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Optical observation of microbubble behaviors in contrast-enhanced active doppler ultrasonography

動的造影超音波法におけるマイクロバブル動態の光学的観測

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1. Introduction

We have proposed contrast enhanced active Doppler (CEADUS) method for detecting lymph channel with high contrast performance. In CEADUS, translation of microbubbles (MBs) as contrast agents is induced by the primary Bjerknes force and quntified by Doppler method. Our previous experiments demonstrated that the translational velocity of MBs was proportional to the pulse repetition frequency and the square of peak negative pressure of incident ultrasound. This trend agreed with the theoretical prediction based on the simulatioin of bubble oscillation and translation for a single bubble. However, it was supposed that the behavior of MBs under ultrasound irradiation should be complicated e.g. due to bubble-buibble intraction induced by secondary Bjerkness force. For depper understanding of MB'a behavior in CEADUS, we incoopoperated the optical observation system into CEADUS system. In this reports, we compare the observed MB's behavior with the translational velocity qunatified by CEADUS.

2. Observation system

Figure 1 shows a self-made spatial flow cell for the simultaneous observation. The cell was filled with agar-based gel, in which a flow channel with square shape (0.3 mm×0.3 mm) was formed The two optical windows facing each other were set on the side wall of the cell. Sonazoid as MBs was injected into the channel by using syringe pump and MB's behaviors was observed from the side of the cell using an optical microscope system (VHX7000, KEYENCE). The magnification of the system was ×100 and the frame rate was 30 frames/s. A single element concave transducer with resonant frequency of 15 MHz and F-number of 2 was located above the flow channel. The focus of the transducer was adjusted so that it was positioned on the upper surface of the flow channel. The focus diameter in lateral direction was 200 μm. The ultrasound was transmitted and received for 1 s with PRF of 1 kHz by using a pulser/receiver (5072 PR, Olympus).

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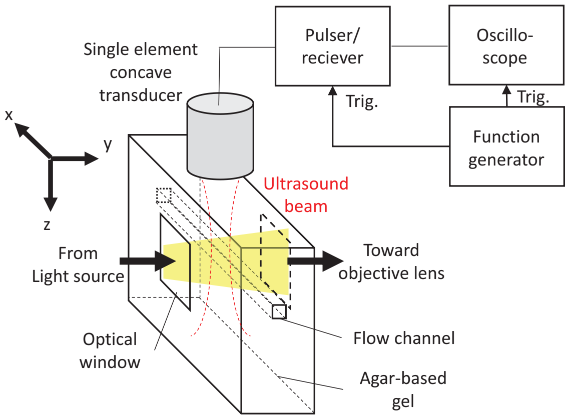

Fig. 1 Optical observation system incorporated in CEADUS system.

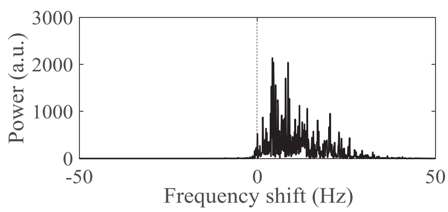

Fig. 2 Typical power spectrum of Doppler signal.

3. Signal processing in CEADUS

The sequence of received echoes for 1 s was converted to analytical signal. Doppler shift frequency was obtained by applied the same signal processing as the pulse Doppler method. We quantified the intensity of dynamic echo and Doppler shift frequency from the Doppler signal. **Figure 2** shows a typical frequency spectrum of Doppler signal. The intensity of the dynamic echo (I_d) was defined as the value subtracted DC (stationary) component (I_s) from the integral (I) of normalized power spectrum (P) of the Doppler signal. I_d and I_s were defined as follows,

$$I = \int P\, df.,$$
$$I_s = P(0), \qquad (1)$$
$$I_d = I - P.$$

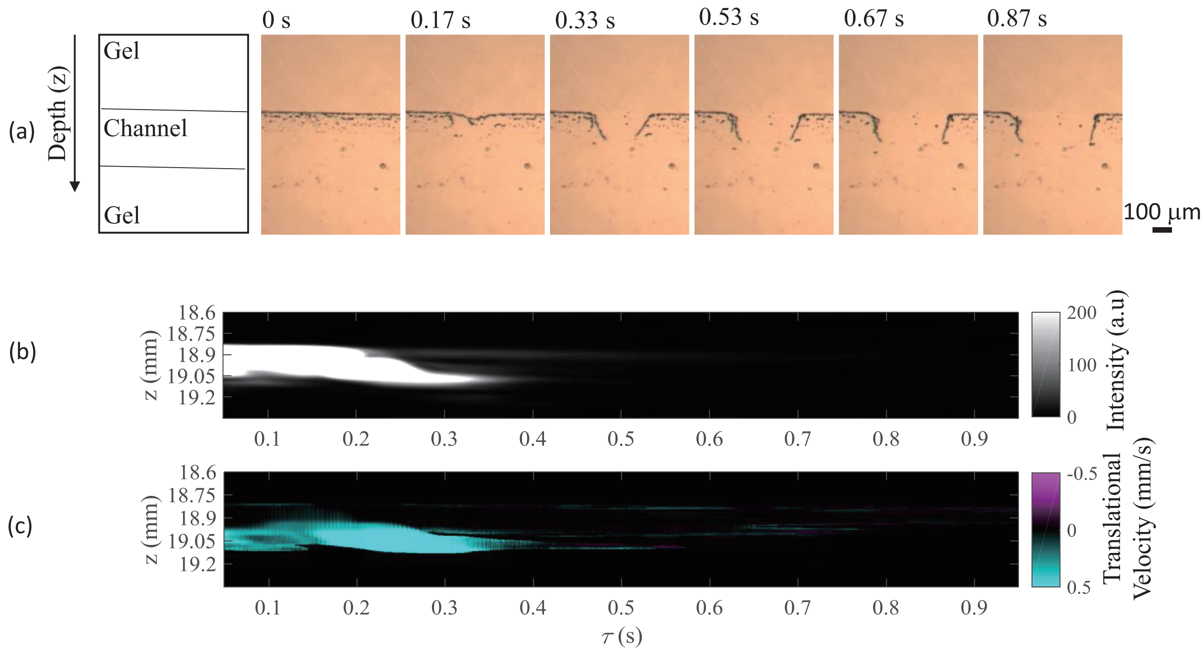

Fig. 3 (a) Observed microbubble's behavior under ultrasound exposure, (b) spatiotemporal analysis of intensity of dynamical echo and (c) translational velocity of MBs by CEADUS. PRF was 1 kHz. In (a), the left figure shows the schematic of the images.

The Doppler shift frequency was defined as the expected value of the normalized power spectrum. Assuming that the UCAs moved only in the sound propagation direction, translational velocity (v_{travel}) of UCAs was calculated from Doppler shift frequency using following equation.

$$v_{travel} = \frac{\Delta f}{2f_0+\Delta f}c, \qquad (2)$$

where f_0 and df mean the center frequency of transmitted ultrasound and Doppler shift frequency, respectively. c is the speed of sound.

4. Results and discussions

Figure 3 shows the MB's behavior observed by the optical microscope. MBs floated and were at the upper surface of the channel before MBs underwent ultrasound exposure. It seemed that MBs moved radially around the upper surface of channel on the sound propagation axis. After 0.33 s, there were few MBs on the sound propagation axis. The disappearance range was approximately 500 μm, which was larger than the beam width. The translational velocity of MBs could be calculated to be several mm/s from the images.

CEADUS analysis demonstrated that significant dynamical echo could be observed at the upper surface of channel before 0.2 ms. Then the hyperechoic portion gradually moved to the lower surface of the channel. After 0.4 s, there were few significant dynamic echoes all over the channel. This result pointed that MB's translation occurred only during first 0.4 s. This fact agreed with the optical observation results.

Above results point that the long and strong ultrasound exposure may prevent from detecting MBs in clinical situation because they disappear around the sound propagation axis. Once MBs disappear on the sound propagation axis, we should re-injected MB's suspension or diffuse pre-existing MBs around the disappearance part.

4. Summary

The optical observation system was constructed for investigating the microbubble's behaviors in CEADUS. We succeeded in the simultaneous observation of bubble translation by the optical microscope and CEADUS. The results demonstrated that the trend analyzed by CEADUS was consistent with the optically observed bubble behaviors.

Acknowledgment

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