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Proposal of liquid viscosity measurement by burst-wave-aided contrast-enhanced ultrasonography

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1. Introduction

Burst-wave-aided contrast-enhanced active Doppler ultrasonography (CEADUS), where ultrasound contrast agents (UCAs) driven by acoustic radiation force are detected by the Doppler method, has been proposed to visualize microvascular vessels with high sensitivity[1)]. The translation of contrast agent caused by acoustic radiation force strongly depends on the viscosity of the surrounding liquid. Assuming that the relationship between the two can be formulated, the burst-wave-aided CEADUS enables the evaluation of the viscosity of body fluid in vivo. In this report, we describe the results of experimental and numerical evaluations of the relationship between the translational velocity of UCAs and the viscosity of the surrounding liquid to develop a calibration curve for estimating the viscosity coefficient.

2. Method

2.1 Experiments

A flow channel with a 1.5-mm diameter was formed in a gel phantom, including acoustic scatterers. Sonazoid was used as UCAs. UCA's suspension was prepared by adding UCA's lyophilized powder to the glycerin solution. The viscosity of the UCA's suspension was carefully controlled by the concentration of glycerin. The glycerol concentrations were 0, 5, 10, 20, and 30wt%, and the corresponding viscosity at each concentration was 1.0, 1.3, 1.8, 2.5, and 3.7 mPa·s[2)]. The number density and size distribution of UCAs were measured by a hemocytometer. UCA's suspension was pumped into the channel by a syringe pump. Experiments were performed under two conditions: with the pumping stopped (stationary condition) and at a flow rate of 1 mL/min.

A programable ultrasonic research system (Vantage256, Verasonics) and a 128-element linear array probe (L11-5v, Verasonics) with a bandwidth of 4.68-10.52 MHz were used for transmitting and receiving signals. **Figure 1**, which illustrates the transmitting sequence, provides a visual aid to accompany the following description. The burst-wave-aided CEADUS method transmits long-burst plane waves during the interval between plane-wave pulses for imaging with different polarities. The

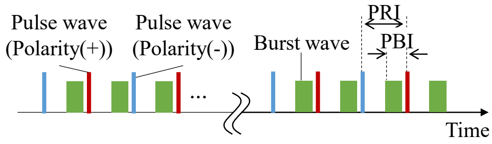

Fig. 1 Sequence of ultrasound transmission.

interval (PRI) between the pulses was 0.44 ms, and the interval (PBI) between the pulse and the burst waves was 0.22 ms. The center frequencies of the pulse and burst wave were 5.2 MHz and 7.5 MHz, respectively. The cycle of the burst wave was 350 (approximately 47 μs). The peak negative pressure of the pulse and burst wave were 0.23 MPa and 0.16 MPa, respectively. The total transmission of the burst wave was 202 times (approximately 89 ms)

The raw RF channel data were processed offline to reconstruct a 256-line image with a scanning interval of 0.15 mm by a delay and sum algorithm. An FIR filter, which only the fundamental component passes through, was applied to the Doppler signal to remove clutter echoes. The translational velocities of UCAs were analyzed by detecting and tracking individual UCAs in the reconstructed consecutive images. The translation of UCAs in the depth direction perpendicular to the sound propagation direction was assumed to be caused by acoustic radiation force. The positions (depth) of UCAs were measured in each frame, and the depth-time curves for individual UCAs were evaluated. The slope of the depth-time curve was measured as the translational velocity of the UCA.

2.2 Numerical simulation

The numerical calculations of the translation of a UCA were performed to verify the experimental results. We calculated the coupled dynamics of a UCA's radial oscillation and translation during the burst wave irradiation with a center frequency of 7.2 MHz, a sound pressure (peak-peak value) of 400 kPa, and 350 cycles. The Marmottant's equation was used to calculate the radial oscillation[3)]. The translation was calculated by solving a governing equation based on Newton's second law, taking into account buoyancy, drag force due to viscosity, inertial force due to the effect of added mass, and acoustic radiation force[4)]. The UCA's travel distance during burst-wave irradiation was calculated and divided by the PRI to obtain the translational velocity.

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4. Results and discussions

Figure 2 shows the relationship between the viscosity coefficient and the translational velocity of UCAs at (a) stationary conditions and (b) flow volume of 1 mL/min. Although there is a large dispersion in the results, the translational velocity decreases nonlinearly with increasing viscosity coefficient. A comparison of the stationary and 1 mL/min flow volume cases shows no difference in the qualitative trends. Therefore, we assumed that the relationship between the velocity and viscosity can be defined by the expression of power law,

$$v_z = A\mu^B, \tag{1}$$

where v_z is the translational velocity and μ is the viscosity of the surrounding liquid. Assuming the power-law dependence, the experimental data was approximated by the least-squares method. The solid and dashed lines in Fig. 2 (a) and (b) show the approximation of all results and that of the mean value at each viscosity condition, respectively. The coefficients A and B ranged from 3.65 to 4.18 and -0.92 to -1.13, respectively.

The numerical calculations were performed to verify the validity of the experimental trend. Since the mean and standard deviation of UCA's radius in the experiments were approximately 1.4 µm and 0.3 µm, the translational velocity of a UCA with a radius from 1.1 to 1.7 µm was calculated. Fig. 2(c) shows the results. We can confirm the similar trend with the experiments at all radius conditions. The coefficients *A* and *B* in Eq. (1) at R_0 = 1.4 µm, close to the mean of the experimental data, were 4.54 and -1.09, not different from the values obtained from experiments. This result confirms the validity of the power law in Eq. (1). It suggests that this equation, with its potential to be used as a calibration curve, can revoltionize the evaluation of viscosity.

Fig. 2(c) indicates that a significant variation in UCA's radius, with the standard deviation of 0.3 µm in the experiments, results in a difference in the translational velocity at the same viscosity. The variation of UCA's radius in the calculation leads to a translational velocity of 2-7 mm/s at, e.g., $\mu = 1$, a trend that agrees with the experiment. This result suggested that the reduction of radius variation may contribute to improved accuracy for viscosity measurement. In addition, it is crucial to note that coefficients *A* and *B* are indices that depend on sound pressure, highlighting the urgent need to address how to compensate for the effect of acoustic attenuation by biological tissues in in-vivo situations.

4. Summary

We examined the relationship between the translational velocity of UCAs and the viscosity of the surrounding liquid. The relation is the power-law dependence.

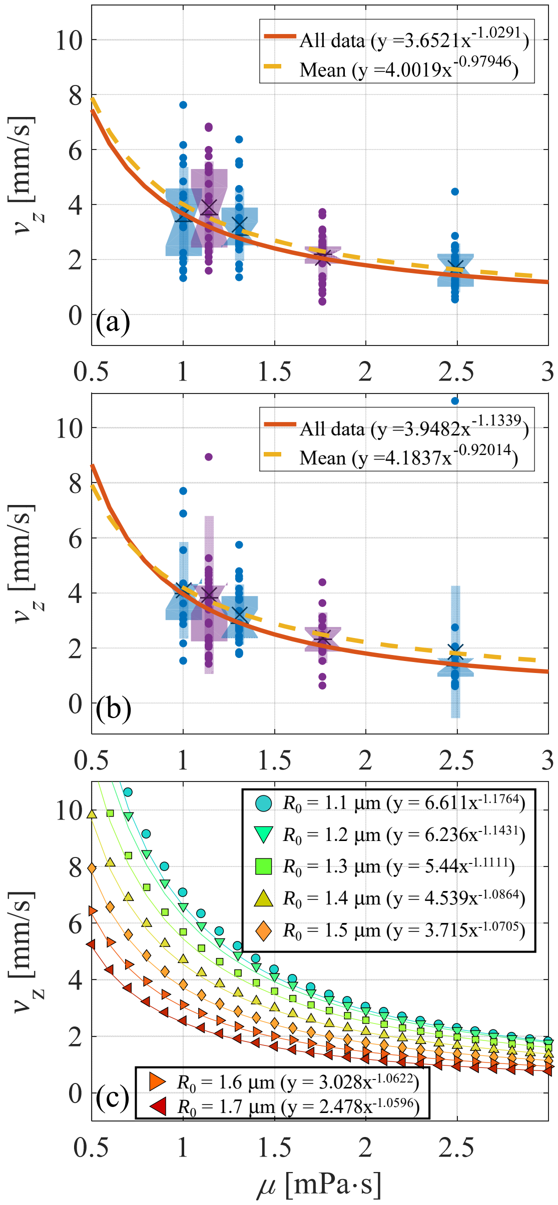

Fig. 2 Translational velocity (v_z) in the depth direction versus viscosity coefficient (μ) in cases of (a) stationary condition, (b) flow volume of 1 mL/min, and (c) numerical calculation. R_0 means the initial radius of UCA

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