

Evaluation of Red Blood Cell Aggregation by Frequency Analysis of 40-MHz Ultrasonic Wave Scattered from Lumen of Vein

静脈内腔からの 40 MHz 超音波散乱波の周波数解析による赤血球凝集度評価

Taku Fukushima^{1†}, Hideyuki Hasegawa^{2,1} and Hiroshi Kanai^{1,2} (¹ Graduate School of Eng., Tohoku Univ.; ² Graduate School of Biomedical Eng., Tohoku Univ.)
福島 拓^{1†}, 長谷川英之^{2,1}, 金井 浩^{1,2} (¹東北大院 工;²東北大院 医工)

1. Introduction

Estimation of red blood cell (RBC) aggregation, which plays an important role in blood rheology and the condition of blood, is one of the useful indices in blood characterization [1]. Conventional ultrasonic images cannot evaluate the condition of blood because RBCs, which are the main components of blood, are much smaller than the wavelength of the ultrasound and the difference in acoustic impedance between blood plasma and RBCs is very small [2]. The purpose of the present study is to establish a noninvasive and quantitative method for evaluation of RBC aggregation.

2. Methods

2.1. Scattering property

To evaluate the level of RBC aggregation, the RF echoes are analyzed in the frequency domain. The power spectrum of ultrasonic RF echo from nonaggregating RBCs, which shows frequency characteristic of scattering, obeys Rayleigh behavior [2, 3]. It means that the power spectrum of the scattered wave is proportional to the fourth power of frequency. On the other hand, ultrasonic RF echo from aggregating RBCs mainly contains the components of reflection, which have no frequency dependence.

In the present study, a scatterer was modeled by placing the infinite number of infinitesimal point sources on the surface of the scatterer. The theoretical power spectrum $Q(ka)/a^2$ of the scattered echo is given by [4]

$$Q(ka)/a^2 = 4\pi \sum_{n=0}^{\infty} \frac{(2n+1)}{(ka)^2} \sin^2[\delta'_n(ka)], \quad (1)$$

where k is the wave number, a is the radius of scatterer, n is the number of point sources on the surface of scatterer and $\delta'_n(ka)$ is the differential of phase difference between incident wave and scattered wave.

2.2. Weighted least-square method

By dividing the power spectrum of the scattered echo by that of reflected echo measured under the similar propagation medium, the transducer's frequency response and attenuation property contained in the power spectrum of scattered wave were removed.

In this report, because of using pulsed ultrasound which has finite frequency band, the available frequency band is limited. By referring to the signal-to-noise ratio (S/N) of scattered RF signal at each discrete frequency, the slope of the normalized power spectrum, which shows scattering properties, was determined using the weighted least-square method as follows [5]:

$$\alpha = \sum_{k=0}^N w_k^2 \{ \log y(x_k) - (ax_k + b) \}^2, \quad (2)$$

where $y(x_k)$ is measured normalized power spectrum, x_k is logarithmic frequency $\log_{10}(f_k)$, and w_k is weighting function. The weighting function is given by the magnitude-squared coherence function (MSCF) $|\gamma(k)|^2$ as follows [5]:

$$w_k = |\gamma(k)|^2 = \frac{|E_i[Y_i^*(k)Y_{i+1}(k)]|^2}{E_i[|Y_i(k)|^2] \cdot E_i[|Y_{i+1}(k)|^2]}, \quad (3)$$

where $Y_i(k)$ is the frequency spectrum at each beam i , $E_i[\cdot]$ and $*$ are the averaging with respect to 1000 beams and complex conjugate, respectively. Evaluating correlation of received RF signals using MSCF, S/N was assessed and the slope was estimated using spectra with high S/N.

Figure 1(a) shows average power spectrum

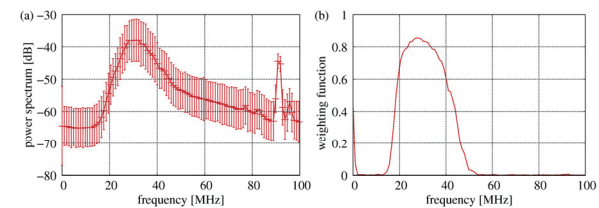


Fig. 1 (a) Power spectrum of echoes from the lumen of the vein. (b) Weighting function obtained from MSCF in *in vivo* experiment.

E-mail: fukushim@us.ecei.tohoku.ac.jp

and the standard deviation of individual power spectra of RF echoes from the lumen of the vein in dorsum manus of a 23-year-old healthy male. **Figure 1(b)** shows the weighting function obtained from MSCF among received RF echoes from the lumen.

3. Basic experiment using microspheres

An ultrasound diagnostic system (UD-1000, Tomey, Japan) was equipped with a mechanical scan probe at a center frequency of 40 MHz (wavelength λ is about 40 μm). Ultrasound RF echoes were acquired at a sampling frequency of 1 GHz and 1000 power spectra were averaged to reduce the influence of random noise.

4 microspheres which have deferent radii simulated RBC and RBC aggregation are measured. **Figure 2(a)** shows the weighting function obtained from the MSCF among received RF echoes from each microsphere. **Figure 2(b)** shows the normalized power spectra of each microsphere. Slope was estimated for each of 7 narrow frequency ranges indicated by the yellow markers. **Figure 3** shows distribution of the slopes and the theoretical slopes obtained by Eq. (1).

As shown in Fig. 3, by comparing the distribution of estimated slopes with the theoretical slopes, scatterer's sizes of 4 microspheres were estimated to be close to respective particle diameters.

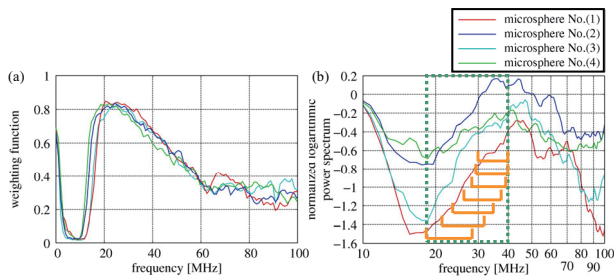


Fig. 2 (a) Weighting function determined from the received RF signals for each microsphere. (b) Normalized power spectrum for each microsphere and 7 narrow frequency ranges.

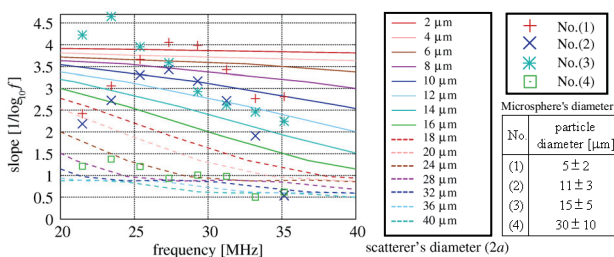


Fig. 3 Distribution of the slopes estimated in each narrow bandwidth for four kinds of microspheres and the theoretical slopes for various scatterer's diameters.

4. In vivo experiment

In *in vivo* measurements, normal blood does not aggregate in large blood vessels because of high blood flow velocity. To measure ultrasonic echoes from aggregated RBCs, blood flow was stopped by pressurizing a cuff surrounding the upper arm at 250 mmHg. Ultrasonic echoes were acquired at rest for 2 min, during avascularization for 5 min, and after recirculation for 3 min.

Slope was estimated in the same procedure as in the basic experiment. **Figure 4** shows distribution of the slopes and the theoretical slopes obtained by Eq. (1).

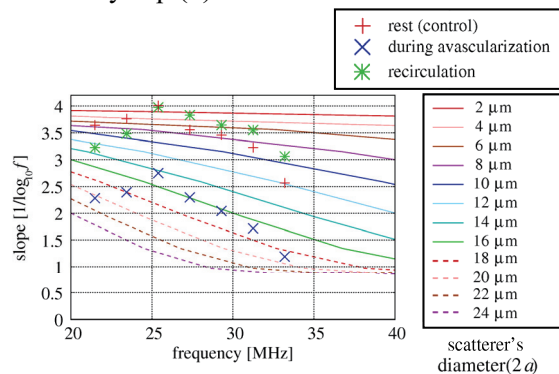


Fig. 4 Distribution of the slopes estimated in each narrow bandwidth at *in vivo* measurement and the theoretical slopes.

5. Conclusion

In *in vivo* experiment, scatterer's sizes at rest and after recirculation were estimated to be about 2~12 μm , which correspond to the size of a single RBC. On the other hand, scatterer's size estimated during avascularization was 14~20 μm , which correspond to aggregated RBCs.

These results showed the possibility of proposed method for the noninvasive assessment of RBC aggregation in vein.

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References

1. C. C. Huang, et al.: Jpn. J. Appl. Phys. **45**(9A) (2006) 7191.
2. N. Saitoh, et al.: Jpn. J. Appl. Phys. **48**(7) (2009) 07GJ08-1.
3. M. F. Insana, et al.: Ultrason. Imaging **12** (1990) 245.
4. P. M. Morse, et al.: *Methods of Theoretical Physics* (McGraw-Hill., New York, 1953).
5. H. Kanai: *Spectrum Analysis of Sound and Vibration* (Corona Publishing Co., Ltd., Tokyo, Japan, 1999) (in Japanese).