Basic study about microbubble localization in contrast-enhanced ultrasound

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1. Introduction

In contrast enhanced ultrasound (CEUS), nonlinear echoes from microbubbles (MBs), which are comprised gas cores encapsulated in shells, in a blood flow are used for contrast-specific image formation. The CEUS images are useful for visualizing the blood flow and are promising for vasculature evaluation[1].

Recently, it has also been applied to super resolution (SR) imaging for microvasculature[2]. In SR imaging, the CEUS images are typically acquired with high-frame rate more than 1000 fps. Then, the isolated MB is detected from the images. The SR image can be formed by the localization and tracking of the center of the MB echo. Previous reports about SR imaging, the SonoVue MB (Bracco Imaging, Italy) is employed as the contrast agent. In this study, employment of the Sonazoid MB (GE Healthcare, Japan) have been considered. Therefore, the suitable number density and a method of localization for the Sonazoid MBs are investigated, as a preliminary study.

2. Image formation

In CEUS, the only nonlinear echoes from the flowing MBs are used for image formation. To cancel the linear echoes from MBs and surrounding tissues, the multi-pulse transmission technique, which are known as pulse inversion (PI), is typically employed. In the PI procedure, an ultrasonic (positive) pulse is transmitted, and the echoes are received. Then, the amplitude-inverted (negative) pulse is transmitted, and the echoes are received. The nonlinear echoes can be extracted by the summation of the positive and negative echoes.

Although most linear echoes can be canceled by PI, the residual linear echoes often make it difficult to detect the isolated MBs. Therefore, the moving target indication (MTI), taking the difference between adjoining flames, is employed in this study. The echoes from stationary surrounding tissues are canceled by MTI.

3. Experimental method

The experimental setup in this study is shown in **Fig. 1**. The silicone tube (ARAM, Japan) with an inner and outer diameter of 0.4 and 0.5 mm was fixed at a depth of 20 mm in the water tank. The diluted suspension of Sonazoid MBs was manually injected into the tube. The research ultrasound system Vantage 256 and the linear-array probe L11-5v (Verasonics, USA) are used to acquire echo data. The central frequency and the bandwidth are 7.47 MHz and 74%.

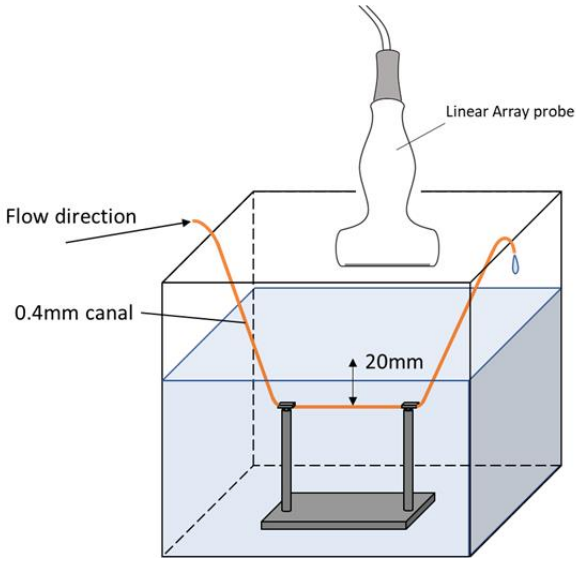

Fig. 1: Experimental setup.

Two cycles of the sinusoidal wave at 5 MHz was transmitted as a plane wave. The steering angles of the plane waves were -10°, -5°, 5° and 10°. In the ultrasound system, therefore, 8 sequences (positive and negative pulses in each angle) for transmission and reception are performed for CEUS. The pulse repetition frequency was 2 kHz. The applied voltage for the transducer elements were set at 5 V. The estimated MI value at a depth of 20 mm in water was 0.1. The received signals were stored at a sampling frequency of 50 MHz. The signal/image processing including the delay and sum beamforming were performed off-line using MATLAB.

4. Result and discussion

The solution of the Sonazoid MBs of 2 ml was diluted 100,000, 200,000 and 1,000,000 times with ultrapure water in 2 steps. The theoretical numbers of MBs are 60, 30 and 6 in the tube of the imaging region within ±20 mm.

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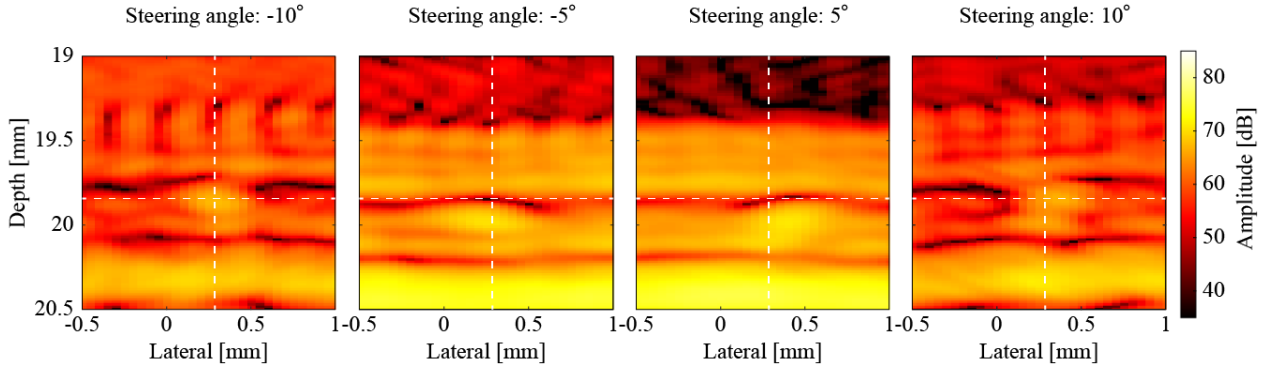

Fig. 2: The CEUS images obtained by PI in the steering angles of -10°, -5°, 5° and 10°.

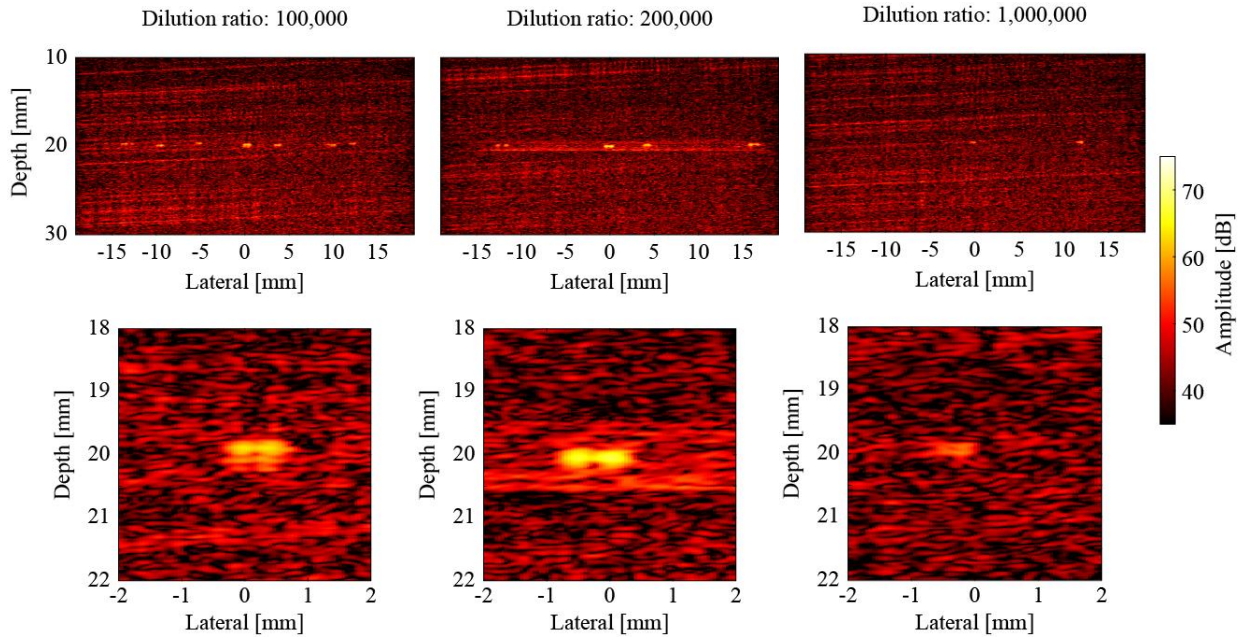

Fig. 2: The CEUS images obtained by PI and MTI in the steering angle of 10°.

The CEUS images obtained by the different steering angles should be compounded to form the high-resolution image. However, the echo positions by all steering angles didn't gather in this system, as shown in **Fig. 2**. Therefore, the CEUS images in the steering angle of 10° are used for MB detection. The CEUS images obtained by PI and MTI are shown in **Fig. 3**. The numbers of the flowing MBs are 7, 4 and 2 in the dilution ratios of 100 k, 200 k and 1M times, respectively. The number of MBs decreases from the theoretical numbers so that the concentration increases. Inhomogeneous distribution of MBs in the pipette for dilution and that in the diluted solution can be considered the cause.

In their close-up view in **Fig. 3**, the MB echoes seem to be divided into right and left. These are the MB echoes in adjacent frames. Therefore, the other stationary echo cancelation such as singular value decomposition should be employed for SR imaging[3].

5. Conclusion

In this report, the number density of the diluted suspension of the Sonazoid MBs is investigated for SR imaging. In this system, the compound of beam-steered images was impossible. However, the flowing MBs could be detected from each steering-angle image. The numbers density of the Sonazoid MBs were less than the theoretical values. Therefore, the pipetting, dilution and injection process have to be revised.

Acknowledgment

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References

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