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Modeling of power spectrum considering density of red blood cells in focal region to estimate red blood cell aggregation size

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1. Introduction

Red blood cell (RBC) aggregation is known to be a clinically meaningful index for the evaluation of blood properties.[1)] We proposed a method to estimate the RBC aggregate size by measuring the ultrasound backscattering characteristics.

In our previous study[2)], the size of RBC aggregates was estimated by fitting the scattering power spectrum obtained from the vascular lumen with the theoretical reference scattering power spectra for a single-sphere scatterer calculated for each diameter. However, since the power spectrum acquired from the vessel lumen is affected by interference among scattering properties from numerous RBCs, there will be errors in the estimated size.

In the present paper, we investigated a method to calculate the reference scattering power spectrum from numerous RBCs, considering the hematocrit value in the focal region, and compared it to the conventional spectrum from a single scatterer. The accuracy of the spectrum was verified by a phantom experiment using a suspension of microparticles simulating blood.

2. Principle and method

2.1 Calculation of power spectrum considering number density of RBCs in focal region

In a cylindrical coordinate system as shown in **Fig. 1(a)**, letting us assume a cylindrical focal region of the ultrasonic beam with diameter L and height W, the scattering power spectrum $S_{\mathrm{RD}}(f,\mathbf{r})$ from a single-sphere scatterer with diameter D existing at position $\mathbf{r}=(r,z,\theta)$ is given by the product of scattering property $S_D(f)$, spectrum $X(f)$ of the applied signal, transmission and reception properties $G(f)$ of the ultrasonic transducer, sound pressure property $H(f,r,z,\theta)$ of the ultrasound probe, and attenuation property $A(f,z)$. Therefore, the scattering spectrum $S_{\mathrm{RD}}(f,\mathbf{r})$ is given by

$$
\begin{aligned}
S_{\mathrm{RD}}(f,\mathbf{r}) &= S_{\mathrm{RD}}(f,r,z,\theta)\\
&= S_D(f)X(f)G(f)H(f,r,z,\theta)A(f,z). \quad (1)
\end{aligned}
$$

The spectrum acquired from the vessel lumen actually includes scattering properties from numerous RBCs corresponding to the hematocrit value in the focal region. The sum $S_{\mathrm{R}D_{\mathrm{SUM}}}(f)$ of the scattering spectra from the N scatterers at the positions $\{\mathbf{r}_i\}$ $(i=0,\cdots,N-1)$ in the focal region can be expressed as

$$
\begin{aligned}
&S_{\mathrm{R}D_{\mathrm{SUM}}}(f)\\
&=\frac{1}{N}\int \delta(\mathbf{r}-\mathbf{r}_i)S_{\mathrm{R}D}(f,\mathbf{r})d\mathbf{r}\\
&=\frac{1}{N}\int_{\theta=0}^{2\pi}\int_{z=z_f-L/2}^{z_f+L/2}\int_{r=0}^{W/2}\{\delta(r-r_{j_i},z-z_{k_i},\theta-\theta_{l_i})\\
&\qquad\qquad \times S_{\mathrm{R}D}(f,r,z,\theta)\}drdzd\theta, \qquad (2)
\end{aligned}
$$

where $\delta(\mathbf{r}-\mathbf{r}_i)$ is a delta function of the presence or absence of a scatterer at position $\mathbf{r}$.

In this study, the scattering spectrum $S_{\mathrm{R}D}(f,\mathbf{r})$ from a single scatterer was acquired by ultrasonic measurements for an ultrafine wire with a hemispherical tip. The scattering spectrum from a wire with a diameter of 20 µm was measured at nine positions in the focal region, as shown in Fig. 1(a). An ultrasonic diagnostic apparatus (UD-8000; Tomey Corp., Nagoya, Japan) was used with a mechanical linear probe (IP21; Tomey Corp., Nagoya, Japan) operating at the center frequency of 30 MHz. The sampling frequency was 240 MHz. The scattering spectra $\{S_{D_{\mathrm{meas}}}(f,r_j,z_k,0)\}$ were prepared in 20-µm intervals along the z direction by interpolation considering amplitude and phase. The number N of scatterers included in the focal region was calculated, then the scattering spectra from N scatterers randomly distributed in the focal region were summed using Eq. (3), to obtain the reference scattering spectrum $S_{\mathrm{R}D_{\mathrm{SUM}}}(f)$ for a single beam.

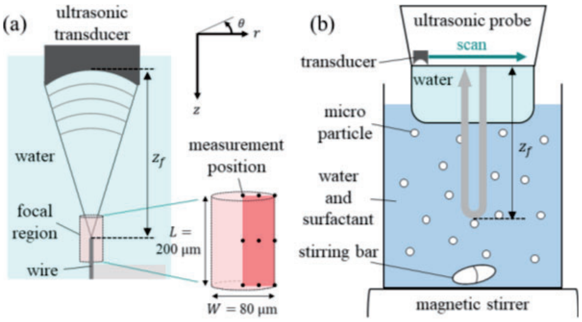

Fig. 1. Schematic diagram of the measurement.
(a) Wire, (b) blood simulating phantom.

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$$S_{\mathrm{R}D\,\mathrm{SUM}}(f) \approx \frac{1}{N}\sum_{j=0}^{\left\lfloor \frac{W}{2D} \right\rfloor}\sum_{k=0}^{\left\lfloor \frac{L}{D} \right\rfloor}\sum_{l=0}^{\left\lfloor \frac{2\pi r_j}{D} \right\rfloor}\{\delta\left(r_j - r_{j_i}, z_k - z_{k_i}, \theta_l - \theta_{l_i}\right) \times S_{D_{\mathrm{meas}}}\left(f, r_j, z_k, 0\right) \times w(z_k)\}, \quad (3)$$

where $\lfloor\cdot\rfloor$ denotes an operation of the floor function and $w(z_k)$ is the Hanning window function with window length L and weighting of depth direction.

2.2 Measurement for blood-simulating phantom

A blood-simulating phantom was prepared by adding a surfactant to a suspension of 20-μm diameter microparticles simulating RBC aggregates and stirring moderately. The volume ratio of the particles was set to 1%. RF signals were acquired from B-mode measurements using the experimental system shown in **Fig. 1(b)**. Power spectra were calculated using windowing the RF signals with the Hanning window at a depth of focus (z_f = 8.55 mm), and 113 power spectra were averaged. The averaged power spectrum was corrected for the propagation attenuation in the microparticle suspension. It was fitted with the two reference scattering power spectra calculated by the previous and proposed methods using the least-squares method.

3. Results

The power spectra $\left|S_{\mathrm{meas}_D}\left(f, r_j, z_k, 0\right)\right|^2$ obtained from the measurement for the wire are shown in **Fig. 2**. It was confirmed that the power differs depending on the measurement position because focused waves were used.

Figure 3 shows the reference scattering power spectrum of a single scatterer and the average and standard deviation of the reference scattering power spectra of 113 beams with a volume ratio of 1% calculated by the proposed method, both corresponding to D = 20 μm. The averaged reference power spectrum calculated by the proposed method has lower power, especially at higher frequencies, and a smaller slope than that for the single scatterer. By considering the scattering from multiple scatterers, the power decrease due to the interference of scattered waves can be simulated.

Figure 4 shows the average and standard deviation of the scattering power spectra obtained from the blood-simulating phantom for 113 beams and the results of fitting with the two reference scattering power spectra. The root means squared errors (RMSEs) of the fitting were 0.59 dB and 1.79 dB for the previous and proposed methods, respectively. This result shows that the reference power spectrum calculated by the proposed method is well-fitted with the measured power spectrum, and the method would estimate the RBC aggregate size more accurately than the previous method.

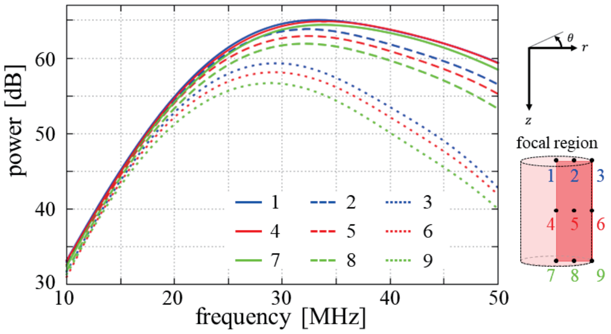

Fig. 2. The power spectra obtained from the wire.

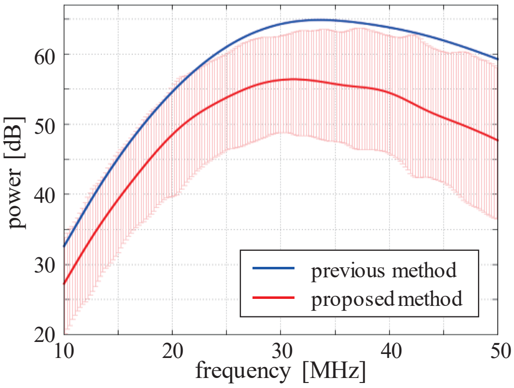

Fig. 3. The power spectra calculated by the previous and proposed methods.

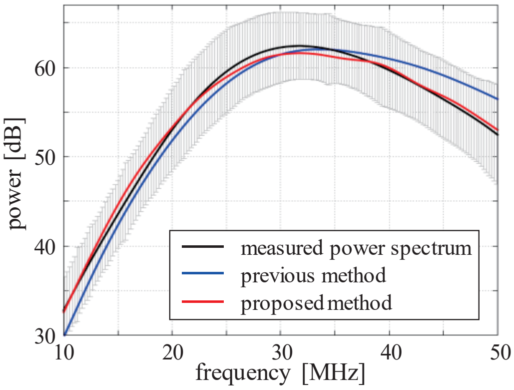

Fig. 4. The fitting results of the measured and reference scattering power spectra.

4. Conclusion

The proposed method could simulate the decrease in power and slope of the power spectrum due to interference of scattered waves from multiple scatterers. Moreover, the spectrum calculated by the proposed method is well-fitted with the spectrum from the blood-simulating phantom, indicating the possibility of accurately estimating the RBC aggregate size. In the future, the proposed method will be applied to *in vivo* measurement to estimate RBC aggregate size.

References

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2) K. Higashiyama, et al., Jpn. J. Appl. Phys. **61**, SG1046 (2022).