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Assessment of Red Blood Cell Aggregation of Diabetics by Analyzing Ultrasonic Scattering Property
超音波散乱特性の解析による糖尿病患者の赤血球凝集度評価

Hiroki Sakaki[1†], Mototaka Arakawa[1, 2], Satoshi Yashiro[3], Yasushi Ishigaki[3] and Hiroshi Kanai[2, 1] ([1]Grad. School of Biomed. Eng., Tohoku Univ.; [2]Grad. School of Eng., Tohoku Univ.; [3]The Department of Internal Medicine, Iwate Medical Univ.)
榊　紘輝 [1†], 荒川元孝 [1, 2], 八代　諭 [3], 石垣　泰 [3], 金井　浩 [2, 1] ([1]東北大院　医工, [2]東北大院　工, [3]岩手医大　内科)

1. Introduction

Red blood cell (RBC) aggregation is a reversible adhesion phenomenon of RBCs, and it is caused by the low shear rate state of blood flow in the presence of high molecular compounds. One-dimensional link of RBCs is known as rouleau formation. When RBCs or other branches of rouleau are attached to the side of the rouleau, three-dimensional clumps are formed. As such excessive RBC aggregation is pathologically related to various cardiovascular diseases such as atherosclerosis and diabetes,[1)] evaluation of blood properties is useful for early detection of such diseases. In our previous study,[2)] the size of an RBC aggregate was estimated by fitting the measured power spectrum of backscatters from the intravascular lumen with the theoretical curve. In the study, the measured power specturm was normalized by that obtained from the posterior wall of the vein. However, variations in the estimated size were large because of the narrow frequency range for the fitting. In the present study, the degree of RBC aggregation was evaluated in the wide frequency range from the changes of the scattering power spectrum of the echos from the intravascular lumen before and after the stop of blood flow.

2. Measurements and Analysis

2.1 Ultrasonic backscattering property

When the scatterer in the target tissue is much smaller than the wavelength of an incident wave, Rayleigh scattering occurs and the backscattering power is proportional to the fourth power of the frequency.[3)] When the scatterer is much larger than the wavelength of an incident wave, reflection occurs and the backscattering power is independent of the frequency. The ultrasonic scattering power spectrum $P_S(f)$ is calculated by Eq. (1) including the scattering property $S(f)$ showing the frequency dependence peculiar to scatterer size.

$$P_s(f) = |S(f)G(f)A(f)X(f)|^2, \qquad (1)$$

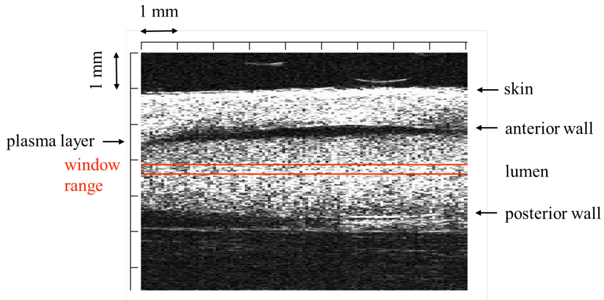

Fig. 1 B-mode image of patient with plasma layer

where $G(f)$ is the frequency response of the transmitting and receiving transducers, $A(f)$ is the attenuation property of the propagation medium, and $X(f)$ is the frequency spectrum caused by the voltage applied to the transducer.

2.2 Relation between shear rate and RBC aggregation

It is reported that RBC aggregation is likely to occur in a low shear rate state.[4)] Therefore, we measured RF signals from the intravascular lumen before and after the stop of blood flow due to avascularization, and extracted the change of scattering property due to a decrease in shear rate.

2.3 Measurement method

The ultrasonic diagnostic equipment (Tomey UD - 8000) with a probe having a center frequency of 40 MHz was used. We applied this method to the dorsal hand vein of multiple diabetics. A plasma layer was observed above the intravascular lumen in the latter half of the avascularization for some patients as shown in **Fig. 1**. Since it is reported that excessive RBC aggregation is affected in the formation of the plasma layer,[5)] only subjects with formation of plasma layer were analyzed.

2.4 Calculation of spectral area

We integrated ultrasound scattering power spectrum in the frequency range from 0 to 60 MHz to calculate the spectral area at rest (before the stop of blood flow) and during avascularization (after the stop of blood flow). An example of measurement of scattering power spectra at rest and avascularization is shown in **Fig. 2**. The frequnecy range from 0 to 60 MHz is appropriate for

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calculation of the change of scattering property because of enough scattering power.

2.5 Selection of analysis frame

We acquired RF signals to form one-frame B-mode image at intervals of 10 seconds, 7 frames were acquired at rest and 6 frames were acquired during avascularization after a lapse of 1 minute from the beginning of the avascularization. The analysis window used for spectrum calculation was set near the focal point of the probe as shown in red lines in Fig. 1. Average RF amplitude intensity was calcualted within the analysis window, and it was compared with those calculated within upper and lower parts with same area of the analysis window. In order to obtain the accurate intensity changes, only frames whose average RF amplitude intensity within the analysis window has a magnitude of 90% or more with respect to the maximum value among the three calculated intensities were selected. The scattering power spectra at rest and avascularization were calculated by averaging the scattering power spectra of each of selected frames.

3. Results

The ratios ρ of spectral area were calculated by

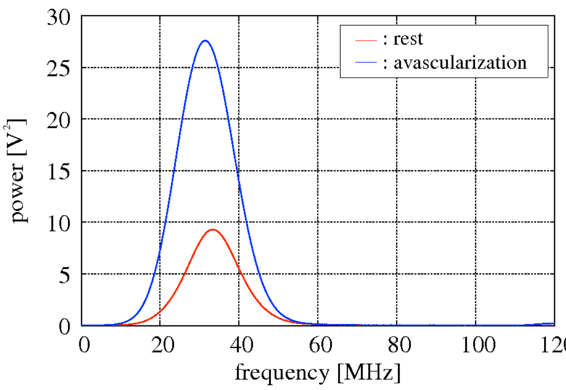

Fig. 2 Scattering power spectra at rest and avascularization.

dividing the spectral area at avascularization by that at rest. The results were compared with the blood glucose, glycated albumin (GA) and hemoglobin A1c (HbA1c) for each subject. GA and HbA1c show the parameters indicating blood glucose indexes in the past 1 and 2 months. **Figures 3 and 4** show the correlation between the blood glucose and the ratio ρ of spectral area without and with frame selection, respectively. The coefficient of determination of the approximate straight line R^2 is defined by

$$R^2 \equiv 1 - \frac{\sum_i (y_i - f(x_i))^2}{\sum_i (y_i - \bar{y})^2}, \tag{2}$$

where y_i is measured data and $f(x_i)$ is a regression model, and $\bar{y}$ is averaged value of y_i. In Figs. 3 and 4, the ratios ρ of spectral area became higher for patients with higher blood glucose, and the frame selection data had a higher coefficient of determination. There was no correlation between GA and the ratio of spectral area ρ, or between HbA1c and ρ ($R^2 < 0.1$). Since GA and HbA1c are long-term blood glucose indicators, it might be caused by the improvement of the subject's symptoms at the time of the ultrasonic measurement.

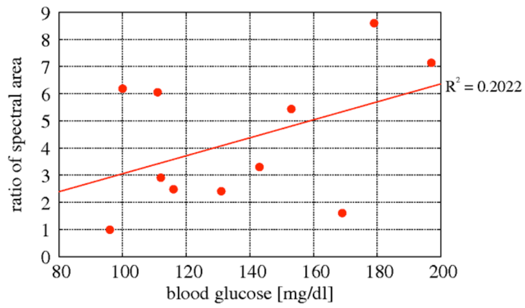

Fig. 3 Correlation between blood glucose and ratio ρ of spectral area without frame selection

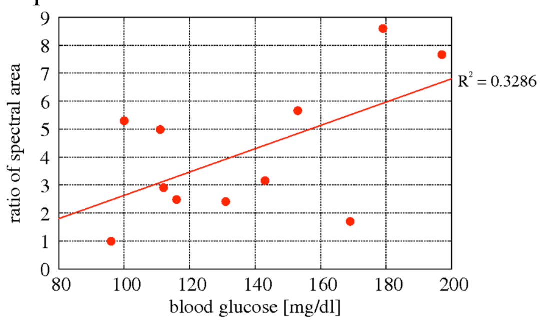

Fig. 4 Correlation between blood glucose and ratio ρ of spectral area with frame selection.

4. Conclusion

The degree of RBC aggregation was evaluated from the ratio ρ of spectral area at rest and avascularization. It was shown that the ratio ρ of spectral area became higher as the blood glucose level became higher. From these results, it is suggested that the ratio ρ of spectral area could be useful as a parameter of the evaluation of RBC aggregation degree in diabetics.

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E-mail address: saka5hiro5@ecei.tohoku.ac.jp
(arakawa, kanai)@ecei.tohoku.ac.jp