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Optically and acoustically simultaneous measurement of phase change nano-droplet vaporization

相変化ナノ液滴気泡化現象の光学的音響的同時計測

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1. Introduction

A phase change nano-droplet (PCND) is being studied by many researchers as contrast agents and therpeutic sensitizers. A PCND is a liquid microbubble precursor which is formulated from superheated perfluorocarbon (PFC). Ultrasound exposure to a PCND would induce liquid to gas phase shift and generate micron-sized bubble which can be utilized as ultraound contrast agents or cavitation nuclei for high intensity focused ultrasound (HIFU) treatment sensitizers.

In order to develop a PCND as an clinical tool, it is necessary to control the vaporization. Nevertheless, acoustic response of a PCND is highly complex that the type of PFC and the applied acoustic parameters would affect the PFC vaporization. Despite the competent ability and wide range of applications, vaporization properties are still unknown. Knowing one of the vaporization properties; extent of vaporization area, is useful when planning a strategy to position adjacent ablation regions.

The purpose of this study is to investigate time-lapse change of ultrasound stimulated PCND vaporization area. Moreover, we investigated the dependency of internal PCND composition.

2. Materials and Methods

A schematic diagram of the experimental setup are shown in **Fig. 1**.

2.1. PCND and gel phantom preparation

In this study we investigated three different internal composition PCNDs; perfluoro-n-pentane (PFP), perfluoro-n-hexane (PFH) and mixture (PFP:PFH = 1:1) [1]. The main characteristic differences are their boiling point (b.p.); PFP (29°C), PFH (57°C) and mixture (40°C). PFP, the most popular PFC droplets used for HIFU enhancement studies, has good acoustic response due to their low boiling point. However, PFP is relatively volatile compared to the other PFC droplet and might vaporized at the undesired timing. As the b.p. rises, it becomes stable in the liquid state but the acoustic response decreases. These three different type of PCNDs (PFP, PFH and Mix) were purchased from Central Research Lab. Hitachi. Polyacrylamide gel solution without PCNDs (w/o PCNDs) and with PCNDs were prepared as same manner as detailed in the ref. [2]. After preparation of both solutions, firstly w/o PCNDs were poured into a mold (50 x 50 x 45 mm). Secondly, after first solution were fixed, solution with PCNDs were poured on top of the w/o PCNDs gel. Parameters investigated were PCND internal composition.

2.2. Experimental setup for ultrasound exposure and high speed imaging

Gel phantoms, placed on inverted microscope (Nikon, TE2000-E) equipped with a 20x objective lens coupled to a high-speed imaging camera (HPV-1A, SHIMADZU), were exposed to an focused ultrasound pulse (central frequency; 5 MHz, Cycle; 5, and peak negative pressure; 3.5 MPa). Only one sequence was irradiated. A programmable research ultrasound system (Verasonics, Redmond, WA) driving a EUP-L73S linear array transducer (Hitachi Aloka Medical) was used to implement this pulse sequence and to measure/record acoustic signals emitted from vaporization of PCND at a sampling frequency of 20 MHz.

3. Results

Representative images taken at frame rate of 1 Mfps by high speed camera are shown in **Fig. 2**. Fig. 2 (a) is images of PFH nano-droplet, (b) is PFP nano-droplet, and (c) is PFP-PFH mixture nano-droplet. For each type of PCNDs, unique vaporization area/shape were observed. Shape of the vaporization area can be distinguished among three type of PFC droplets; PFP = combination of pre-focal and focal, PFH = cigar, PFP-PFH mixture = arrowhead.

In Fig. 2 (a), focal region PCND induced microbubble disappeared at least in 4 μsec while at the pre-focal region microbubble continued to grow their size and remain as a bubble for 10 μsec.

Moreover, vaporization event which is high intensity and wide band frequency signal [2] were captured simultaneously shown in **Fig. 3** by ultrasound transducer. This acoustic signal corresponds to the time scale of Fig. 3 (a) frame number 1 to 3.

4. Discussions

Lifespan of generated bubble differ among type of PFC and can be separated into two group; remaining group and disappearing group. PFP can be separated into remaining group and PFH and PFP-PFH mixture into disappearing group. Remaining group (PFP) might be useful for HIFU treatment sensitizer since remaining microbubble can be used as a pressure-resistant source (ultrasound cannot penetrate) which induce increase of the temperature at the vaporization area by converting ultrasound energy to thermal energy. In the disappearing group (PFH and mixture of PFP and PFH), vaporization concentrated in pre-focal areas which would associate with a risk of ablating away from the intended targeted site. Also we can set up a hypothesis that the vaporized droplet return to the liquid state again or dissolved to the surrounding medium. Further investigations are needed to categorize whether the vaporized droplet returned to the liquid state again or dissolved, by changing the ultrasound exposure sequence (adding 20 μsec pulse interval and exposing ultrasound pulse 2 times).

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References

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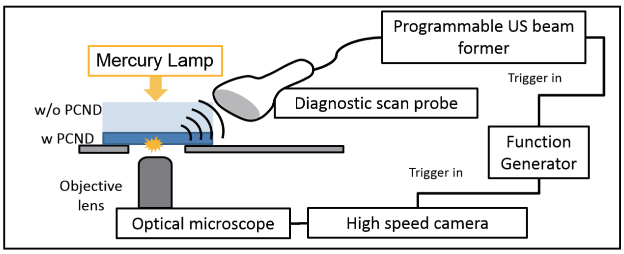

Fig. 1　A schematic diagram of experimental setup

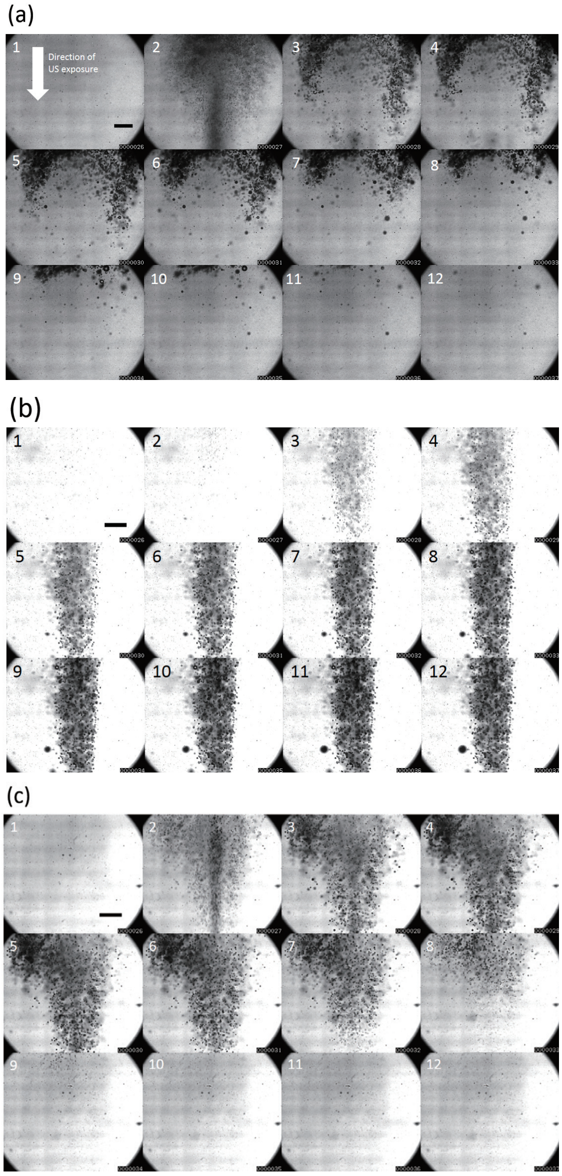

Fig. 2　High speed images of ultrasound exposed PCNDs; (a) PFH, (b) PFP and (c) PFP-PFH mixture. Scale bars represent 100 μm.

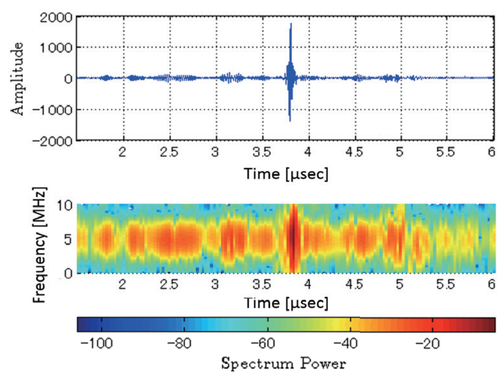

Fig. 3　Acoustic signal corresponding to the time scale of Fig. 3 (a) frame # 1 to 3