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Stabilization of red blood cell aggregation evaluation using short-axis view of vein of ultrasound

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Red blood cell (RBC) aggregation is the reversible adhesion of RBCs among themselves. We previously reported a positive correlation between blood glucose level and the degree of RBC aggregation (the brightness of the B-mode image). In the present study, we investigated the contribution to the brightness according to the deviation from the central axis in measurements along with the long-axis view of the vein. The results show that the brightness changed significantly for a slight change in the lateral position in the short-axis image. We found that the stability of the measurements was not guaranteed in the long-axis view and estimated the correct analysis window range for the short-axis view.

Red blood cells (RBCs) adhere reversibly to each other in blood vessels with a low shear rate or stasis. The phenomenon is called RBC aggregation, and its progression can be confirmed by an increase in the brightness of the B-mode image,[1)] which is a warning for thrombus formation in the heart chambers.[2–4)] The degree of RBC aggregation depends on various factors that determine blood properties, such as blood viscosity and hematocrit.[5–7)] There are many studies using techniques such as in vitro experimentation[8–15)] and non-invasive methods for evaluating blood properties.[16–22)] However, it is difficult to quantify, and the blood components have not been evaluated using ultrasound so far. The realization of non-invasive and quantitative evaluation of blood properties will be useful for monitoring blood properties in patients in cases where blood sampling is difficult[23)] and for checking blood glucose levels for daily treatment in diabetics.[24,25)] Our previous studies have shown a positive correlation between the degree of RBC aggregation (the brightness of the B-mode image) and the blood glucose level,[26)] but the precision of blood glucose level determination using ultrasound was low. One of the causes was considered to be the lack of ability to fix position in the elevation direction of the measurement target during the long-axis measurement.

We performed measurements along with the short-axis view instead of the long-axis view of the vein.[27)] The brightness distribution in the lateral direction of the short-axis image and the stability of the repeated measurements were evaluated. In the present study, the brightness distribution in the beam direction of the short-axis image of the vein was also evaluated and an analysis method that can perform a stable evaluation of the degree of RBC aggregation was established.

The brightness of the intravascular B-mode image was used as a parameter for evaluating the degree of RBC aggregation. Considering the large propagation attenuation of ultrasound in the living body and ease of avascularization, the dorsal vein of a person's hand was selected as the measurement target. Measurements were performed under the conditions of natural blood flow and avascularization in which RBC aggregation was likely to occur. Under the natural flow condition, the natural state of blood can be observed. However, the obtained values greatly fluctuate even with the data measured at 1 s intervals due to the blood flow. On the other hand, under avascularization, it is possible to measure the brightness value of the vessel lumen in a more stable state with no blood flow (0 mm s^{-1}) although it is not possible to observe blood in its natural state.

An ultrasound diagnostic apparatus (UD-8000; Tomey Corp., Nagoya, Japan) was used with a mechanical linear ultrasound probe (IP210; Tomey Corp., Nagoya, Japan) operating at the center frequency of 40 MHz and having a focal length of 9 mm.

To investigate the lateral brightness distribution in the vessel lumen at rest, data for one frame was acquired. To investigate the brightness distribution in the direction of the ultrasound beam, data were acquired by changing the focal position of the probe from the near wall to the far wall of the vein at intervals of 0.1 mm. The brightness distributions in the vein were investigated under the conditions of rest and avascularization. At rest, RF echoes were obtained with a cuff wrapped around the forearm without tightening and applying pressure (0 mmHg). After that, RF echoes were obtained 50 s after the start of avascularization, with a cuff pressure of 120 mmHg on the forearm, to obtain the data during avascularization. The subject was relaxed and fixed in an untightened mold that fitted the entire arm. The reproducibility of the data was also examined by taking measurements in the short-axis view using the following protocol. Ultrasound data for a frame were acquired 11 times at 3 s intervals. For each frame, the acquired RF signals were enveloped and averaged within the area near the center of the vessel.

Figure 1(A) shows the B-mode images of the dorsal vein, and Fig. 1(B) shows the average brightness along the depth direction in the area indicated by the red and green frames in Fig. 1(A). The brightness was 20 dB around the center in the area indicated by the red frame and it became darker when the brightness reduced to 8 dB near the vessel wall. The intima-media complex (IMC) is visible only when the ultrasound beam is incident normal to the vessel wall. From the brightness distribution in the lateral position, it can be seen that a brightness gradient exists even in the range where the IMC can be identified (the region between the two yellow lines).

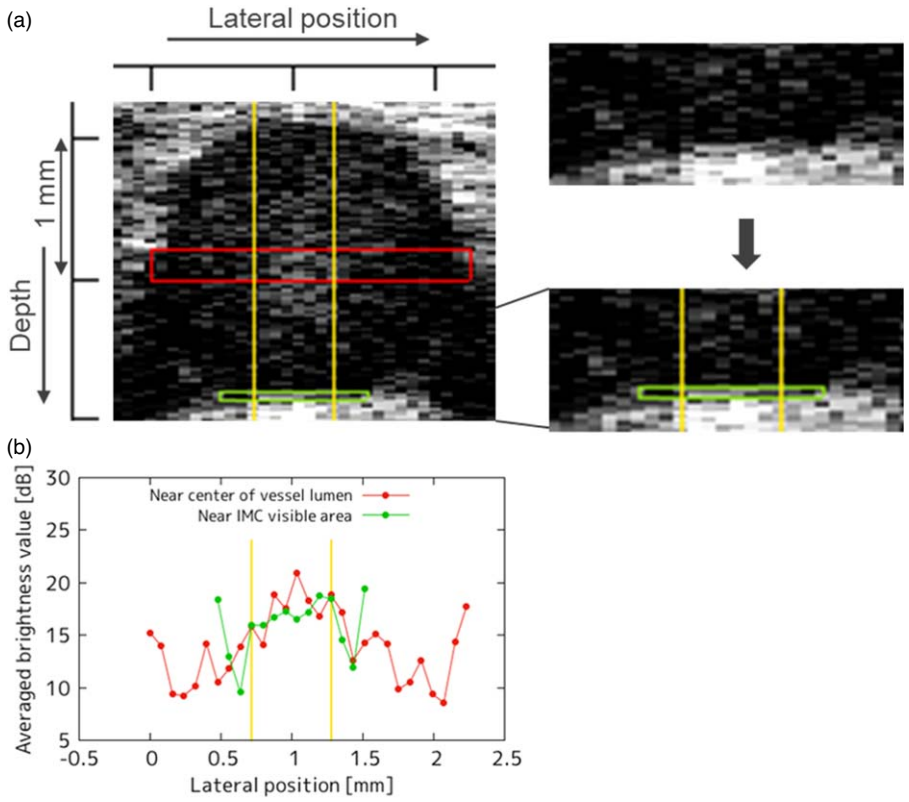

Fig. 1. (Color online) Brightness distribution in the lateral position in the dorsal vein at rest. (A) B-mode image; (B) brightness values for the lateral position.

Figures 2(A) and 2(B) show the results at rest. Similarly, Figs. 2(C) and 2(D) show those during avascularization. Figures 2(A) and 2(C) show the brightness distributions in the direction of the beam in the vein and Figs. 2(B) and 2(D) show the B-mode images at the time of data acquisition for each depth, and the red dashed line is the focal point and the yellow frame is the analysis window. The left sides of Figs. 2(B) and 2(D) correspond to the upper side (probe side). Figures 2(A) and 2(C) show the brightness values, averaged in the analysis windows (0.8 mm × 0.06 mm) shown in Figs. 2(B) and 2(D), respectively, for the data acquired at each position from the near wall to the far wall. The variation

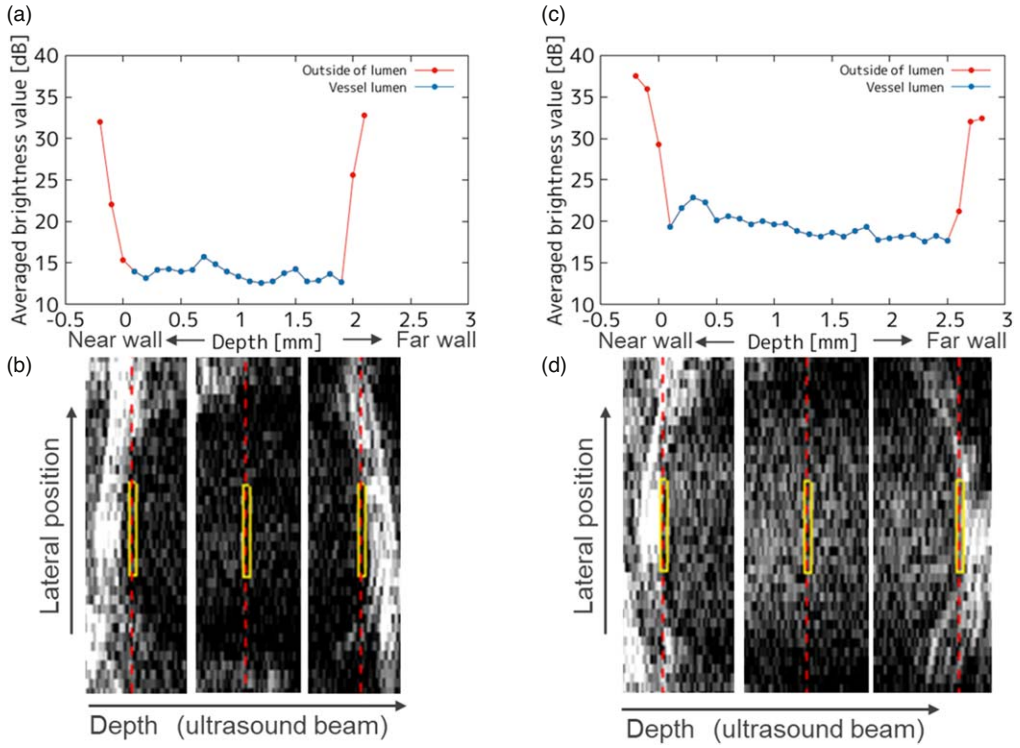

Fig. 2. (Color online) Brightness distribution in the direction of the beam in the vein. (A), (B) at rest. (C), (D) at avascularization; (In (B) and (D), red dashed line: focal points, yellow frame: analysis window).

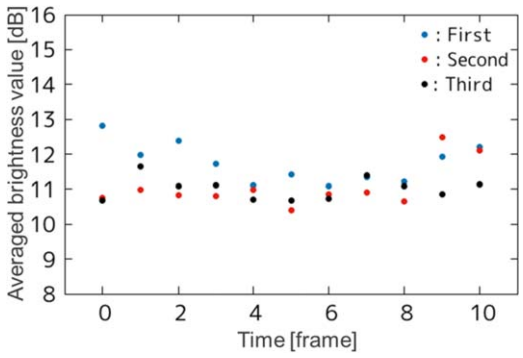

Fig. 3. (Color online) Average brightness value for each frame.

in the averaged brightness values in the vein (at a depth of 0.1–1.9 mm) at rest was 3.2 dB, and that in the vein (at a depth of 0.1–2.5 mm) during avascularization was 5.3 dB. There was no sudden brightness change due to the change in depth in the vein, both at rest and during avascularization. However, a slightly higher brightness was observed at a depth of 0.7 mm than at other depths at rest.

Figure 3 shows the average brightness around the center of the blood vessel for each frame. For each of the three measurements, the variation was within 2 dB. Moreover, for all the measurements, the variation was within 2.5 dB.

In our previous experiments,[26] scattering signals were measured along with the long-axis view, and the data in the IMC visible range were used to evaluate the degree of RBC aggregation. Figure 1(B) suggests that the result greatly changes due to a slight change in the position of the vein even if the data from the IMC visible slice is acquired. Therefore, there were large fluctuations in the brightness value measured in the long-axis view.

From the results of the brightness distribution in the beam direction (Fig. 2), it can be observed that the brightness decreased linearly with depth, and the change in brightness increased during avascularization. This is because the attenuation of ultrasound increased as RBC aggregation was enhanced.[28]

Considering the shear rate (velocity gradient) distribution in the radial direction of the blood vessel at rest, the brightness distribution was expected to be higher in the center of the vessel and lower near the vessel wall in both the lateral and beam directions,[29,30] but such a result was not obtained in the beam direction. It is considered that the brightness distribution due to the shear rate gradient could not be detected as it was smaller than the temporal brightness fluctuation due to the blood flow in the vein. Moreover, in the blood vessel and below the blood vessel, as shown in Fig. 1(A), both the sides have lower brightness than that at the center. Therefore, the brightness distribution would be affected by the shape of the blood vessel. The effects of refraction and interference, due to the phase shift in the focused ultrasonic waves, caused by different sound velocities of blood and tissues increased at both ends of the blood vessel.

The brightness was higher at the depth of 0.7 mm ($p = 0.03$) at rest. This may be because the increased RBC aggregation occurred due to: (1) stagnation of the blood flow due to some physiological causes, such as straining or breathing, and (2) the passage of blood, including accidentally increased RBC aggregation, due to changes in blood flow accompanied by the opening and closing of venous valves.

The fluctuation range of the brightness in the beam direction was almost the same as that for repeated measurements at the same position except for the effect of the attenuation. Therefore, when the degree of RBC aggregation is evaluated from the brightness, it is considered that there is no problem if the analysis window is set at the focal position, even if the center of the blood vessel deviates from the focal point by approximately 0.2 mm.

The brightness distribution in the lateral direction was high near the center of the blood vessel and the gradient was steep, whereas, the gradient in the beam direction was gradual. It is necessary to examine whether this is due to the influence of the shape of the blood vessels. Therefore, it is necessary to strictly set the analysis window range in units of several beams (with a beam interval of 0.08 mm) in the lateral direction. As shown in Fig. 3, the data with small fluctuations were obtained from the temporal measurements in the short-axis view. A slight variation in the blood flow might be the main cause of these small fluctuations. The permissible fluctuation range will be determined in subsequent work by considering the fluctuation range of RBC aggregation due to the changes in blood glucose level.

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