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Study on methods of microbubble visualization and localization in three-dimensional contrast-enhanced ultrasound

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1. Introduction

In contrast-enhanced ultrasound (CEUS), nonlinear echoes from microbubbles (MBs) 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 vascular evaluation [1]. Recently, super resolution (SR) imaging is applied to CEUS for the microvasculature [2]. In SR imaging, the CEUS images are acquired with diluted MBs at high frame rate. Then, the isolated MBs are detected in the images, and the center of the MB echoes are localized and tracked to form the SR image.

However, it is difficult to accurately detect the microvasculature with complex structures from the ultrasound tomogram. In this study, SR imaging in the three-dimensional (3D) image is investigated. It is expected that the stable detection will be possible by visualizing the microvasculature in 3D. In this paper, MBs flowing through micro channels in a tissue-mimicking phantom were visualized by two-dimensional (2D) array probe. Then, a method to visualize and localize the MB echoes in the 3D-CEUS images is studied.

2. Method

2.1. Ultrasound imaging

The 3D ultrasound images were acquired with the 1024-element 2D array probe (8 MHz, Vermon) driven by the single research ultrasound system (Vantage 256, Verasonics). The 1024 elements were divided into four sub-apertures due to the limitation of the number of channels in the system. Each sub-aperture has 256 elements, aligned on a 32×8 grid with a pitch of 0.3 mm. Since there are 0.3 mm intervals between the sub-apertures, the area of the 32×32 grid full aperture is 9.6×10.5 mm. Each sub-aperture received echoes provided by the transmission of each sub-aperture, leading to 16 sequences of all combinations of 4 sub-apertures per frame.

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), was employed. First, the ultrasonic (positive) pulse was transmitted, and the echoes were received. Then, the amplitude-inverted (negative) pulse was transmitted, and the echoes were received. The positive and negative echoes were summed before other signal processing. As a result, 32 sequences of transmission and reception per frame were performed.

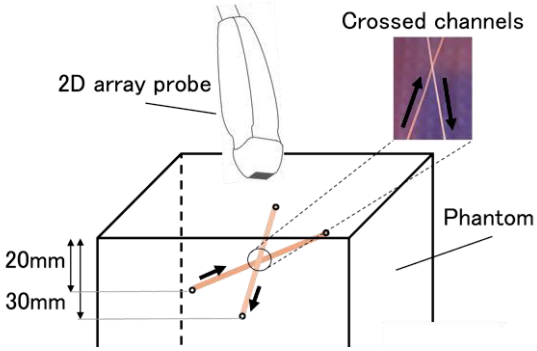

Fig. 1 Experimental setup for 3D-CEUS imaging.

Although most linear echoes can be canceled by PI, the residual linear echoes often make it difficult to detect the isolated MBs. Therefore, clutter-filtering method using the singular value decomposition (SVD) approach was employed in this study [3]. The echoes from stationary surrounding tissues and electrical noise are canceled by the filter.

2.2 Experimental setup

The experimental setup in this study is shown in **Fig. 1**. Two silicone tubes (ARAM, Japan) with an inner and outer diameter of 0.3 and 0.4 mm were fixed in a diagonal crossed shape at a depth from 20 to 30 mm in the homogeneous agar phantom. The components of the agar phantom were 92.5 wt% ultrapure water, 5 wt% polyamide (ORGASOL 2001 UD NAT 1, Arkema) particles of 5 μm diameter (as scatterers), 2 wt% agar, and 0.5 wt% dispersant. A suspension of MBs (Sonazoid®, GE Healthcare) diluted 1000 and 20,000 times with ultrapure water were injected into the tubes in opposite directions to each other at a flow rate of 10 mm/s using a syringe pump. The probe was fixed at the top surface of the phantom directly above the cross section of the two tubes.

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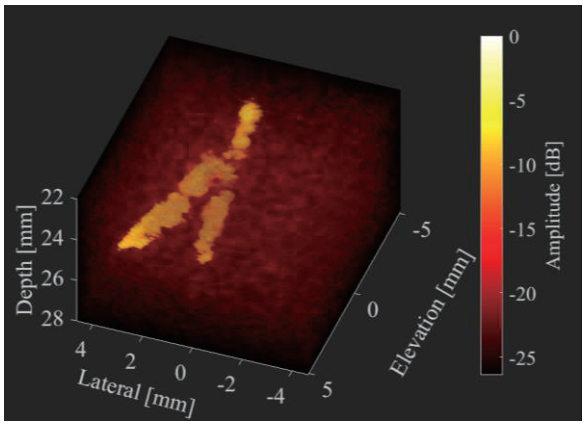

Fig. 2 3D-CEUS image obtained by PI and transparent processing for the dilution ratio of 1000 times.

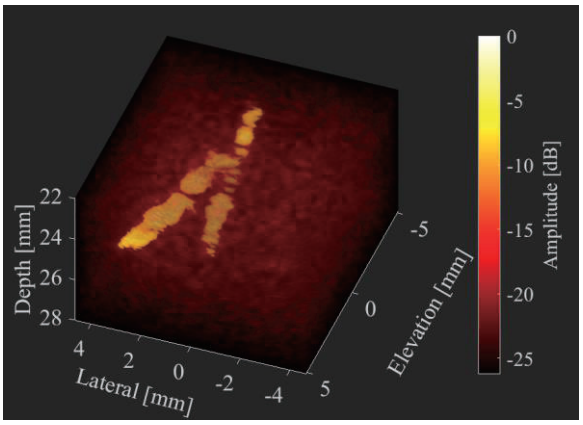

Fig. 4 3D-CEUS image obtained by PI and transparent processing for the dilution ratio of 20000 times.

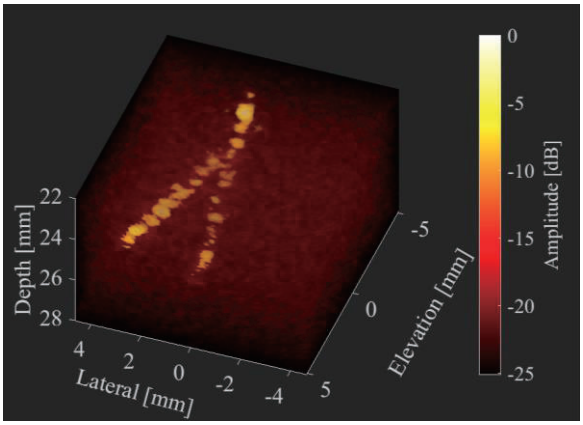

Fig. 3 3D-CEUS image obtained by PI, SVD filter, and transparent processing for the dilution ratio of 1000 times.

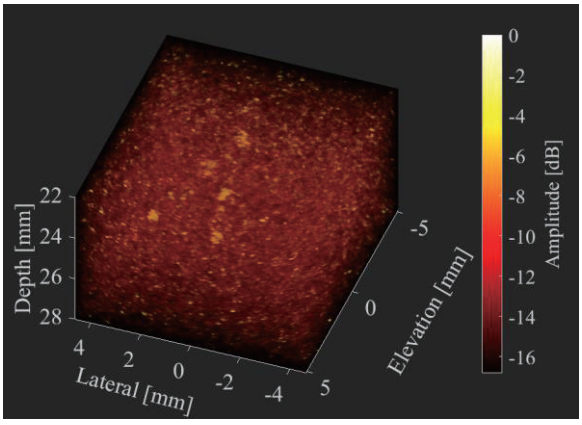

Fig. 5 3D-CEUS image obtained by PI, SVD filter, and transparent processing for the dilution ratio of 20000 times.

Two cycles of the sinusoidal wave at 4.629 MHz was transmitted as a plane wave. The applied voltage for the transducer elements were set at 10 V. A total of 60 frames (1920 sequences of transmission and reception) were acquired with MBs flowing continuously. The received signals were stored at a sampling frequency of 62.5 MHz. The synthesis of full-aperture echo signals and signal/image processing were performed off-line using MATLAB.

3. Result and discussion

All 3D images were formed by 3D delay-and-sum beam forming (DAS) of RF signals. For the dilution ratio of 1000 times, the 3D-CEUS image with PI and transparent processing is shown in **Fig. 2**. The region of the tube and MBs appears to be enlarged beyond their actual boundaries. Therefore, the SVD filter was applied to the image, as shown in **Fig. 3**. The echoes from MBs appears to be extracted by the filter. However, identifying the isolated MBs is difficult due to the high density of MBs.

For the dilution ratio of 20000 times, the 3D-CEUS image is shown in **Fig. 4**. As in Fig. 2, echoes from the tube to have persisted. **Fig. 5** shows the 3D-CEUS image with PI, SVD filter, and transparent processing. Although the echoes from individual MBs were weak, several isolated MBs were observed at the tube locations. From Fig. 3 and Fig. 5, 3D images make it easier to detect MBs flowing through complex channels.

4. Conclusion

In this report, as a study for the visualization and localization of MBs in the 3D image, we performed the experiment using 2D array probe. By applying PI, SVD filter, and transparent processing, MBs can be visualized in 3D-CEUS image.

Acknowledgment

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References

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