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Estimation of viscoelasticity of radial artery during flow-mediated dilatation using a single ultrasound probe based on blood pressure measurement via pulse transit time method

Yuto Shoji[1], Shohei Mori[2], Mototaka Arakawa[1,2*], Shigeo Ohba[2], Kazuto Kobayashi[3], and Hiroshi Kanai[1,2]

[1]*Graduated School of Biomedical Engineering, Tohoku University, Sendai 980-8579, Japan*
[2]*Graduated School of Engineering, Tohoku University, Sendai 987-8579, Japan*
[3]*Honda Electronics Co. Ltd., Toyohashi 441-3193, Japan*

[*]E-mail: arakawa@ecei.tohoku.ac.jp

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We developed a single ultrasound probe to simultaneously measure blood pressure and changes in the diameter of the radial artery to estimate the wall viscoelasticity during flow-mediated dilatation (FMD). This probe can be used for the early diagnosis of arteriosclerosis. This paper introduces the pulse transit time method to accurately measure changes in blood pressure during FMD. Using the single ultrasound probe and the proposed method, in vivo experiments involving three subjects were conducted, and reasonable results on blood pressure were obtained. Thus, the usefulness of the pulse transit time method was experimentally confirmed. © 2021 The Japan Society of Applied Physics

Vascular endothelial dysfunction occurs during the early stages of arteriosclerosis. As the dysfunction can be treated through medication and relevant lifestyle modification,[1)] an evaluation of the vascular endothelial function is important for the early diagnosis and treatment of arteriosclerosis. To assess the vascular endothelial function, several methods have been clinically employed including invasive plethysmography[2,3)] and non-invasive plethysmography,[4)] which use ischemic reactive hyperemia and flow-mediated dilatation (FMD) test.[5–7)] Among them, the FMD test is widely used clinically because it is simple and non-invasive.[8,9)] However, it does not directly evaluate the mechanical properties of the vessels, as it only measures the rate of vasodilatation as an indicator. During FMD, the shear stress in a vessel increases owing to the rapid increase in blood flow after avascularization, and nitride oxide (NO) is secreted by the vascular endothelial cells. NO acts on the smooth muscle in tunica media causing the vessel wall to relax and vessel diameter to dilate.[10,11)] In other words, vascular dilation is caused by changes in the mechanical properties of the vessel wall. Therefore, elasticity measurement during FMD is a direct evaluation of the vascular endothelial function.

We developed a single ultrasound probe that simultaneously measures vessel diameter and blood pressure waveforms at the same position to precisely determine the viscoelastic properties of the vessel wall.[12)] The developed probe detects blood pressure waveforms by separating a central element from the conventional ultrasound probe and using it as a piezoelectric sensor. Because the pressure waveform is measured as a voltage value, it is necessary to calibrate it to the blood pressure. Moreover, determining the change in viscoelasticity during FMD requires measuring the blood pressure over time. However, it is difficult to measure blood pressure using a cuff for calibration during FMD. We have confirmed that viscoelastic properties are measured with high accuracy by calibrating the blood pressure waveform at rest.[13)] However, accurate blood pressure measurement is difficult in this procedure because the acquired voltage is affected by the change in the pushing pressure of the ultrasonic probe to the blood vessel caused by the unintended body movement during the FMD measurement.[14)]

In this study, fluctuations in viscoelastic properties during FMD were experimentally corrected by introducing the pulse transit time (PTT) method to determine the systolic and diastolic blood pressures, regardless of the absolute value of the voltage acquired by the probe.[15)] Because the PTT method estimates the blood pressure values using only PTT, it is possible to calibrate the blood pressure waveform during FMD without using a cuff.

Because the blood pressure waveform measured by the developed ultrasound probe is output as voltage, the waveform should be calibrated at each heartbeat, as previously mentioned. The blood pressure value after calibration $\widehat{p(t)}$ is given by

$$\widehat{p(t)} = \frac{p_{\mathrm{sys}} - p_{\mathrm{dias}}}{p_{\mathrm{max}} - p_{\mathrm{min}}}\{p(t) - p_{\mathrm{min}}\} + p_{\mathrm{dias}}, \tag{1}$$

where p_{max} and p_{min} are the maximum and minimum values of $p(t)$, respectively, and p_{sys} and p_{dias} are the systolic and diastolic blood pressures, respectively. p_{max}, p_{min}, and $p(t)$ were obtained as voltage values.

In conventional methods,[13,14)] systolic and diastolic blood pressures measured using a sphygmomanometer at rest were used as p_{sys} and p_{dias} in Eq. (1), respectively, whereas in this study, those determined by the PTT method were used to accurately reflect the changes in blood pressure during FMD. Blood pressure measurement using PTT is a reliable method currently being studied for cuff-less blood pressure measurements.[16–18)] The method can determine the blood pressure using only the transit time of the blood pressure pulse wave, as described below.

Using the Moens–Korteweg equation,[19)] the pulse wave velocity PWV is described by the elastic modulus E of the artery as

$$PWV = \frac{d}{T_{\mathrm{PT}}} = \sqrt{\frac{Eh}{2\rho r}}, \tag{2}$$

where T_{PT} is the transit time of the blood pressure between distance d from the heart to the artery, h is the thickness of the vessel wall, ρ is the density of the blood, and r is the radius of the vessel. An exponential relationship between the vascular modulus E and mean blood pressure is given by[20)]

$$E = E_0 e^{\alpha P}, \tag{3}$$

where E_0 is an intercept, α is a constant specific to each measurement object, which can be approximated by a constant for the parent population, and P is the mean blood pressure within a heartbeat.[20] From Eqs. (2) and (3), the mean blood pressure $P(T)$ of an arbitrary heartbeat T is given by

$$P(T) = \frac{1}{\alpha} \ln \frac{2\rho r d^2}{E_0 h} - \frac{2}{\alpha} \ln T_{\mathrm{PT}}. \tag{4}$$

The changes in PTT significantly affect changes in blood pressure when compared to those in other coefficients from Eq. (4). Here, by assuming that E_0, h, ρ, r, and d remain unchanged during the period from the reference heartbeat T_0 to the heartbeat T, the mean blood pressure $P(T_0)$ in Eq. (4) holds for T_0, and the change in the mean blood pressure ΔP is given by the ratio of T_{PT} to $T_{\mathrm{PT_0}}$ as

$$\Delta P = P(T) - P(T_0) = \frac{2}{\alpha} \ln \frac{T_{\mathrm{PT_0}}}{T_{\mathrm{PT}}}, \tag{5}$$

which shows that the change in ΔP depends only on the pulse transit time of the blood pressure.

The elasticity E_θ of the wall circumference direction can be defined as

$$E_\theta = \frac{p_{\mathrm{sys}} - p_{\mathrm{dias}}}{2\pi(r_{\mathrm{sys}} - r_{\mathrm{dias}})/2\pi r_{\mathrm{dias}}}, \tag{6}$$

where r_{sys} and r_{dias} are the radii during systole and diastole, respectively. Equation (6) holds for heartbeats T and T_0. By substituting E of Eq. (2) with E_θ of Eq. (6), we obtain

$$T_{\mathrm{PT}}^2(p_{\mathrm{sys}} - p_{\mathrm{dias}}) = T_{\mathrm{PT_0}}^2(p_{\mathrm{sys_0}} - p_{\mathrm{dias_0}}), \tag{7}$$

where $p_{\mathrm{sys_0}}$ and $p_{\mathrm{dias_0}}$ are the systolic and diastolic pressures, respectively, for the reference heartbeat T_0. From Eq. (7), p_{sys} is determined as

$$p_{\mathrm{sys}} = p_{\mathrm{dias}} + (p_{\mathrm{sys_0}} - p_{\mathrm{dias_0}}) \frac{T_{\mathrm{PT_0}}^2}{T_{\mathrm{PT}}^2}. \tag{8}$$

By substituting the relation $P(t) = (p_{\mathrm{sys}} + 2p_{\mathrm{dias}})/3$ and p_{sys} of Eq. (8) in Eq. (5), p_{dias} is determined as

$$p_{\mathrm{dias}} = \frac{p_{\mathrm{sys_0}}}{3} + \frac{2p_{\mathrm{dias_0}}}{3} + \frac{2}{\alpha} \ln\left(\frac{T_{\mathrm{PT_0}}}{T_{\mathrm{PT}}}\right) - \frac{p_{\mathrm{sys_0}} - p_{\mathrm{dias_0}}}{3} \frac{T_{\mathrm{PT_0}}^2}{T_{\mathrm{PT}}^2}. \tag{9}$$

In this study, the pulse transit time T_{PT} was obtained as the time difference from the R wave of the electrocardiogram to the peak of the blood pressure waveform in the same cardiac cycle. Thus, systolic blood pressure p_{sys} and diastolic blood pressure p_{dias} can be determined without relying on the output voltage obtained from the ultrasound probe because they are determined using only T_{PT}, systolic blood pressure $p_{\mathrm{sys_0}}$, and diastolic blood pressure $p_{\mathrm{dias_0}}$ at the reference heartbeat T_0.

The change in the vascular diameter $2r(t)$ was measured using the phased-tracking method,[21] and the relationship between the blood pressure $p(t)$ and vascular diameter $2r(t)$ was fitted to the Voigt model to estimate the viscoelasticity of the vessel wall.

We measured the blood pressure $p(t)$ and vessel diameter $2r(t)$ for three healthy men in their 20 s during FMD in the radial artery, and estimated changes in the elasticity $E(t)$ and viscosity $\eta(t)$ of the radial arterial wall. The experimental system and protocol were the same as those described in Ref. 14. Informed consent was obtained from all subjects, and the study was approved by our institutional ethics committee for human research.

Figures 1–3 show the measurement results of PTT, systolic (solid line) and diastolic (dashed line) blood pressures, and estimates of the elastic modulus $E(t)$ (solid line) and viscosity $\eta(t)$ (dashed line), respectively. Further, the results for subjects A–C are shown with red, blue, and green lines, respectively, and figures (a) and (b) show the results obtained at rest and after recirculation, respectively.

Figure 1 shows that the PTT immediately increased after recirculation in all subjects and gradually approached the resting values, which correspond to the decrease in elasticity after recirculation in the FMD. This result reflects the decrease in the elasticity due to the FMD because the pulse transit time T_{PT} increases as the elasticity E decreases, as given by Eq. (2).

Figure 2 shows that p_{sys} and p_{dias} decreased after recirculation and gradually increased to near-resting values for all subjects. The results are reasonable because the blood pressure, which decreased immediately after recirculation, was lower than that at rest because of vasodilatation owing to FMD. This trend was not observed through the conventional method,[14] thus indicating the effectiveness of the proposed method.

In Fig. 3, although the magnitude of elasticities differed from the three subjects, they at rest were of the same order of magnitude. However, the elasticity, which changed after recirculation, showed a different trend among the subjects, although the trends of the blood pressure change were similar. This might be because the vessel was deformed such that the upper part of the vessel was flattened for the measurement of the blood pressure waveform using the ultrasound probe. If the shape of the artery changed during the measurement, the estimated viscoelasticity was affected even when the actual mechanical properties did not change. This is because the viscoelastic property was estimated from the relationship between the applied blood pressure and

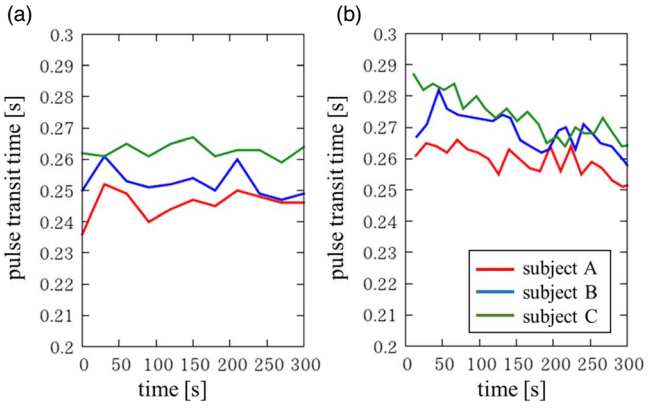

Fig. 1. (Color online) Pulse transit time during the FMD measurement (a) at rest, (b) after the recirculation.

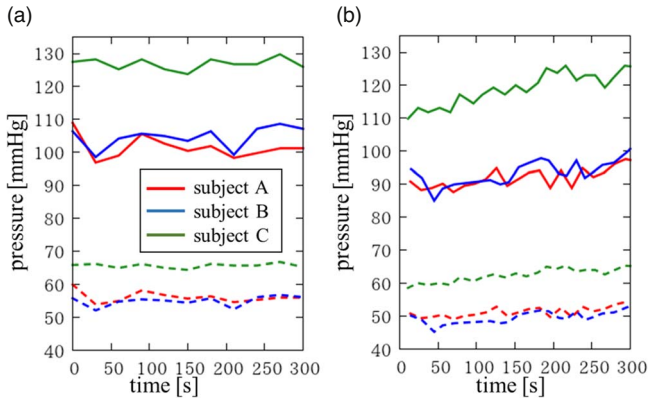

Fig. 2. (Color online) Systolic (solid line) and diastolic (dashed line) blood pressure during the FMD measurement (a) at rest, (b) after recirculation.

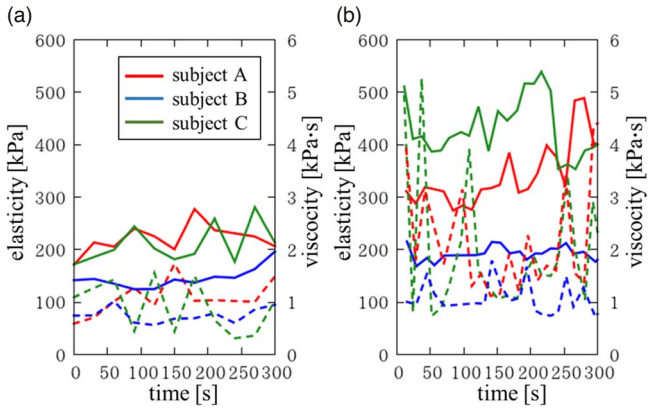

Fig. 3. (Color online) The elasticity (solid line) and viscosity (dashed line) during the FMD measurement (a) at rest, (b) after recirculation.

resultant deformation due to the change in the vessel diameter by assuming that the circular shape of the artery was maintained. These results suggest that the shape of the artery should be considered in the viscoelasticity estimation in addition to the accurate measurement of blood pressure.

To evaluate the endothelial function from the viscoelastic properties, the circular arterial shape should be maintained during the measurement. However, it is difficult to maintain the arterial shape during the measurement because the FMD test requires more than 10 min and dilation of the artery occurs. Therefore, in the future, it is important to develop a new viscoelastic model by considering the cross-sectional shape of the arteries.

As shown in Fig. 3(b), the estimated viscosity showed a stable value for subject B, while the values showed large variabilities for subjects A and C. The viscosity reflects the widening of the hysteresis loop between the blood pressure and vessel diameter during one heartbeat. The viscosity estimate became large when the diameter estimate did not return to its original value for each heartbeat. Therefore, more stable measurement of the vessel diameters is required to obtain more accurate viscosity.

In this study, we showed that the PTT method is useful for measuring blood pressure because the measurement values do not depend on the pressure applied by the ultrasound probe. The measured blood pressure changes showed a similar trend in all the subjects. The results reflect the change in the elastic modulus during the FMD. However, Eq. (2) suggests that the PTT may change depending on the vessel diameter. Therefore, vasodilatation due to FMD may affect the estimation of blood pressure. Moreover, the importance of viscoelasticity estimation considering the shape of the vessel is suggested. In the future, we plan to study the construction of a viscoelasticity estimation model to evaluate the viscoelasticity during FMD.

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