



Noninvasive Estimation of Arterial Viscoelastic Indices Using a Foil-type Flexible Pressure Sensor and a Photoplethysmogram

Harutoyo Hirano, Hiromi Maruyama, Abdugheni Kutluk, Toshio Tsuji, Osamu Fukuda, Naohiro Ueno, Teiji Ukawa, Ryuji Nakamura, Noboru Saeki, Masashi Kawamoto, and Masao Yoshizumi

Hiroshima university, The National Institute of Advanced Industrial Science and Technology,
Nihon Kohden Corporation, Japan
harutoyo@bsys.hiroshima-u.ac.jp

Abstract: This paper proposes a noninvasive method for estimating the viscoelastic characteristics of arterial walls using pulse waves measured in various parts of the body using a foil-type pressure sensor (FPS) and a photoplethysmogram. The FPS was employed to measure pulse waves based on the tonometry approach for its characteristics of high sensitivity and flexibility as well as its ability to continuously measure the alternating-current component of pulse waves. First, in order to accurately measure the amplitude variation of blood pressure waves, suitable mechanical forces externally applied to the FPS were examined, and it was found that values of 5 – 25 [N] yielded the best performance. Next, to verify the time characteristics of pulse waves, the brachial-ankle pulse wave velocity (baPWV) was measured. The results showed that baPWV determined using the FPS and that found with a noninvasive vascular screening device were almost the same. Estimation was then performed to establish arterial viscoelastic indices for the radial artery and the dorsal pedis artery during the application of mechanical pain stimuli. The results suggested that the estimated indices could be used to quantitatively assess vascular response caused by sympathicotonia. Thus, it was concluded that the proposed method enabled noninvasive measurement of pulse waves and estimation of viscoelastic indices.

Keywords: mechanical impedance, arterial wall, pressure sensor, arterial pressure, photoplethysmogram

1. Introduction

Blood vessels can be thought of as pipes used to transport blood throughout the entire body. They have viscoelastic characteristics because they consist of smooth muscles and elastic fibers [1]. When blood circulates in them, blood pressure is created. This is the amount of pressure applied by blood to the walls of blood vessels, and is linked to dynamic changes in the characteristics of arteries. It is widely used as a metric in health examinations, especially for the diagnosis of hypertension.

Blood pressure and blood flow are controlled by vascular smooth muscles, which contract and relax as a result of adjustments in the autonomic nervous and humoral regulation systems. The structural make-up of arterial walls differs from that of other physiological elements, with arterioles having the highest percentage of smooth muscles in the body [1]. Accordingly, accurate and simultaneous measurement of blood pressure and blood vascular diameter enables estimation of the condition of arteries, and can also be applied to evaluation of arterial viscoelastic properties and autonomic nervous activity.

A variety of noninvasive methods for blood pressure measurement have already been proposed. For instance, the oscillometric method [2] and the tonometry method [3] are well known and widely utilized. In the oscillometric method, a cuff is wrapped around one of the subject's extremities, and is pressured and depressurized to enable measurement. Systolic and diastolic pressure are then determined from variations in the pressure of the cuff. However, it is not possible to measure continuous blood pressure using this method. Conversely, the tonometry method allows

measurement not only of systolic and diastolic pressure but also of continuous blood pressure. In this approach, a pressure sensor is placed on the skin surface, and an appropriate amount of pressure is applied to the skin to make the artery wall as flat as possible. The level of pressure measured by the sensor is then converted into an electrical signal. This method can measure blood pressure with a level of detail close to that of invasive techniques without interference from the influences of vascular stiffness and tension.

In the field of estimating autonomic nervous activity, some research groups have evaluated the dynamic characteristics of arterial walls using data obtained via noninvasive methods. For example, Bank *et al.* [4] estimated the stiffness of the brachial artery from vessel diameter and blood pressure values measured using an ultrasound device. Sakane *et al.* [5] measured blood pressure and obtained finger photoplethysmograms, and then used these data to quantitatively estimate the dynamic characteristics of arterial walls in peripheral parts. Ikeshita *et al.* [6] also estimated the stiffness and viscosity of the radial artery using a similar method. However, in previous studies, the continuous blood pressure values used to estimate the dynamic characteristics of blood vessels were measured only in the fingers and wrists. To estimate arterial viscoelasticity in the distal foot, for example, blood pressure needs to be measured in that part. However, other than techniques involving the fingers and wrist, no noninvasive method of continuously measuring blood pressure in a specific part of the body has so far been proposed.

This paper therefore proposes a noninvasive method of continuously measuring pulse waves based on the tonometry approach and estimating the viscoelastic characteristics of arterial walls in various parts of the body using a small lightweight foil-type pressure sensor (FPS) [7]. In particular, pulse waves in the dorsal pedis artery were measured in this study, and changes in vascular response caused by autonomic nerves were evaluated.

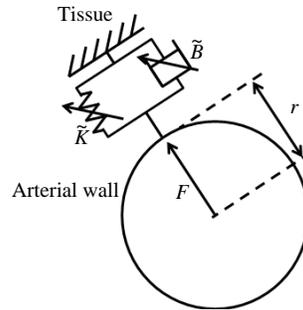


Figure 1. Schematic outline of the arterial wall impedance model

2. Arterial impedance model

Figure 1 shows an impedance model of the arterial wall [5] representing only the wall characteristics in an arbitrary radius direction. When any reference time (for example, R-wave timing) in the cardiac cycle is set, the impedance characteristic can be described using stress and displacement values for the arterial wall as follows:

$$dF(t) = Kdr(t) + Bd\dot{r}(t_0) \quad (1)$$

where $dF(t) = F(t) - F(t_0)$, $dr(t) = r(t) - r(t_0)$, and $d\dot{r}(t) = \dot{r}(t) - \dot{r}(t_0)$. $F(t)$ is the stress acting in the normal direction of the arterial wall, $r(t)$ and $\dot{r}(t)$ are the diameter of the wall and its first derivative, respectively, t_0 denotes the reference time (defined in this paper as the time at which the R wave appears in each electrocardiogram (ECG) recognition cycle), and K and B are coefficients of stiffness and viscosity, respectively. To estimate the impedance parameters given in (1), it is necessary to measure $F(t)$ and $r(t)$. The stress exerted on the arterial wall is proportional to the arterial pressure, as shown by the following equation:

$$F(t) = k_f P_b(t_0) \quad (2)$$

where k_f is a constant and $P_b(t)$ is the arterial pressure.

However, blood flow variations caused by pulsations of the heart are transmitted peripherally in arteries, and cause peripheral-part volume fluctuations that show up in photoplethysmograms. The heart repeats rhythmic contraction and dilation, and a photoplethysmogram shows periodical changes in line with this pulsation. Accordingly, we focus here only on a single plethysmogram period.

Let I_0 denote the intensity of incident light on a blood vessel with diameter D , and I_D represent the intensity of light transmitted through the apex of the finger. According to Lambert-Beer's law [8], the following equation can be obtained:

$$A_0 \equiv \log(I_0 / I_D) = ECD \quad (3)$$

where A_0 is a level of optical density proportional to the concentration of the absorptive substance C and the diameter of a blood vessel D , and E is a specific absorption coefficient depending on the material. When the blood vessel diameter $D(t)$ changes to $D_0 + \Delta D(t)$, and the light transmitted through the apex of the finger becomes $I_D - \Delta I(t)$. The variation in absorbance $\Delta A(t)$ can therefore be given as:

$$\Delta A(t) = A(t) - A_D = \log(I_D / (I_D - \Delta I(t))) = EC\Delta D(t) \quad (4)$$

The variation in absorbance $\Delta A(t)$ is defined as the photoplethysmogram value $P_l(t)$, which changes in proportion to the pulsation of blood vessels. In this paper, the summation of the vessel diameter in the measurement location is denoted as r_v , and is assumed to be proportional to the photoplethysmogram value $P_l(t)$:

$$r_v(t) = \frac{P_l(t) + A_D}{k_p} \quad (5)$$

where k_p is a proportional constant. From the above relationship, (1) can therefore be expressed as follows:

$$dP_b(t) = \tilde{K}dP_l(t) + \tilde{B}d\dot{P}_l(t_0) \quad (6)$$

where $dP_b(t) = P_b(t) - P_b(t_0)$, $dP_l(t) = P_l(t) - P_l(t_0)$, $d\dot{P}_l(t) = \dot{P}_l(t) - \dot{P}_l(t_0)$, and $\tilde{K} = K / k_f k_p$ and $\tilde{B} = B / k_f k_p$ are the stiffness and viscosity of the arterial wall, respectively. In this paper, \tilde{K} and \tilde{B} are defined as the arterial viscoelastic indices.

To estimate these indices, the arterial blood pressure must be measured in fulfillment of the following requirements:

- 1) The sensor must measure continuous blood pressure.
- 2) The sensor must have high sensitivity in order to measure pulse waves in various parts of the body.
- 3) The sensor must have sufficient flexibility to correspond to the shapes of various body parts.
- 4) In long-term measurement, the sensor should be robust against drift.

In this study, an FPS designed to measure pulse waves was used because it satisfied these four requirements.

Arterial wall impedance was estimated based on the following steps: First, electrocardiogram (ECG), noninvasive arterial pressure $P_b(t)$ and photoplethysmogram $P_l(t)$ measurements were taken simultaneously. The data were then pre-processed offline and used to estimate the impedance parameters based on the standard least-squares method.

Figure 2 shows an example of measured data from Subject A. It plots the electrocardiogram, noninvasive arterial pressure and photoplethysmogram values. As measured signals are usually affected by external influences such as noise from the power source or the body movement of the subject, the frequency characteristics of the noninvasive arterial pressure and photoplethysmogram values were regulated using a second-order infinite impulse response (IIR) low-pass filter (10 [Hz]) and a first-order IIR high-pass filter (0.3 [Hz]). As R waves generally have a distinctly large amplitude, they were used in this study to create an ECG recognition cycle, represented as t_0 .

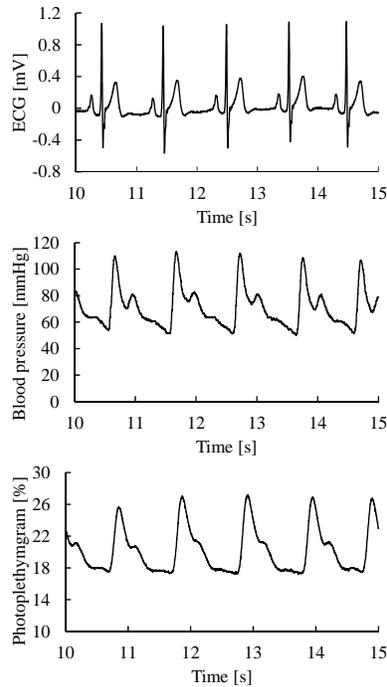


Figure 2. Examples of biological signals measured from Subject A

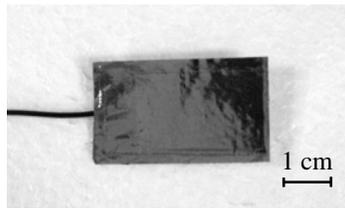


Figure 3. Foil-type flexible pressure sensor

The noninvasive arterial pressure dP_b and photoplethysmogram dP_l values for the interval between one R wave and the next one (referred to as the RR interval) were then used to determine the impedance parameters of Equation (6) via the least-squares method. As the previous RR interval was established when the subsequent R wave was detected, the beat-to-beat arterial wall impedance parameters \tilde{K} and \tilde{B} could be estimated during the subsequent RR interval.

3. Noninvasive pulse wave measurement

Figure 3 shows the FPS (foil-type pressure sensor) used to measure pulse waves [7]. Formed using the sputtering method, it consists of platinum as the base material, polyimide film (8.5 [μm]) as the electrode, and highly C-axis-oriented nitride aluminum (AlN) thin film as the piezoelectric material. The sensor has seven layers and a thickness of 50 [μm]. In sensors with a piezoelectric element, electrodes are generally located on both surfaces, giving them a configuration similar to that of a parallel-plate capacitor. With an FPS, however, unexpected leakage of electric charge and electric charge induced by unknown external electric fields is avoided through the inclusion of a sensor with a laminated structure. The aluminum nitride thin film on both sides of the inner electrode also makes it approximately twice as sensitive as previous sensors. FPSs therefore fulfill

the need for flexibility and high sensitivity in sensors used to measure pulse wave pressure in various parts of the body.

When the distance between electrodes is l and the area of electrode application force $F(t)$ is S_p , the voltage $V(t)$ can be described as follows:

$$V(t) = g \frac{l}{S_p} F(t) \quad (7)$$

where g is the specific output voltage constant for the piezoelectric element. When the electrode area is S and the permittivity of the piezoelectric element is ϵ , the electrostatic capacitance C can be expressed as $C = \epsilon S / l$. The charge $q(t)$ generated by the pressure $P(t)$ on the electrode can therefore be described as follows:

$$q(t) = \epsilon g S P(t) = P_D S P(t) \quad (8)$$

where $P_D = \epsilon g$ is the piezoelectric constant [9] and $q(t)$ does not depend on the thickness of the piezoelectric element. In measurement, pressure variations are converted from the measured output charge of the sensor using a charge amplifier.

The low-frequency component of the induced charge $q(t)$ of the sensor is attenuated under the inner structure of the sensor, but the higher-frequency component of the pulse wave is not. Thus, only the pressure variation of the alternating-current (AC) component of pulse waves can be measured [7]. The influence of drift in the output signal of the sensor can therefore be eliminated in long-term measurements using an FPS.

In this study, the tonometry method [10] was adopted to measure pulse waves using an FPS. Generally, the arterial tonometry method is adopted when measuring arteries supported by stiff components such as bone or tendon, and its use is limited to thick blood vessels near the skin surface. The technique also works well in the measurement of pulse waves for the radial artery [3].

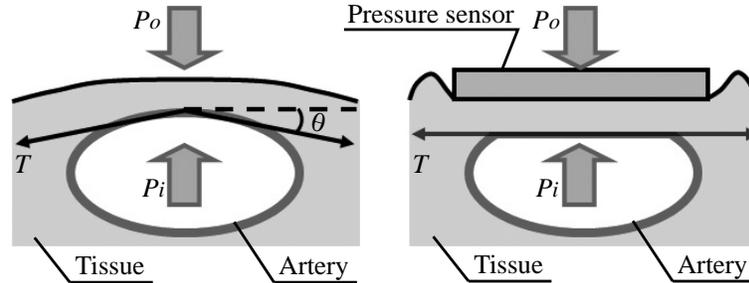


Figure 4. Principle of arterial tonometry

Figure 4 shows the principle of the arterial tonometry method. If an arterial wall is thin, the relationships between the arterial wall tension T , intravascular pressure P_i and external force P_o can be described as follows:

$$P_o = P_i - T \sin \theta \quad (9)$$

where θ is the angle between the tangential component of the arterial wall and arterial wall tension T . If pressure is applied using a plate so that the arterial wall is flattened as shown in Figure 4, θ becomes 0 [degrees]. In addition, P_o becomes P_i in the normal direction of the plate because arterial wall tension T occurs only in the plate's tangential direction.

In line with the relationship described above, a device for measuring pulse waves was developed based on an FPS (Figure 5). It was arranged with the sensor and a rubber plate placed on the artery to be monitored, and was fixed so that an external force of 1 [N] was applied to the measurement site using a wrap-around band. The external force was applied in the normal direction of the FPS so that the arterial wall was flattened during pulse wave measurement. The output values of the FPS did not contain the direct-current component of the measured pulse wave. The output voltage $V(t)$ was then converted to a variation of arterial pressure $\tilde{P}_b(t)$ around the mean arterial pressure.

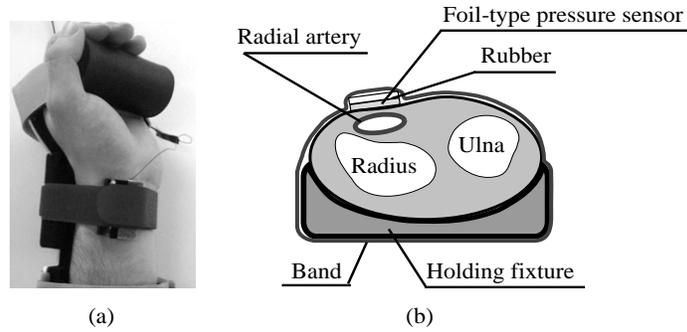


Figure 5 Pulse-wave measuring apparatus ((a) apparatus, (b) schematic cross-sectional view)

The arterial pressure variation $\tilde{P}_b(t)$ can be described as follows:

$$\tilde{P}_b(t) = \frac{PP_{Pf}(t)}{V_{Pf}} V(t) \quad (10)$$

where PP_{Pf} is the pulse pressure measured using an automated sphygmomanometer, and V_{Pf} is the corresponding peak-to-peak voltage measured using the FPS. PP_{Pf} and V_{Pf} were measured simultaneously at the beginning of the measurement period. Thus, the values of $\tilde{P}_b(t)$ were assigned to $dP_b(t)$, and noninvasive arterial viscoelastic index estimation was successfully completed.

4. Experiment

A. Experimental setup

Figure 6(a) shows the experimental setup. The signal measurement unit was used to measure pulse waves from the left radial artery with the FPS. Blood pressure and electrocardiogram signals

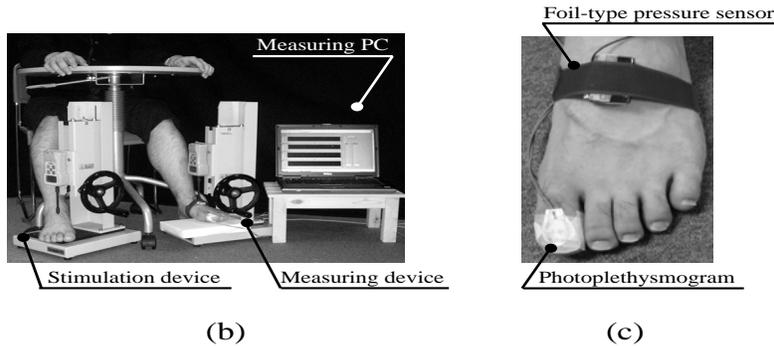
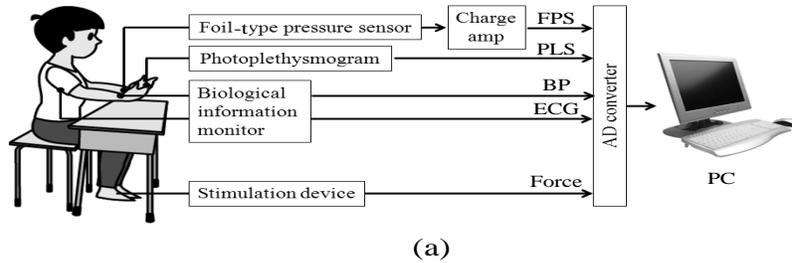


Figure 6. Pulse-wave measuring apparatus ((a) overview of experimental set-up, (b) experimental apparatus for measuring dorsal pedis artery pulse waves, (c) close-up of measuring devices)

were also measured from the left radial artery and the chest using a physiological monitor (BP-608, Omron Colin), and photoplethysmogram signals were measured from the second finger of the right hand using a pulse oximeter (OLV-3100, Nihon Kohden). Mechanical stimuli were employed as noxious influences to increase sympathetic nerve activity. These stimuli were applied using a digital force gauge (FGP-5, Nidec-Shimpo) with a cone-shaped attachment (point diameter $\phi = 0.36$ [mm]) that was pushed onto the dorsum of the subject's right foot while the pushing intensity was monitored. All signals were simultaneously measured at 1,005 [Hz] using an analog-digital card (CSI-360116, Interface), and the values were entered into a computer. The signal from the FPS was converted to a voltage signal using a charge amplifier (CH-1200, Ono Sokki), and the results were also input into the computer.

B. Experiment for pulse wave measurement

First, to accurately measure blood pressure amplitude variation, pulse waves recorded using the proposed method were compared with those recorded using the conventional arterial tonometry method. The seven healthy male subjects were seated in a resting state, and signals were measured over a period of one minute. An external force of 0 – 40 [N] was then applied in a direction perpendicular to the FPS using a force gauge with a columnar attachment ($\phi = 12$ [mm]). To evaluate an appropriate amount of mechanical force, the amplitude of the pulse waves (i.e., the piezoelectric pulse wave amplitude) was measured using the sensor with respect to each RR interval of the ECG. Subsequently, the correlation coefficient of the wave shape seen within the one-minute period and in one beat between the pulse waves measured using the FPS and blood pressure values was calculated. The coherence function and the phase of the cross-spectrum were also calculated to enable comparison of the linearity of the pulse waves measured using the FPS with blood pressure values in the frequency domain.

Next, to verify the time characteristics of the pulse waves detected using the FPS, the brachial-ankle pulse wave velocity (baPWV) – a well known and widely utilized index of arteriosclerosis [11] – was measured. Two FPSs were attached to the subject's skin surface – one near the brachial artery and one near the ankle artery – to enable simultaneous recording of FPS output voltages corresponding to the pressure pulse waves of the two arteries. The measured signals were then passed through a second-order infinite impulse response (IIR) low-pass filter (50 [Hz]) and a first-order IIR high-pass filter (5 [Hz]) to identify the rise time per beat of the measured pulse waves [12], and the difference between the rise times of the brachial artery and the ankle artery was taken as the pulse wave propagation time. The distance from the heart to the ankle artery L_a and that from the heart to the brachial artery L_b are given by the following equations [12]:

$$\begin{aligned} L_a &= 0.2195 \times h - 2.0734 \\ L_b &= 0.8129 \times h + 12.328 \end{aligned} \quad (11)$$

where h is the subject's height. baPWV values can therefore be estimated using the following equation:

$$\text{baPWV} = \frac{L_b - L_a}{t_b - t_a} \quad (12)$$

where t_a is the propagation time from the heart to the ankle, and t_b is the propagation time from the heart to the brachial artery. In order to verify the results of FPS-based baPWV measurement, values were also measured using a noninvasive vascular screening device (BP-203RPE II form PWV/ABI, Omron Colin) for comparison. For this purpose, four healthy male subjects (G – J) were asked to assume a supine position in a resting state, and signals were measured over a period of two minutes. baPWV values were measured on both sides of the body.

C. Experiment for evaluation of blood vessel function

Pulse waves were measured while mechanical pain stimuli were delivered to the subject by applying an appropriate external force to the FPS. The same seven male subjects discussed in

Section IV-B were used. To avoid any psychological influence from the sight of the stimulator, the subjects were not allowed to see it. The external force that yielded the best performance in the experiment described in Section IV-B was used for the FPS. To evaluate the effectiveness of the proposed method, pulse waves from the dorsal pedis artery were measured, and the arterial viscoelastic indices were estimated. Figure 6 (b) shows the experimental environment. Five of the subjects discussed in Section IV-B (B, C, D, F and G) were asked to assume a sitting posture, and biosignals were measured from the left dorsal pedis artery and the digitus secundus of the left foot using the FPS and a pulse oximeter, respectively (Figures 6 (b) and (c)). A force of 15 [N] was applied to the FPS, as determined in the experiment described in Section IV-B. To avoid any psychological influence from the sight of the stimulator, the subjects were not allowed to see it. The measurements were repeated once for each level of stimulation intensity, and were taken in a resting state (0 – 60 [s]), a stimulated state (60 – 80 [s]), and a resting state again (80 – 140 [s]). A stimulation intensity of 3 [N] was applied to the dorsum of the subject's right foot using a digital force gauge.

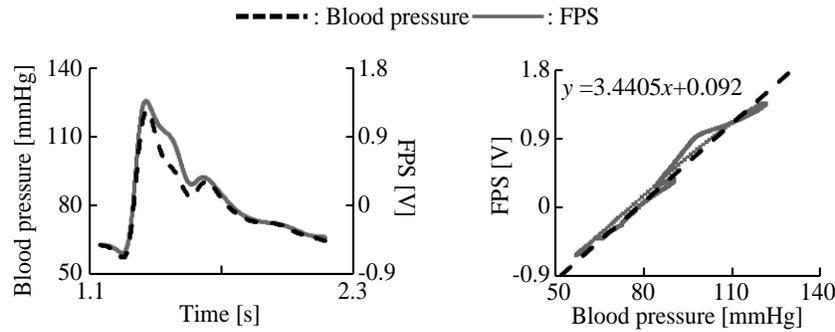


Figure 7. Results of measurement for Subject A at rest ((a) comparison of FPS-measured pulse wave and wave based on blood pressure values, (b) correlation between FPS-measured pulse wave and wave based on blood pressure values)

viscoelastic indices seen in a resting state with those seen in a stimulated state.

Due to blood pressure and photoplethysmogram differences, absolute values of viscoelasticity generally vary among individuals [13]. The estimated values were therefore normalized based on the corresponding standard values seen in a resting state. \tilde{K} and \tilde{B} were normalized using the following equations:

$$\begin{aligned} K_{BPn} &= \frac{\tilde{K}_{BP}}{K_{BPr}} & B_{BPn} &= \frac{\tilde{B}_{BP}}{B_{BPr}} \\ K_{FPSn} &= \frac{\tilde{K}_{FPS}}{K_{FPSr}} & B_{FPSn} &= \frac{\tilde{B}_{FPS}}{B_{FPSr}} \end{aligned} \quad (13)$$

where K_{BPr} and B_{BPr} are the stiffness and viscosity estimated using an automated sphygmomanometer in a resting state, and K_{BPn} and B_{BPn} are the normalized values of stiffness and viscosity, respectively. Also, K_{FPSr} and B_{FPSr} are the stiffness and viscosity estimated using the FPS in a resting state, and K_{FPSn} and B_{FPSn} are the normalized values of stiffness and viscosity, respectively. Welch's t -test was used to compare the arterial

5. Results

A. Experiment for pulse wave measurement

Figure 7(a) shows a comparison of wave shapes for Subject A between the pulse waves measured using the FPS with an external force of 10 [N] (which resulted in the maximum amplitude) and blood pressure values. Figure 7(b) shows the correlation of the wave shape and the

regression line between the pulse wave of the FPS and blood pressure values shown in Figure 7(a).

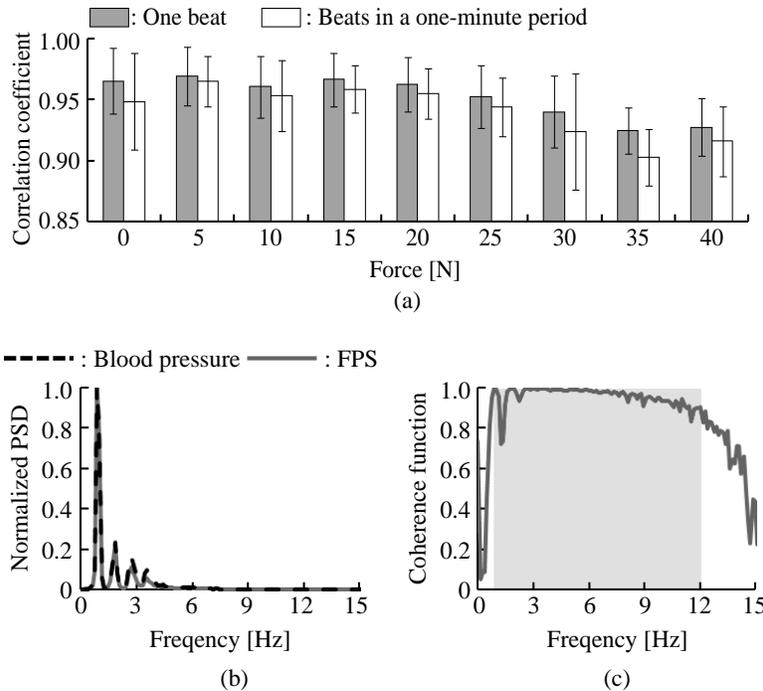


Figure 8. Results of measurement with the subject at rest ((a) coefficients of correlation between FPS-measured pulse waves and waves based pm blood pressure values (Subject A), (b) power spectral density, (c) coherence function (Subject A))

In both figures, the FPS wave shape shows a strong similarity to that for blood pressure. The correlation coefficient is 0.99 ($p < 0.01$), which is significantly high. Figure 8(a) shows the average correlation coefficients of the wave shapes for all subjects over a one-minute period and one heartbeat between pulse waves measured using the FPS and blood pressure levels seen when various mechanical forces were applied. The coefficients are 0.9 or more for all subjects with the application of an external force of 10 – 25 [N]. Figures 8(b) and (c) show the power spectral density normalized by the maximum value and the coherence function of Subject A when an external force of 10 [N] was applied. The results shown in Figure 8 (b) indicate that the pulse waves measured using the FPS had the same properties as those for blood pressure. Moreover, Figure 8 (c) shows that the coherence function is approximately 1 for frequencies of 0.74 – 12 [Hz]. The FPS-measured pulse waves and blood pressure values also show a high degree of linearity, and the phase of the cross-spectrum between the FPS and blood pressure values was almost 0 in the frequency domain of 0 – 15 [Hz]. These tendencies were seen in the results of all subjects. Thus, it was confirmed that the wave shapes and frequency characteristics of pulse waves measured using the FPS showed a close correlation with those of blood pressure when an external force of 5 – 25 [N] was applied. Consequently, this range of external force is recommended for pulse wave measurement using the proposed method.

Figure 9(a) shows an example of measured FPS output voltages, and Figure 9 (b) shows the corresponding filtered signals. It is confirmed that the propagation time from the heart to the ankle t_a and that from the heart to the brachial artery t_b can be measured appropriately. Figure 6 shows the results of baPWV measurement using an FPS and a noninvasive vascular screening device, and indicates a significant similarity between the two. Also Figure 9 shows comparison of baPWV values measured on both sides of the body using the noninvasive vascular screening device and FPSs.

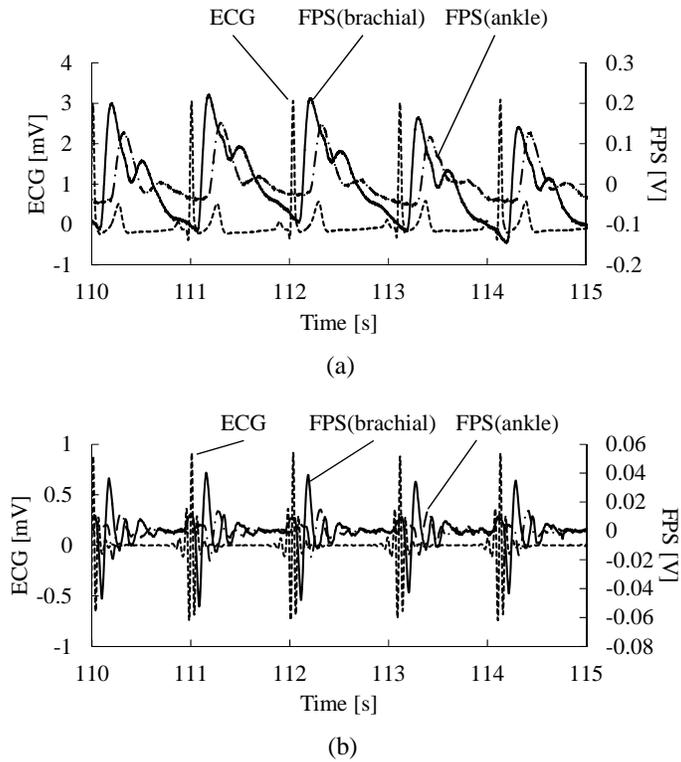


Figure 9. Results of ECG and FPS output voltage measurement. FPS values were measured on the right side of the body of Subject G ((a) raw waves, (b) filtered waves)

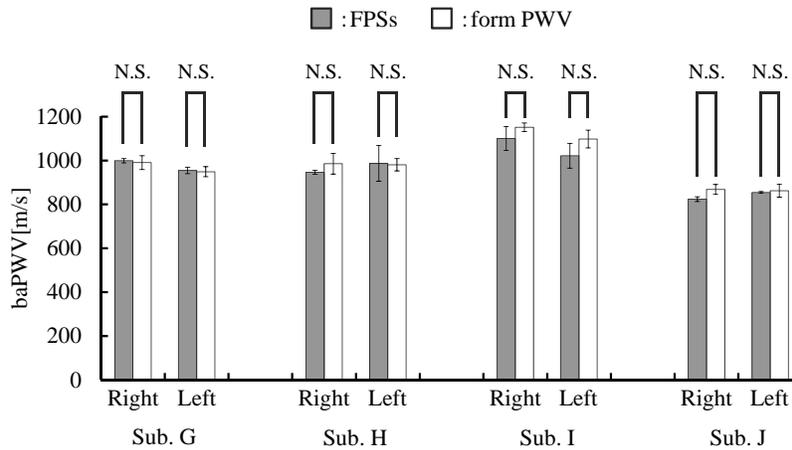


Figure 10. Comparison of baPWV values measured on both sides of the body using the noninvasive vascular screening device and FPSs

B. Experiment for evaluation of arterial viscoelasticity in a peripheral part

Figure 11 shows an example of signals measured from the radial artery. The different parts of the figure show the electrocardiogram, photoplethysmogram, blood pressure and pulse waves measured using the FPS. The results indicate small changes in the photoplethysmogram, blood pressure and

pulse waves during the stimulation period (59 – 70 [s]).

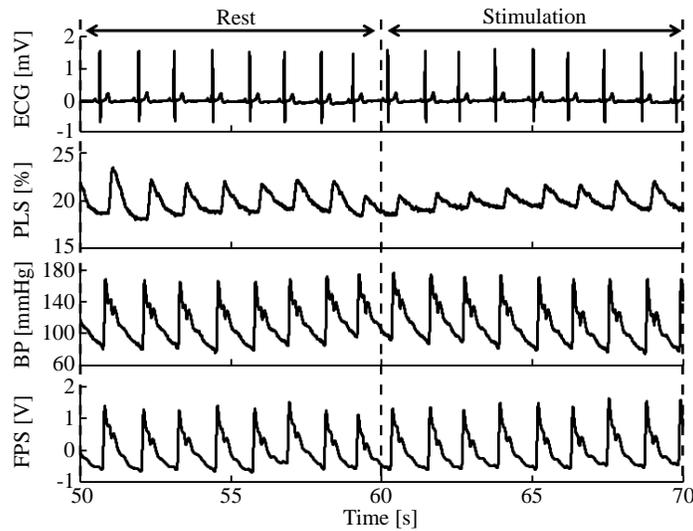


Figure 11 Results of measuring biological signals from the right radial artery at the wrist

Figure 12 shows the experimental results for Subject A when an external force of 10 [N] was applied. The different parts of the figure show pulse pressure, stiffness \tilde{K}_{BP} and viscosity \tilde{B}_{BP} estimated from blood pressure values, piezoelectric pulse wave amplitude, and values of stiffness \tilde{K}_{FPS} and viscosity \tilde{B}_{FPS} estimated using the proposed method. The time from 60 to 80 seconds shown in this figure is the period during which the dorsum of the right foot was stimulated.

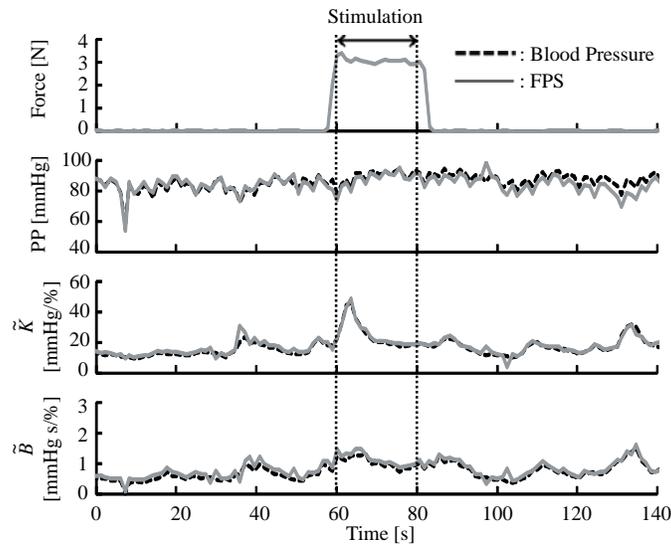


Figure 12 Arterial wall viscoelasticity changes in response to mechanical stimuli

The results show small changes in the pulse pressure \tilde{B}_{BP} and \tilde{B}_{FPS} as a result of this stimulation, and indicate that \tilde{K}_{BP} and \tilde{K}_{FPS} increased drastically and rapidly during the stimulation period. The results also show that changes in the piezoelectric pulse wave amplitude

\tilde{K}_{FPS} and \tilde{B}_{FPS} tended to follow those of the pulse pressure \tilde{K}_{BP} and \tilde{B}_{BP} estimated from blood pressure values, respectively.

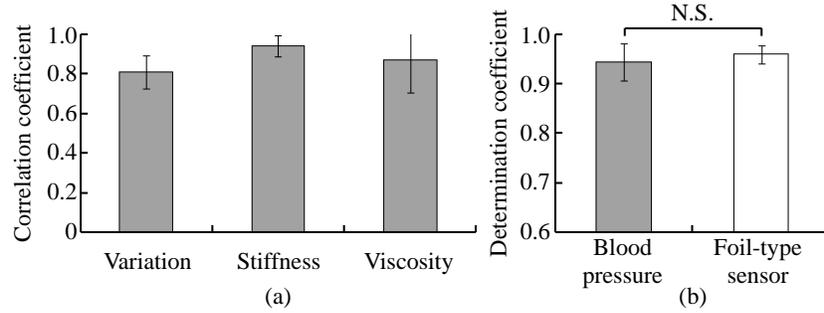


Figure 13 Results of measurement with the subject at rest and during application of stimulation to the dorsal skin of the right foot ((a) correlation coefficients of variation, stiffness and viscosity between FPS and blood pressure values, (b) comparison of coefficients of determination between FPS and blood pressure values)

Figure 13(a) shows that the average correlation coefficient between the piezoelectric pulse wave amplitude and pulse pressure was 0.810 ± 0.084 ($p < 0.01$). The results also show that the average correlation coefficient of estimated stiffness between the proposed method and that based on blood pressure values was 0.937 ± 0.053 ($p < 0.01$), while that of viscosity was 0.868 ± 0.162 ($p < 0.01$).

Figure 13(b) shows that the determination coefficient of the proposed method was 0.944 ± 0.038 , and that based on blood pressure values was 0.959 ± 0.019 . This confirms that estimation of stiffness and viscosity values using the proposed method was as accurate as that based on blood pressure values.

Figure 14 shows the correlations between the results obtained with the FPS and those obtained with the automated sphygmomanometer. Figures 12 and 14 (c) – (f) indicate that the mean values of \tilde{K}_{FPS} , \tilde{K}_{BP} , \tilde{B}_{FPS} and \tilde{B}_{BP} increased when the mechanical stimulus was applied. These figures also show that variations in PP_{FPS} , \tilde{K}_{FPS} and \tilde{B}_{FPS} tended to follow those of PP_{BP} , \tilde{K}_{BP} and \tilde{B}_{BP} , respectively. The correlation coefficients between PP_{FPS} and PP_{BP} , between K_{FPSn} and K_{BPn} , and between B_{FPSn} and B_{BPn} were 0.810 ± 0.084 , 0.936 ± 0.058 and 0.886 ± 0.121 , respectively. Figures 14 (g) and (h) show that all mean values of normalized parameters K_{FPSn} , K_{BPn} , B_{FPSn} and B_{BPn} were more than 1; the stiffness and viscosity values increased as a result of stimulation. The slopes of the regression lines show values of approximately 1. This confirms that arterial viscoelastic index changes seen during the application of mechanical pain stimuli can be captured as accurately using the proposed method as with that based on blood pressure values.

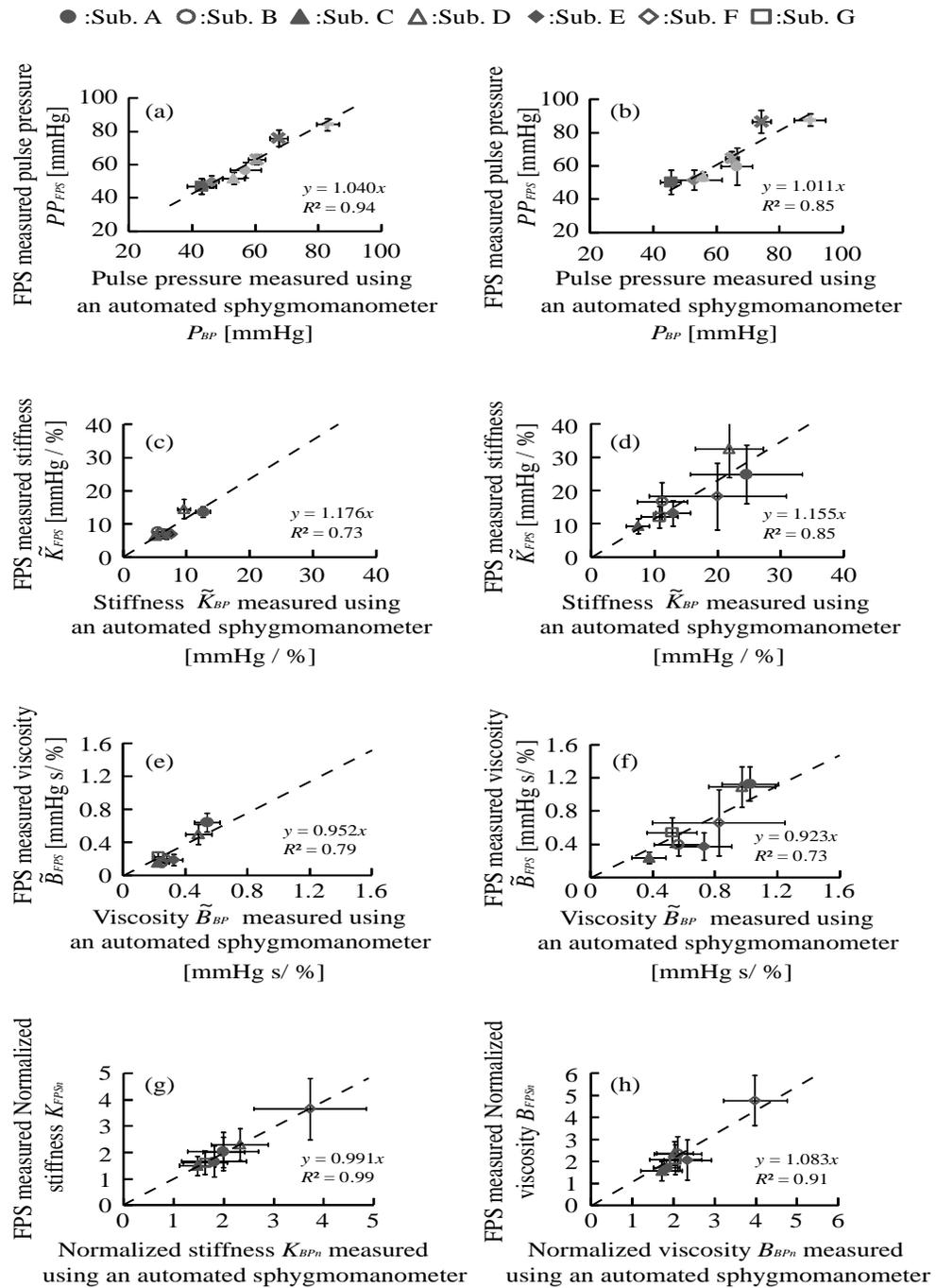


Figure 14 Comparison of results obtained using an FPS and those obtained using an automated sphygmomanometer: (a) PP at rest, (b) PP during stimulation, (c) \tilde{K} at rest, (d) \tilde{K} during stimulation, (e) \tilde{B} at rest, (f) \tilde{B} during stimulation (g) normalized K , (h) normalized B

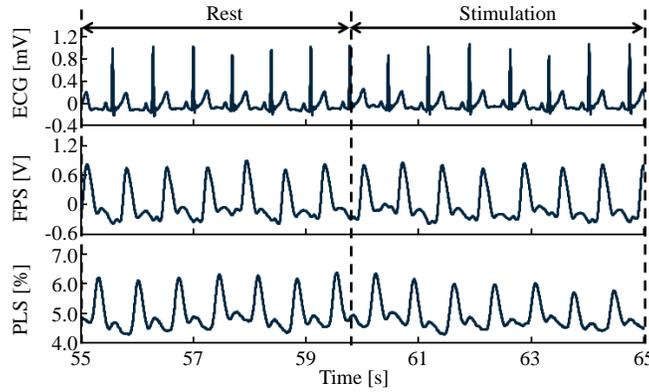


Figure 15 Results of measuring biological signals from the left dorsal pedis artery

Figure 15 shows an example of measured signals for the dorsal pedis artery. The different parts show the electrocardiogram, pulse waves measured using the FPS and the photoplethysmogram. Figure 16 (a) shows an example of measured signals for the dorsal pedis artery for Subject C. The tendencies seen here are similar to those of Figure 12. These figures plot the stimulation intensity, piezoelectric pulse wave amplitude, \tilde{K}_{FPS} and \tilde{B}_{FPS} . Figures 16 (b) and (c) show the average values of K_{FPSn} and B_{FPSn} seen during the rest and stimulation periods. Both values increased significantly in the stimulation period compared to those of the rest period.

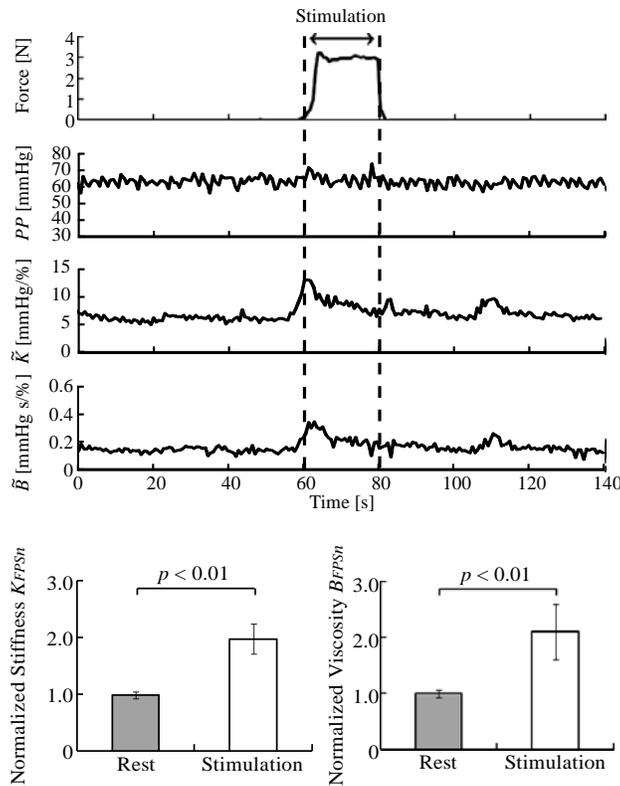


Figure 16 Results of measurement with the subject at rest and during application of stimulation to the dorsal skin of the right foot ((a) changes in arterial wall viscoelasticity (Subject C), (b) comparison of results for normalized stiffness between periods of rest and stimulation, (c) comparison of results for normalized viscosity between periods of rest and stimulation)

6. Discussion

Figure 8(a) shows that the wave shape and frequency characteristics of FPS-measured signals exhibit a close correlation to those of blood pressure during the relevant period for the external-force range of 5 – 25 [N] in which the maximum value of the piezoelectric pulse wave amplitude was obtained for all subjects. This confirms that measurement using the proposed method was as accurate as that based on blood pressure values when considering individual differences seen during the application of constant external forces of 5 – 25 [N]. Figure 10 also shows that the baPWV values measured using the noninvasive vascular screening device and those from the FPS were quite similar. This confirms that the proposed method can be used to successfully measure the amplitude and time variation of blood pressure. As the FPS can detect and measure pressure pulse waves in various physiological locations, regional PWV values around the body can be evaluated. This may be useful in determining the development of regional arteriosclerosis.

Figures 12 and 14 show that the output voltage of the FPS can be converted to a variation of arterial pressure. This confirms that index changes seen during the application of mechanical stimuli can be captured as accurately using the proposed method as with that based on blood pressure values. Kohno *et al.* [13] previously confirmed that values of stiffness estimated from pulse pressure and photoplethysmogram amplitude were significantly influenced by different stimulation intensities and different shapes of objects used for stimulation. The proposed method may be considered capable of quantitatively evaluating changes seen in response to mechanical stimuli. Figure 16 shows that the proposed method can be used to measure pulse pressure waves not only in the radial artery but also in the dorsal pedis artery. In addition, the mean value of the determination coefficients obtained in the estimation of arterial viscoelastic indices for all subjects was 0.979 ± 0.002 . It was thus confirmed that the proposed method can be used to successfully estimate arterial viscoelastic indices.

Conclusion

This paper proposed a noninvasive method for measuring pulse waves and estimating changes in the dynamic characteristics of arterial walls using an FPS and a photoplethysmogram. The results showed successful measurement of pulse waves in the dorsal pedis artery and estimation of arterial viscoelastic indices, thereby confirming the technique's effectiveness.

In future work, a calibration algorithm of average blood pressure based on converting FPS output values to blood pressure values should be considered, and testing should be carried out with older subjects. A method of evaluating organic and functional changes in arterial viscoelastic characteristics should also be explored.

References

- [1] R. Ohchi, "Physiology text 4th Edition", BUNKODO, 2003.
- [2] T. G. Pickering, J. E. Hall, L. J. Appel, B. E. Falkner, J. Graves, M. N. Hill, D. W. Jones, T. Kurtz, S. G. Sheps, E. J. Roccella, "Recommendations for blood pressure measurement in humans and experimental animals: Part 1: blood pressure measurement in humans: a statement for professionals from the Subcommittee of Professional and Public Education of the American Heart Association Council on High Blood Pressure Research", *Am. J. Hypertension* Vol.45, pp.142 – 61, 2005.
- [3] R. P. Kelly, C. S. Hayward, J. Ganis, J. M. Daley, A. Avolio and M. F. O'Rourke: "Noninvasive Registration of the Arterial Pressure Pulse Waveform Using High-Fidelity Applanation Tonometry", *Journal of Vascular and Medical Biology*, Vol. 1, pp. 142 – 149, 1989.
- [4] J. Bank, R. F. Wilson, S. H. Kubo, J. E. Holte, T. J. Dresing and H. Wang, "Direct Effects of Smooth Muscle Relaxation and Contraction on In Vivo Human Brachial Artery Elastic Properties", *Circulation Res.*, vol. 77, pp. 1008 – 1016, 1995.
- [5] Sakane, K. Shiba, T. Tsuji, N. Saeki and M. Kawamoto, "Non-invasive monitoring of arterial wall impedance", *Proc. 1st Int. Conf. Comp. Med. Eng.*, pp. 984–989, 2005.

- [6] K. Ikeshita, H. Hasegawa and H. Kanai, "Ultrasonic Measurement of Transient in Elastic Property of Radial Artery Caused by Endothelial-Dependent Vasodilation", *IEICE Technical Report*, vol. 107, no. 96, pp. 29–32, 2007.
- [7] N. Ueno, M. Akiyama, K. Ikeda and H. Tateyama, "A Foil Type Flexible Pressure Sensor Using Nitelide Aluminum Thin Film", *SICE Trans.*, vol. 38, no. 5, pp. 427–432, 2002.
- [8] M. J. Goldman, *Principles of Clinical Electrocardiography*, 12th edition. Lange Medical Publications, 1986.
- [9] R. Maeda, R. Sawada, and K. Aoyagi, "Advanced Technologies and Applications of MEMS/NEMS", P.45-54, Frontier Publishing, Tokyo, 2006.
- [10] G. L. Pressman and P. M. Newgard, "A Transducer for the Continuous External Measurement of Arterial Blood Pressure", *IEEE Trans. Biomed. Eng.*, vol. 10, pp. 73–81, 1963.
- [11] Yamashina, H. Tomiyama, K. Takeda, H. Tsuda, T. Arai, K. Hirose, Y. Koji, S. Hori, Y. Yamamoto, "Validity, Reproducibility, and Clinical Significance of Noninvasive Brachial-Ankle Pulse Wave Velocity Measurement", *Hypertension Res.*, vol. 25, no. 3, pp. 359–364, 2002.
- [12] M. Munakata, N. Ito, T. Nunokawa and K. Yoshinaga, "Utility of automated brachial ankle pulse wave velocity measurements in hypertensive patients", *Am. J. Hypertens.*, Vol. 16, pp. 653–657, 2003.
- [13] Kohno, A. Kutluk, T. Tsuji, T. Ukawa, R. Nakamura, N. Saeki, M. Yoshizumi and M. Kawamoto, "Quantitative Evaluation of Pain with Mechanical Nociceptive Stimuli by the Change of Arterial Wall Viscoelasticity", *Japanese J. Med. inst.*, vol. 80, no. 3, pp. 196–204, 2010.



Harutoyo Hirano received his B.E. degree in Electrical, Computer, and Systems Engineering from Hiroshima University, Japan, in 2008 and his M.E. degree in Artificial Complex System Engineering from Hiroshima University, Japan, in 2010. Now he is a doctoral student in Systems Cybernetics, Hiroshima University, Japan. His research interest includes medical devices for vascular assessment and treatment. He is a student member of the Institute of Electrical Engineers of Japan.



Hiromi Maruyama received his B.E. degree in Electrical, Computer, and Systems Engineering from Hiroshima University, Japan, in 2009 and his M.E. degree in Artificial Complex System Engineering from Hiroshima University, Japan, in 2011. His research interest includes medical devices for circulatory organ.



Abdugheni Kutluk received the B.E. degree in textile engineering and computing from Xi'an Polytechnic University, Xi'an, China, in 2001, and received the M.E. degree in electric and computer engineering from Tokyo Denki University, Japan, in 2005, respectively. He received the Ph.D degree in systems engineering from Hiroshima University, Japan, in 2011. From March 2011, he is an International Guest Researchers in Faculty of Engineering, Hiroshima University, Japan. His current research interests include monitoring of autonomic nervous system activity, measuring of arterial elasticity, and biosignal analysis.



Toshio Tsuji received his B.E. degree in industrial engineering in 1982, his M.E. and Doctor of Engineering degrees in systems engineering in 1985 and 1989, all from Hiroshima University. He was a Research Associate from 1985 to 1994, and an Associate Professor, from 1994 to 2002, in the Faculty of Engineering at Hiroshima University. He was a Visiting Professor of University of Genova, Italy for one year from 1992 to 1993. He is currently a Professor of Department of System Cybernetics at Hiroshima University. Prof. Tsuji won the Best Paper Award from the Society of Instrumentation and Control Engineers in 2002 and 2008, and the K. S. Fu Memorial Best Transactions Paper Award of the IEEE Robotics and Automation Society in 2003. His current research interests have focused on Human-Machine Interface, and computational neural sciences, in particular, biological motor control. Prof. Tsuji is a member of the Institute of Electrical and Electronics Engineers, the Japan Society of Mechanical Engineers, the Robotics Society of Japan, and the Society of Instrument and Control Engineers in Japan.



Osamu Fukuda received his B.E. degree in mechanical engineering from Kyushu Institute of Technology, Iizuka, Japan, in 1993 and the M.E. and Ph.D. degrees in information engineering from Hiroshima University, Higashi-Hiroshima, Japan, in 1997 and 2000, respectively. From 1997 to 1999, he was a Research Fellow of the Japan Society for the Promotion of Science. He joined Mechanical Engineering Laboratory, Agency of Industrial Science and Technology, Ministry of International Trade and Industry, Japan, in 2000. Since 2001, he has been a member of National Institute of Advanced Industrial Science and Technology, Japan. His main research interests are in human interface and neural networks. Also, he is currently a guest professor of Department of System Cybernetics at Hiroshima University. Prof. Fukuda is a member of the Society of Instrument and Control Engineers in Japan and Japanese Society of Physical Fitness and Sports Medicine.



Naohiro Ueno received his B.S. degree in physics from Kyushu University, Japan, in 1984 and received his Ph.D. degree from Hiroshima University in 1998. He joined 5th Research Center, Technical Research and Development Institute, the Defense Agency, Japan from 1984 to 1985. He joined department of structures and urban planning, Fukuoka Prefectural government, Japan from 1985 to 1990. He joined the Kyushu National Industrial Research Institute, Ministry of International Trade and Industry, Japan, from 1990. Now He joins National Institute of Advanced Industrial Science and Technology, Saga, Japan. Also he is currently a guest Professor of Department of System Cybernetics at Hiroshima University. His current research interests are active sensing and functional material for devices. Prof. Ueno is a member of the Institute of Electrical and Electronics Engineers and the Society of Instrument and Control Engineers in Japan.



Teiji Ukawa received the Bachelor of Engineering degree from department of applied physics of Waseda University, Tokyo, Japan, in 1980. He joined Nihon Kohden Corp., Tokyo, Japan, from April 1980. He is a Ph.D. student in systems engineering at Hiroshima University, Higashi-Hiroshima, Japan, from October 2009.



Ryuji Nakamura received the B.A. degree from Hiroshima University, Japan and the Ph.D. degree from Hiroshima University, Japan, both in medical science, in 1999 and 2010, respectively. He was a graduate school student of biomedical sciences at Hiroshima University, Japan, from April 2005 to March 2010. Since April 2010, he is Assistant Professor in the Department of biomedical sciences, Faculty of Medicine, Hiroshima University. His current research interests are monitoring of autonomic nervous system function.



Noboru Saeki received the B.A. degree from Hiroshima University, Japan, and the Ph.D. degree from Hiroshima University, Japan, both in medical science, in 1990 and 2000, respectively. He was an Assistant Professor in the Graduate School of Biomedical Sciences, Hiroshima University, from April 2000 to March 2010. His current research interests are cardiovascular and brain monitoring during the surgery, vascular permeability regulation under inflammatory stimuli.



Masashi Kawamoto was certified the Medical license in Japan and the Ph.D. degree from Hiroshima University Faculty of Medicine, in 1989. He dedicated as an Instructor, an Assistant Professor, an Associate Professor at Hiroshima University, Japan, and since April 2007, he is Professor in the Department of Anesthesiology and Critical Care, Division of Clinical Medical Science, Graduate School of Biomedical Sciences, Hiroshima University. His current research interests are both in Autonomic nervous system and Clinical anesthesia.



Masao Yoshizumi received the doctor of medicine from the University of Tokyo, Japan, in 1981, and the doctor of philosophy in medical science from the University of Tokyo, Japan, in 1997. After completion of fellowship in cardiology and molecular cardiology research at the University of Tokyo, Japan, he was a Research Associate in molecular biology and an Instructor in Medicine at Harvard University, U.S.A., from January 1992 to April 1996. He was an Assistant Professor in the Department of Geriatric Medicine, Faculty of Medicine, the University of Tokyo from August 1998 to March 2002. Since April 2002, he is a Professor in the Department of Cardiovascular Physiology and Medicine, Faculty of Medicine, Hiroshima University. His current research interests are molecular mechanism in cardiovascular diseases and biomedical engineering in cardiology.