Studying Peripheral Vascular Pulse Wave Velocity Using Bioimpedance Plethysmography and Regression Analysis

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ABSTRACT

In this study, a simple bioimpedance plethysmography method was employed to measure the pulse wave velocity (PWV) from the radial artery in the wrist to the middle finger of a patient. Subsequently, electrocardiography was combined with a bioimpedance method to calculate the PWV from ECG and pulse waves to the middle finger. Experiments were conducted by employing cuffs that temporarily block blood flow to produce observable changes in the PWV. Statistical results indicated that temporary blockage of blood flow did not influence the PWV of typical healthy people. Moreover, multiple regression analysis was used to establish an equation for estimating two types of PWV and their relevance with other physiological parameters. Multiple regression analysis indicated that the abdomen circle and height are independent predictors of the PWV from the radial artery in the wrist to the middle finger (wfPWV) ($r = 0.893$). Systolic blood pressure (SBP) and diastolic blood pressure (DBP) are independent predictors of the PWV from the EGC T wave to the middle finger (tfPWV) ($r = 0.898$). Correlation analysis showed the wfPWV is significantly associated with tfPWV ($r = 0.770$, $p < 0.01$).

Keywords: Bioimpedance, Pulse wave velocity, multiple regression

1. INTRODUCTION

According to a report released by the World Health Organization in 2014, cardiovascular disease, cancers, chronic respiratory diseases, diabetes, and other non-communicable diseases accounted for 37%, 27%, 8%, 4%, and 24%, respectively, of all causes of death among people under the age of 70 years in 2012 [1]. The report elucidated the relevant threat of cardiovascular diseases to the health of the general population in modern society. Moreover, vascular sclerosis is an irreversible disease. Once the blood vessels are affected by aging, one can only maintain their current state and prevent further deterioration. It is impossible to regain the former flexibility of the blood vessels. This loss of flexibility can be attributed to the gradual proliferation of atherosclerotic plaque that thickens the vascular walls resulting in hardening of the walls. Consequently, it narrows the blood vessels causing reduced blood flow or the rupturing of plaques that form thrombus leading to blocked arteries, tissues or organs that may lead to ischemic necrosis. In the event that the carotid artery or the cerebral artery is obstructed, it can result in a stroke, while blocked coronary arteries can cause myocardial infarction. Therefore, prevention is better than a cure, especially in terms of the hardening of blood vessels. However, many are unable to have regular check-ups due to their busy lifestyle. Once symptoms are detected, it is difficult to restore the original health state of the person. In addition to diagnosing the illness, a check-up at this time may help to control the disease and inhibit further deterioration.

Preventive measures for cardiovascular diseases are beneficial for early detection of symptoms. Real-time cardiovascular monitors can be used to detect cardiovascular disease and estimate its severity. A specific form of arteriosclerosis, called atherosclerosis, is known as hardening of the arteries that begins at the intima of the artery [2]. Currently, various methods have been developed for the detection of the degree of arteriosclerosis. A particular method for analyzing the situation is the pulse wave velocity (PWV) method. PWV is by definition the propagation velocity of the arterial pulse and is also the distance traveled by a wave divided by the time required for it to travel that distance. PWV measurements can be either invasive or non-invasive. Invasive measurement methods include angiography, fiberoptic angioscopy [3], intravascular ultrasound (IVUS) [4] and MRI [5]. These types of measurements can be used to directly investigate the presence of fat accumulation or intimal hyperplasia in an artery. However, it is likely to cause fear and health risks to the patient. Furthermore, it is also very time-consuming and requires the operator to have professional knowledge and training to exercise appropriate judgment. Due to the inherent inconvenience and limitations of invasive methods, current medical practice uses non-invasive measurements to assess the degree of early vascular disease[6]. Non-invasive methods include ul-

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trasound [7], cuff [8], pressure sensing, infrared sensing [9], and pulse rate, among others. Many studies have found that vascular wall elasticity is affected by personal health factors or disease [10, 11], and the measured aortic pulse-wave velocity (PWV) changes due to the elasticity of the arterial wall. In hardened arteries, PWV is faster, while in more elastic arteries, it is reduced. Arterial elasticity has been associated with various cardiovascular diseases [12]. Therefore, PWV parameters may serve as useful indicators in the assessment of human arteries. Consequently, medical practitioners frequently employ non-invasive measurement methods (e.g., ultrasound, cuff, and infrared sensing methods) to estimate early vascular lesions.

The most frequently used non-invasive approach is the cuff method. Here, a cuff is used to measure the pulse at the upper arm and ankle and calculate a brachial-ankle PWV and ankle-brachial index. A previous study [13] indicated that brachial-ankle PWV measurement is a valid approach with high reproducibility. It has been reported that the measured PWV of patients with cardiovascular diseases are substantially higher than those of healthy people [14,15]. However, the difficulty of estimating vessel length creates problems in practical application of this method. Currently, there have been numerous studies of PWV, but most were directed toward the study of baPWV or aortic PWV with limited literature discussing peripheral blood vessels. Subsequently, prior to the hardening of the aorta, peripheral vascular blood flow should show changes. Therefore, deducing the health of the aorta through long-term monitoring of the peripheral blood vessels will be beneficial for patients with cardiovascular disease. When there is flow in blood vessels, aside from producing mechanical expansion, a change in the bioelectrical impedance is generated. Bioimpedance measurement is a technique that is useful because it is cost-effective, portable and poses no radioactive exposure to patients. Research teams have measured PWV and heart rate by employing a bioimpedance technique at the forearm [16], indicating that bioimpedance can be used to measure PWV. For these reasons, the current research utilized changes in bioelectrical impedance by measuring the pulse rate through the bioelectrical impedance changes from the radial artery in the arm to the finger. Simultaneously, the obtained rate and physiological parameters (such as anthropometric parameters, heart rate and blood pressure). The values of these parameters were used in regression analysis to estimate the relationship between PWV and physiological parameters.

2. SYSTEM ARCHITECTURE

2.1 Bioimpedance Plethysmography Measurement System

Fig. 1 presents the bioimpedance plethysmography measuring system used in the current study. It includes a bioimpedance circuit, cuff control, pressure sensing circuit, and electrocardiography (ECG). The received physiological data were interpreted using an analogue-to-digital converter and subsequently transmitted to a computer. The user interface and data storage function was developed using National Instruments (NI) LabWindows. The signal analysis to obtain PWV parameters was accomplished using MATLAB software.

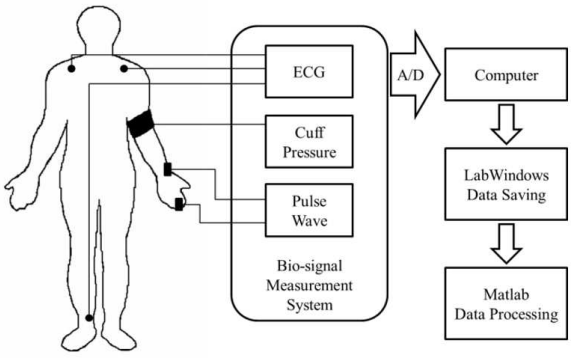

Fig.1: *System architecture of physiological signal measurement.*

2.2 Bioimpedance Circuit and Electrode

When arteries pulsate from the heart's pumping of blood, their vascular caliber changes. The change causes an increase in intravascular blood volume that alters bioimpedance. Therefore, vessel pulsation can be considered a parameter determined via a bioimpedance signal that varies as blood flow changes. Bioimpedance electrodes were constructed using eight copper electrodes with the following dimensions: size: 10×3 mm; thickness: 0.2 mm; and inter-electrode separation: 3 mm. These were affixed to a patient's radial artery and middle finger to measure PWV, as shown in Fig. 2. A quad-electrode method was used to create a constant current within two electrodes and apply the created current to the participants. The voltage differences between the other two electrodes affixed to the participants were also measured [8]. In this experiment, a constant current source was operated at a 50 kHz frequency with a 1 mA current. One of two outer electrodes was inserted into the constant current source and the other was used as the constant current sink. The two middle electrodes were used to measure the changes in pulse wave impedance.

The electric signals received by the electrodes were transmitted to an instrumentation amplifier (AD620,

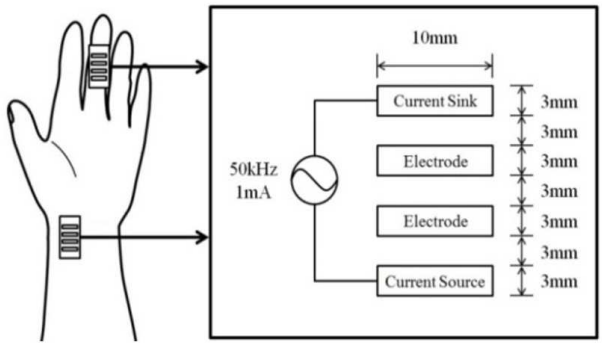

Fig.2: *Schematic diagram of a bioimpedance electrode.*

Analogue Devices) with a high common-mode rejection ratio to amplify differential signals. The AD620 operational amplifier is advantageous because of its following properties: high input impedance, high common-mode rejection ratio, and low noise. The measured alternating current signal was fed to the modulator. Then, a direct current signal was obtained. This signal was sent to an amplifier. Thus, the arterial pulsations reflected the magnitude of the voltage modulated. Subsequently, a bandpass filter was used to filter all noise other than the pulse frequency. The measurement system used a high-pass filter with a cut-off frequency of 0.48 Hz and a low-pass filter with a cut-off frequency of 5.3 Hz. Since the electric noise frequency of 50 Hz was higher than the cut-off frequency range of the low pass filter, no band exclusion filter was used in this study. After the aforementioned circuits were used, level adjustment and circuit amplifiers were implemented to transmit signals to a 12-bit analogue-to-digital converter to capture the digital data. Fig. 3 presents a circuit block diagram of this apparatus.

2.3 Cuff Pressure Sensing Circuit

The cuff pressure sensing circuit detects air pressure changes in the cuff and is measured with the aid of a differential pressure sensing element (SCC05DN, Honeywell Sensing and Control Co., Ltd). A pressure sensing component was adapted to measure cuff pressure changes to reduce the influence of temperature. The sensor also incorporates a temperature compensation circuit designed using the Wheatstone bridge principle. When a pressure was applied to the sensor, changes were generated in the electrical resistance of the bridge as shown in Fig. 4. The generated voltage difference is the output voltage defined as:

$$V_{os} = V_B \cdot \frac{2\Delta R}{R} \tag{1}$$

where V_{os} indicates the offset voltage (the output voltage was 0 when the pressure was applied), and V_B indicates the offset bridge voltage.

Electrical resistance is directly proportional to pressure, and the output voltage is as follows:

$$V_o = s \cdot p \cdot V_B + V_{os} \tag{2}$$

where V_o, s, and p denote output voltage, sensitivity coefficient, and pressure, respectively.

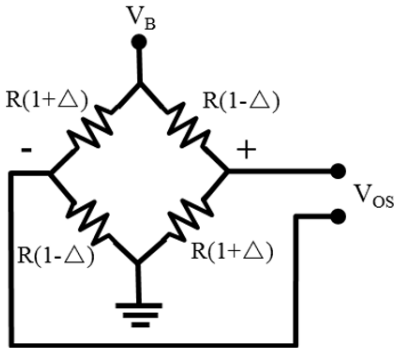

Fig.4: *The cuff pressure sensing circuit diagram.*

2.4 Electrocardiogram Measurement Instrument

The Ultraview SL2200, manufactured by Spacelabs Healthcare, was selected to measure and capture ECG signals. This equipment can output measured physiological signals through an analog output method, and facilitate back-end data processing. The aforementioned data received by the circuit were stored by a DAQ card USB-6351, manufactured by National Instruments, in the computer, and on the DAQ card. The DAQ card had a 16-bit ADC resolution that could accommodate 8 differential modes or 16 single-ended connections. Its sample rates were 1.25 MHz and 1.0 MHz for single channel and multichannel, respectively. In our system, the sampling rate was 10 kHz, and data were recorded into a raw data file, and simultaneously displayed to ensure the authenticity of the signals. After the measurements were completed, the raw data file was loaded into a customized MATLAB program for back-end signal processing.

2.5 Signal Processing

Before data were processed, the arm length, shoulder length, and length from the wrists to middle fingers of the participants were input for PWV calculation as shown in Fig. 5. After the participant data were read, signals were processed using a digital filter, and the pulse signal was processed using a third-order Butterworth low-pass filter with a cut-off frequency of 5.3 Hz. The ECG used a third-order high-pass filter and a low-pass filter with cut-off frequencies of 0.1 Hz and 20 Hz, respectively. The digital filter could further eliminate motion noise. Subsequently, the trough of the pulse wave was captured. The R

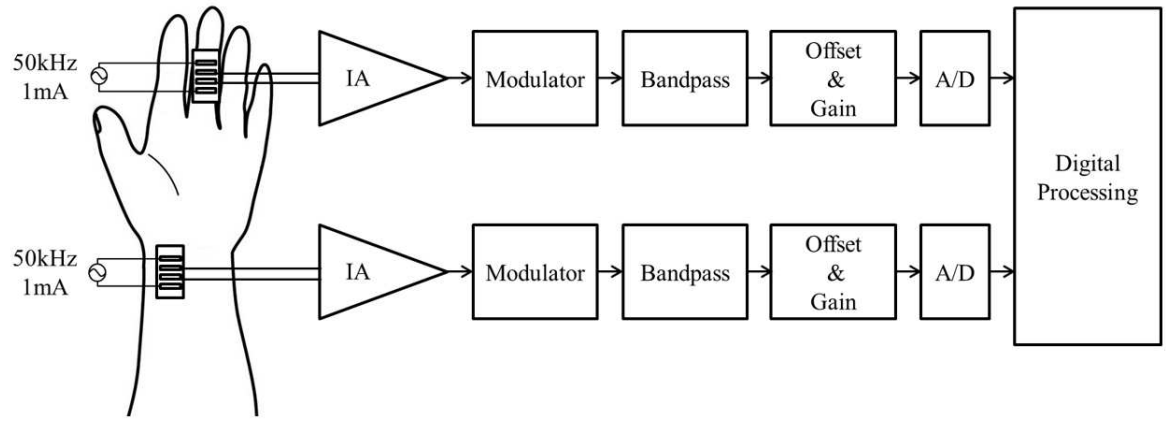

Fig.3: *Block diagram of the bioimpedance circuit.*

and T waves of the ECG were then obtained, and the PWV and heart rate were calculated. Finally, the results were shown on a screen, and the PWV was recorded for statistical analysis.

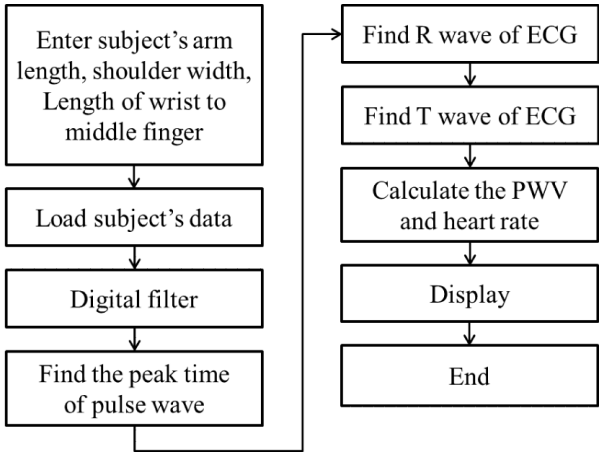

Fig.5: *Block diagram of signal processing.*

2.6 Graphical User Interface

Fig. 6 shows the graphical user interface (GUI) developed using LabWindows software (National Instruments). The far left boxes display the channel parameters and sample rate that could be adjusted accordingly. To ensure that the signal was not distorted, the sample rate was set at 10k Hz. Data were obtained and simultaneously stored in data files, which were then loaded by the system into the MATLAB program for back-end analysis. The graphic interface on the left displayed two electrical impedance pulse waves and the interface on the right showed the ECG signal and cuff pressure.

3. RESULTS AND DISCUSSION

3.1 Experimental Design

Demographic information of the participants was obtained at the beginning of the experiment. This included height, weight, body mass index (BMI), body fat, length from wrist to the middle finger, arm length, shoulder width, waistline, and blood pressure. These demographic data were then combined with PWV parameters for statistical analysis. Table 1 gives the demographic information of the ten participants in this study. After the demographic information was measured, the participants were asked to rest for 5 minutes, after which the measurement electrodes were affixed to the participants' bodies. The total measurement time was 5 minutes. During the first 2 minutes, the PWV and ECG signals of the participants were collected while the participants were in a relax state. Thereafter, the cuffs were inflated until the participant's blood flow was blocked. This was maintained for 5 seconds before the cuff was deflated, releasing the cuff pressure. Subsequently, participant PWV and ECG signals were measured for 2 minutes. Fig. 7 presents a flow chart of this experiment.

Table 1: *Basic physiological parameters of the participants.*

	Mean±SD	Max/Min
Height(cm)	169.5±4.27	176/163
Weight(kg)	67.29±7.98	81.8/54.6
Arm length(cm)	72.85±2.53	76/68
Shoulder width(cm)	44.4±2.33	48/41
Waistline (cm)	91.5±4.77	97.5/83
SBP(mmHg)	121.2±6.88	131/111
DBP(mmHg)	71.1±7.61	83/60
BMI(kg/m^2)	23.53±2.43	78/56
Body fat(%)	18.63±4.06	27.65/19.34
Age(years)	22.9±1.79	27/21
Length of wrist to middle finger(cm)	16.41±1.16	18/14

3.2 PWV Analysis

After data were measured, 2 minutes of pulse wave and ECG raw data were collected, before the cuffs were inflated and after they were deflated. Fig. 8 shows measuring electrodes and the image of the fixed electrode on a participant's hand. Several defined distances are shown in Fig. 9. This experiment defined three types of PWV parameters: (1) the PWV from the radial artery in the wrist to the middle finger (wfPWV), (2) the PWV from the ECG R wave to the middle finger (rfPWV), and (3) the PWV from the ECG T wave to the middle finger (tfPWV) which are computed as follows:

$$\text{wfPWV} = \text{D}_{\text{wf}}/\Delta\text{T}_{\text{wf}} \tag{3}$$

where D_{wf} refers to the distance from the electrode on the radial artery of the wrist to the electrode on the middle finger. $\Delta\text{T}_{\text{wf}}$ indicates the pulse wave time difference from the radial artery to the middle finger as in equation (3) and

$$\text{rfPWV} = \text{D}_{\text{rf}}/\Delta\text{T}_{\text{rf}} \tag{4}$$

Since the distance from the aorta to the middle finger was difficult to measure, the half shoulder width plus arm length was considered the distance defined as D_{rf}, and $\Delta\text{T}_{\text{rf}}$ represents the time difference of the peak ECG R wave to the middle finger of equation (4). The definition of tfPWV is as follows:

$$\text{tfPWV} = \text{D}_{\text{tf}}/\Delta\text{T}_{\text{tf}} \tag{5}$$

where $D_{tf} = D_{rf}$, and ΔT_{tf} indicates the time difference of the peak ECG T wave to the middle finger. Fig. 10 presents the pulse wave of the radial artery in the wrist, pulse wave of the middle finger, ECG, and a waveform with a length of approximately 3 seconds.

(a) (b)

Fig.8: *(a) Measuring electrodes, (b) Photo of fixed electrode on the wrist and finger.*

Table 2 shows the mean, standard deviation, maximum value and minimum value of the three types of PWV values of the participants before the cuffs were inflated and after they were deflated. According to Table 2, the numerical value of rfPWV was lower than that of wfPWV. Furthermore, the rfPWV distance was the length from the heart to the middle finger, representing the path from the aorta to the peripheral artery. The cardiac action corresponding to the ECG signal must be determined to evaluate whether rfPWV and tfPWV were substantial. According to

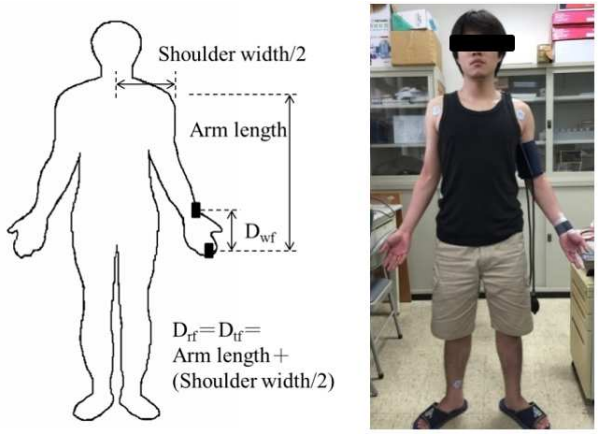

Fig.9: *Defined distances of D_{wf}, D_{rf}, and D_{tf}.*

medical literature, the phase in which the R wave occurs is the time immediately before the heart enters the systolic phase, during which the heart has not yet contracted. In other words, the heart does not pump blood at this phase. T-waves occur immediately after the heart completes the systolic phase and immediately before it enters the diastolic phase. During this phase, the aorta pumps blood systemically because of the recent contraction. The pulse wave measured in this study could be verified when the troughs between two pulse waves that occurred after the T wave. Since the definition of PWV is the speed at which a pulse wave propagates, the time reference point defined by rfPWV is unreasonable. Therefore, rfPWV values were discarded, and only wfPWV and tfPWV data were used for analysis. The results of this analysis were as follows.

Table 2: *Three types of PWV before cuff inflation and after cuff deflation.*

Status	Mean±SD	Max/Min
wfPWV before inflating	5.33±1.18	7.0/3.31
wfPWV after deflating	5.22±1.25	7.38/3.15
rfPWV before inflating	2.28±0.14	2.47/2.04
rfPWV after deflating	2.29±0.14	2.47/2.03
tfPWV before inflating	5.36±0.79	7.24/4.45
tfPWV after deflating	5.36±0.92	7.68/4.55

In this experiment, statistical analysis was used to determine whether PWV significantly differed before inflation and after deflation. A paired sample t-test was used to compare the results. The paired sample t-test employs data of the same individuals in a small sample (sample number < 30) measured at two different times. The confidence interval was 95%. According to Table 3, wfPWV and tfPWV were not significantly different. In other words, a temporary blood flow blockage caused no significant difference in the PWV of healthy people.

Multiple regression analysis was conducted to elucidate whether the physiological parameters (e.g.,

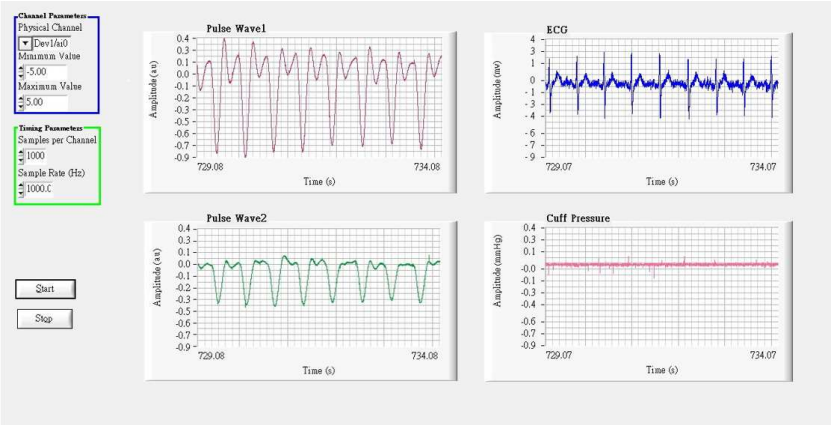

Fig.6: *Data display and storage interface using LabWindows.*

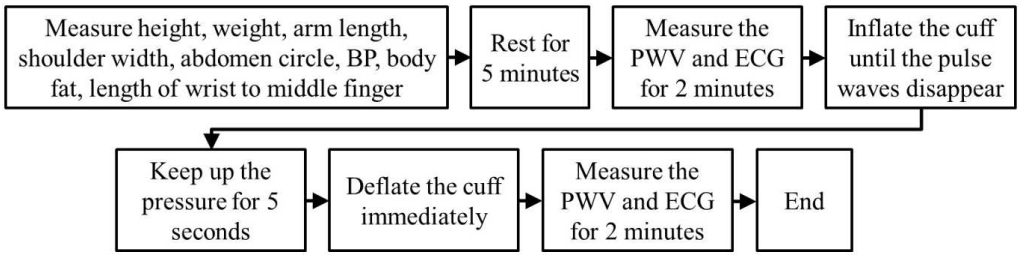

Fig.7: *Experiment flowchart.*

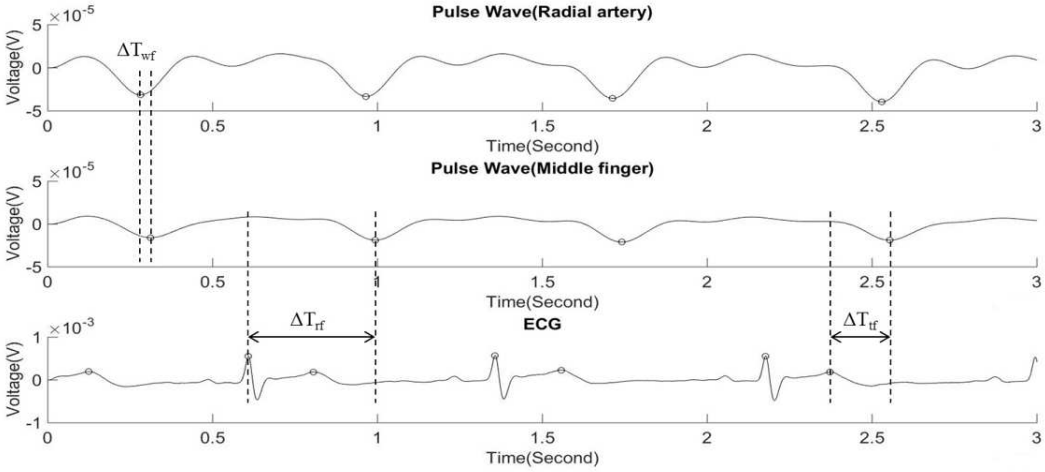

Fig.10: *Measured pulse waves and ECG.*

Table 3: *Paired sample t-test for wfPWV and tfPWV.*

Status	Mean	SD	Std. Error	Lower	Upper	t	df	Sig.(two-tailed)
wfPWV before inflating wfPWV after deflating	0.114	0.485	0.153	-0.233	0.462	0.745	9	0.475
tfPWV before inflating tfPWV after deflating	0.001	0.274	0.087	-0.195	0.196	0.007	9	0.995

height and weight) influenced PWV and could be used to estimate PWV. Multiple regression analysis is a statistical method that uses several parameters to predict reaction variables (i.e., PWV in this study). However, these physiological parameters were correlated to PWV. Thus, stepwise selection was used in the regression model. This model introduces one variable at a time and examines all previously selected variables after introducing a new variable into the equation to ensure that the variables retain statistical significance. In this way, a regression equation for PWV can be obtained using these variables. Before cuff inflation, the PWV was equal to the PWV measured at an ordinary state. Thus, in the subsequent evaluations, PWV obtained before cuff inflation to conduct statistical analyses. After the analyses, the variables selected for wfPWV were waistline and height, with R = 0.893 and R^2 = 0.798. The regression equation was:

$$\text{wfPWV} = -0.195 \cdot X_{ab} + 0.168 \cdot X_h - 5.315 \quad (6)$$

where X_{ab} and X_h denote waistline and height, respectively. The variables selected for tfPWV were systolic blood pressure (SBP) and diastolic blood pressure (DBP), with R = 0.898 and R^2 = 0.806. The regression equation was:

$$\text{tfPWV} = 0.109 \cdot X_{SBP} - 0.05 \cdot X_{DBP} - 4.226 \quad (7)$$

X_{SBP} represents SBP and X_{DBP} denotes DBP.

Table 4 presents a correlation of wfPWV and tfPWV with various physiological parameters. It indicates that wfPWV and tfPWV were significantly correlated. Several physiological parameters were also significant. SBP was significantly correlated with wfPWV and tfPWV. Additionally, after multiple regression analysis was done, two physiological parameters were used as the input variables of the equation. According to the regression model selected in this study, even though the other parameters could be surmised to be correlated to PWV, the multiple regression analysis indicated that they were not significant after these variables were incorporated. Moreover, the other physiological parameters may exhibit severe collinear relationships, which can influence the results of the regression analysis.

Table 4: *Correlation coefficient table for wfPWV and tfPWV.*

Parameters	wfPWV	tfPWV
wfPWV	1	0.77**
tfPWV	0.77**	1
Height	0.445	0.354
Weight	-0.333	-0.273
Arm length	0.426	0.778*
Shoulder width	0.08	0.092
Waistline	-0.699*	-0.389
SBP	0.673*	0.728*
DBP	-0.34	-0.152
Heart rate	-0.252	-0.763
BMI	-0.624	-0.43
Body fat	-0.648*	-0.6
Age	-0.104	0.045
Length of wrist to middle finger	0.395	0.31

$^{*}p < 0.05, ^{**}p < 0.01$

4. CONCLUSIONS

In this study, pulse waves were measured from the finger, indicating that they can be measured from peripheral areas of the body in addition to the radial artery in the wrist. The pulse waves measured from these two areas were combined with ECG data to calculate the three types of PWV (i.e., wfPWV, rfPWV, and tfPWV). Considering the stages of a cardiac cycle, this study determined that the time defined by rfPWV was inappropriate for evaluating PWV. For statistical analyses, a paired sample t-test was employed, and temporary blood flow blockage was shown to have no substantial influence on the PWV of healthy people. Moreover, a multiple regression analysis was done to establish an equation to estimate wfPWV and rfPWV and determine the correlation between the physiological parameters (e.g., height and weight) and PWV. Results showed that the independent variables for the regression equation of wfPWV were waistline and height (r = 0.893). The independent variables for the regression equation of tfPWV were the systolic and diastolic blood pressures (r = 0.898). Additionally, correlation between other physiological parameters such as height and PWV was shown. wfPWV and tfPWV were significantly correlated (r = 0.770, $p < 0.01$) and were also associated with waist circumference, systolic blood pressure, and body fat (r = −0.699, r = 0.673 and r = −0.648, $p < 0.05$). tfPWV and arm length (r = 0.778, $p < 0.01$), systolic blood pressure and heart rate were correlated (r = 0.728 and r = −0.763, $p < 0.05$).

During the experiment, the noise caused by bodily movements strongly influenced signal quality. Thus, reduction or elimination of these noises was necessary to improve the measurement system. Moreover, in this experiment, only the PWV of healthy people was measured. Future experiments should incorporate measurement data of patients with cardiovascular diseases for comparison with the data of healthy people to increase the reference data that can be applied for diagnosing peripheral vascular arteriosclerosis.

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