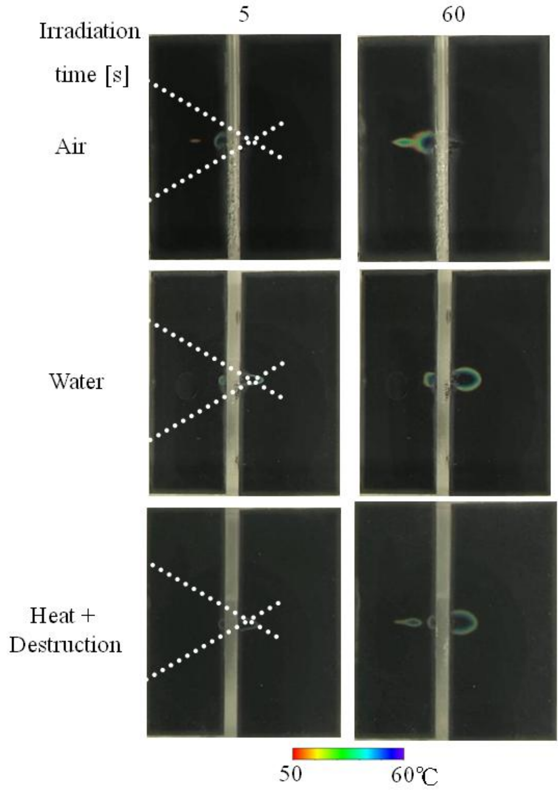


Fig. 3 Temperature distribution of microbubble enhanced HIFU with flow model.


### Acknowledgment

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