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Theoretical verification of ultrasonic peak-frequency shift during red-blood-cell-aggregation-degree measurement

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1. Introduction

Blood viscosity has been considered an index of lifestyle disease. Various factors are involved in blood viscosity, and the red blood cell (RBC)-aggregation diameter has a strong correlation with blood viscosity. Our research group previously investigated the effectiveness of obtaining ultrasonic-peak frequency by transmitting ultrasonic waves into a blood sample for estimating the RBC-aggregation degree[1)]. For this study, we carried out a theoretical verification of the relationship between the average RBC-aggregation diameter and peak frequency on the basis of the losses of acoustic energy.

2. Method

2-1 Attenuation factors of ultrasound transmitted in suspension

Our aim with this study was to carry out a theoretical verification of the relationship between the average RBC-aggregation diameter and peak frequency on the basis of the losses of acoustic energy. Blood can be regarded as a suspension dispersed with RBCs. The main attenuation factors of ultrasound propagated in this suspension are viscosity loss, thermal loss, and scattering loss[2)]. Due to the diameter of the human RBC, i.e., 7 to 8 µm, and the wavelength of the ultrasonic transducer used in this study, i.e., about 75 µm, scattering loss was found to be dominant.

2-2 Experimental conditions of our previous study

The measurement environment of our previous research is illustrated in Fig. 1. We used a 20-MHz transducer with an element diameter of 6.3 mm and non-focus. A suspension prepared by dispersing fine acryl particles in water was used as a blood-mimicking sample and porcine blood as an actual blood sample because of its proximity to the RBC size of human blood and availability. The ultrasonic wave transmitted with the transducer was reflected on a reflection board and attenuated with the acryl particles or RBCs inside the beam form. The peak frequency was obtained by conducting fast Fourier transform (FFT) to the reflected wave received with the transducer.

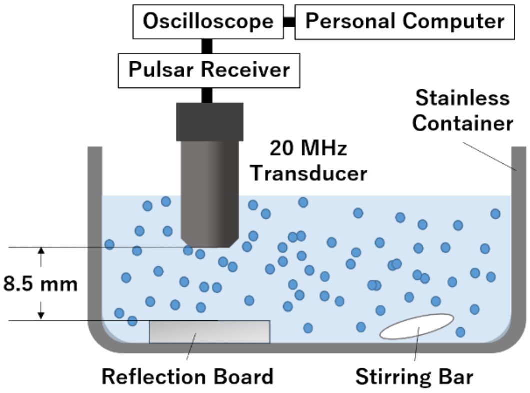

Fig. 1 Experimental setup in our previous study.

2-3 Derivation of attenuation coefficient

In this study, we derived the ultrasonic energy loss by applying sphere approximations to acryl particles and RBCs as the attenuation coefficient using the Epstein-Carhart-Allegra-Hawley (ECAH) theory[3)4)]. The parameters used in these theoretical calculations were the same as those under the experimental conditions in our previous study. The attenuation coefficients were derived as follows.

$$\alpha = -\frac{2}{3}\frac{\epsilon}{k^2 a^3}\sum_{n=0}^{\infty}(2n+1)Re\,A_n, \qquad (1)$$

where A_n denotes the expansion coefficients obtained with a continuity equation and wave equation, k is the wave number, a is the particle diameter, and ϵ is the fractional ratio.

For calculating only expansion coefficients A_0 and A_1, we used the ECAH theory to simply derive viscosity loss, thermal loss, and scattering loss. The scattering loss coefficient α_s viscosity loss coefficient α_v, and thermal loss coefficient α_T were obtained as follows.

$$\alpha_s = \epsilon k\frac{k^3 a^3}{6}\left(\left(\frac{K_p - K_m}{K_m}\right)^2 + \frac{1}{3}\left(\frac{3(\rho_p - \rho_m)}{\rho_p + \rho_m}\right)^2\right) \qquad (2)$$

$$\alpha_v = \epsilon k\frac{18(s-1)^2 b^2 (b+1)}{81(b+1)^2 + b^2[(4s+2)b+9]^2} \qquad (3)$$

$$s = \rho_p/\rho_m \qquad (4)$$

$$b = (\omega/2\nu)^{1/2} \qquad (5)$$

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$$\alpha_T = \frac{3\varepsilon T c_m \rho_m \tau_m T}{2a^2}\left(\frac{\beta_m}{C_p^m \rho_m} - \frac{\beta_p}{C_p^m \rho_p}\right)^2 \ \mathrm{ReH} \qquad (6)$$

$$H^{-1} = \frac{1}{1 - jz_m} - \frac{\tau_m tanhz_p}{\tau_p tanhz_p - z_p} \qquad (7)$$

$$z_{m,p} = a(1+j)\sqrt{\frac{\omega C_p^{m,p} \rho_{m,p}}{2\tau_{m,p}}}, \qquad (8)$$

where ρ is the weight density, c is sound velocity, ν is kinematic viscosity, and β is thermal diffusivity, τ is thermal resistance, and the subscriptions of p and m describe the parameters of the acryl particle and solvent, respectively. The attenuation coefficients were calculated using two different means; thus, the expansion coefficients derived from Eq. (1) were treated as the attenuation coefficients, and the total attenuation coefficient obtained as the sum among the three loss coefficients was derived from Eqs. (2), (3), and (6).

2-4 Calculation of ultrasonic spectra

We used Lambert-Beer's law to calculate the ultrasonic reflection spectra from the attenuation coefficients. The reflection wave is obtained as follows.

$$I = I_0 \exp(-2d\alpha)\,, \qquad (9)$$

where I_0 is the incident wave, α is the attenuation coefficient derived from Eq. (1), and d is the distance between the transducer and reflection board.

$$I = I_0 \ \exp\{-2d(\alpha_s + \alpha_v + \alpha_T)\} \qquad (10)$$

For the experiments, we prepared blood samples dispersed with aggregated RBCs having controlled average diameters of 7, 16, 21, and 26 μm using dextran 70 as a coagulant. The particle concentration of the blood-mimicking suspension was 5%, although the hematocrit value of human blood is around 40%. For the suspensions dispersed with acryl particles, particles with diameters of 6, 15, 32, 46, and 110 μm were selected. To prevent sedimentation, a suitable amount of carboxymethyl cellulose was added to the suspension as a thickener.

3. Results

Figure 2 shows the experimental results with the acryl particle suspensions. Regardless of the theoretical calculation or experiments, the peak frequencies decreased as the particle or aggregation diameter increased. When using the ECAH theory, due to its theoretical limit, valid results could not be obtained with average aggregation diameters of 30 μm or larger. The three approximate straight lines in Fig. 2 are close to each other in a semi-logarithmic graph. Figure 3 shows the comparison among the experimental results and the two results from the theoretical calculation obtained by substituting the blood parameters. A decrease in peak frequencies were observed with the increase in the aggregation diameter, similar to the results of the acryl-particle suspensions. The results from the ECAH theory indicate closer values to the experimental results than those calculated as the total of the three losses.

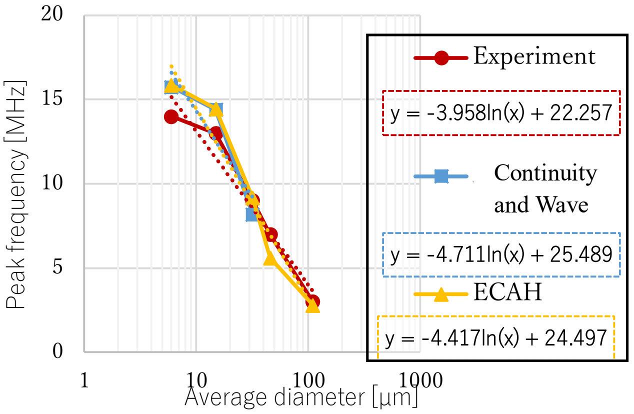

Fig. 2 Changes in peak frequencies with acryl-particle diameters.

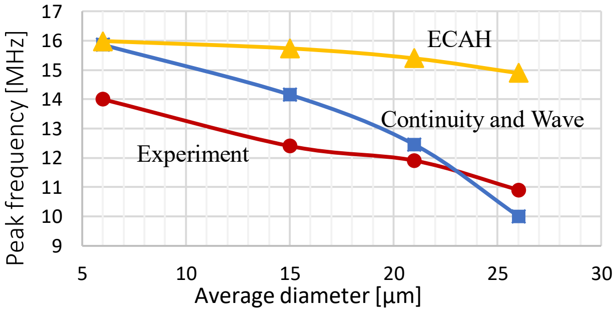

Fig. 3 Changes in peak frequencies with RBC-aggregation diameters.

4. Conclusions

We evaluated the effectiveness of the theoretical calculation of RBC-aggregation-diameter estimation using ultrasound. The next challenge is to investigate the relationship between peak frequency and RBC-aggregation diameter under a high-hematocrit condition.

References

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