Correlation of Harmonic Components between the Blood Pressure and Photoplethysmography Waveforms Following Local-Heating Stimulation

H. Hsiu, C. L. Hsu, C. T. Chen, W. C. Hsu, H. F. Hu, and F. C. Chen

Abstract—**Photoplethysmography (PPG) involves measuring an optic signal related to the arterial volumetric pulsations of blood, and has great potential in clinical applications due to its simplicity and noninvasiveness. In the present study, we aimed to verify if the induced vasodilation and increase in terminal blood supply by local heating stimulation (LH) could help to improve the correlation of harmonic components between radial BP and finger PPG waveforms. Trials were performed on male healthy volunteers (n=17) aged 25-31 years. LH was performed by placing a waterbag filled with 35°C water around the lower arm. BP and PPG spectra were calculated from the averages of all of the pulses during the entire measurement period for the amplitude proportion. For the first three harmonics, the correlation coefficients for the regression lines between BP and PPG waveforms were significantly increased following LH. The present result illustrated improved BP-PPG correlations of harmonic components following LH. It implies that an appropriate environmental temperature could improve the reconstruction of the BP waveform from noninvasive PPG measurements. The present frequency-domain analysis method could thus provide an alternative and more convenient method for acquiring the BP waveform, and hence bring new study directions for further applications such as in evaluating whole-body responses of the microcirculatory blood supply to various treatment strategies, the augmentation index calculation, and telemedicine.**

Index Terms—**Harmonic analysis, local heating, photoplethysmography.**

I. Introduction

Photoplethysmography (PPG) is an optical measurement technique used to monitor blood volume changes in microvascular beds of peripheral tissue, and also to monitor arterial pressure and compliance, with great potential in clinical applications due to its simplicity and noninvasiveness. Since the blood pressure (BP) inside an artery distends the vessel wall, changes in BP can be correlated with changes in the vessel volume and thus the PPG signal [1], [2].

The arterial stiffness is suggested to affect the propagation velocity of the pulse wave (PWV), and the wave reflection can be altered by changes in the perfusion condition of the peripheral vascular beds. Time-domain index based on arterial pulse-wave analysis, such as PWV and augmentation index, could thus help in establishing the extent of cardiovascular disease and in monitoring the effects of therapies [3].

However, time-domain waveforms can be distorted by various types of small perturbation, especially on the peak point (which leads to an erroneous PTT value) or the other parts of the pulsatile PPG waveform (which can lead to errors in calculating the pulse width) [1], [2]. It might limit practical applications of the time-domain PPG waveform index. Since the frequency ranges can be separated from the main components of the signal of interest, frequency-domain analysis can be less affected by some important types of interferences (e.g., motion artifacts and 50-/60-Hz noise) compared with time-domain analysis. For example, frequency-domain analysis has been applied to BPW to monitor the distribution function of the blood supply and to predict outcomes for important cardiovascular diseases [4, 5], and to the PPG signal to study autonomic nervous control of the peripheral circulation [6].

Nonpainful local heating (LH) evokes vasodilation that is mediated by neurogenic reflexes and locally released substances. The enhancement the blood circulation following LH may result in an increased metabolic rate and transport of metabolities and other essential biochemical compounds. Thermal hyperemia has been used to assess endothelial function, allowing the assessment of NO-dependent vasorelaxation reported as the amplitude of the second peak.

We previously demonstrated that an appropriate contact pressure could improve the reconstruction of the BP waveform (BPW) from noninvasive PPG measurements and frequency-component analysis [1]. In the present study, we aimed to verify if the induced vasodilation and increase in terminal blood supply by local heating stimulation (LH) could help to improve the correlation of harmonic components between radial BP and finger PPG waveforms. Such a technique might be useful in developing a new noninvasive index for monitoring the blood-flow condition at local vascular beds induced by LH or other types of treatment strategies that improve local blood supply.

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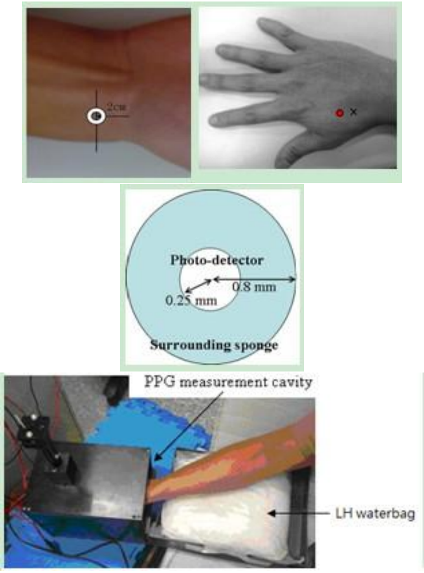

Fig. 1. Illustration of the setup for the sensors and LH apparatus. (a) Location of BP measurements. The pressure transducer was placed on the skin surface above the radial artery at 2 cm from the wrist. (b) The LDF measurement site (O) and the thermistor site (X) located on the back of the right hand. (c) A view looking vertically down on top of the finger for the PPG measurement. The hole beneath the middle finger allows light from the LED to reach the photodiode. (d) Illustration of the PPG measurement and Illustration of the PPG measurement and LH setup. The finger was inserted into the black-walled measurement cavity, and the LH was applied to the skin surface of the right upper arm.

II. Methods and Materials

A. Experimental Procedure

17 trials were performed on male healthy volunteers aged 25-31 years and without signs or symptoms of cardiovascular or neurological disease. The subjects were lightly clothed, supine, and were allowed to stabilize for at least 10 minutes before recording commenced. The subjects were enquired about their psychological condition to prevent the interference effect. The environmental temperature was within 23-25 ℃ during the entire measuring period. All subjects gave their informed consent before experiments commenced, were asked to not take any medication for 3 days before experiments, and did not consume food at least 1 hour before each experiment. All subjects were non-smokers, and did not take coffee or drinks containing alcohol at least 1 day before experiments [1], [2].

The LH was applied by placing a waterbag filled with 2000-cc 35-37oC water around the right lower arm, and ECG, PPG, LDF and BPW signal were measured simultaneously and noninvasively. ECG signals were measured by surface electrodes, and acquired by a preamplifier (lead II, RA-LL; 6600-series, Gould, USA). BPW was measured by a pressure transducer (Kyowa_KFG-2-120-D1-11). This device is linear within ±0.1% of the rated output and has a flat frequency response between 0-5 kHz. A 1.5-cm-wide plastic belt was used to hold the pressure sensor around the right wrist. LDF (MBF3, Moor Instruments, UK) was used for measuring the skin-surface MBF on the back of the right hand. The PPG signal from a 940-nm-wavelength infrared LED (QED233, Fairchild Optoelectronic) penetrating the finger tissue was acquired by a photodiode (L-SB1R9PD1D1, Para, Japan). When performing PPG measurements, subjects were instructed to put the right middle finger into a self-made measurement cavity that had a black inner wall to reduce interference from light leakage. A hand-shaped mold was placed under the palm to improve the positioning reproducibility of the hand and finger. A contact pressure was applied around the first knuckle of the finger using a 3-mm-thick sponge as a force cushion. The vertically applied pressure was precalibrated and monitored by a force gage (1000gw, OHBA SIKI, Japan) to be around 60 mmHg to improve the PPG measurement stability and to reduce user discomfort. The BP signal was connected to a preamplifier (UV-10, Sensotec), the PPG signal was connected to a self-made current-to-voltage converter circuit, and all signals were then connected to an analog-to-digital converter card (PCI-9111DG, Adlink Technology, Taiwan) operating at a sampling rate of 1024 Hz [1], [2].

The experimental and measurement procedure is shown in Fig. 2. For each experiment, we recorded a 3-minute baseline-data sequence (*M*0), applied local mild LH and recorded a 3-minute effect sequence (*M*1), and then recorded another 3-minute effect sequence right after stopping the stimulation (*M*2). Before and after the whole procedure, we measured fundamental physiological parameters of the subject, including HR, systolic BP (SBP), and diastolic BP

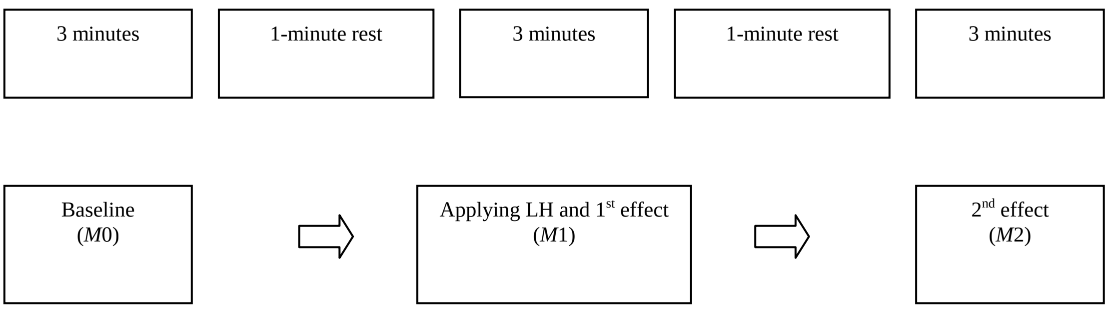

Fig. 2. Experimental and measurement procedure.

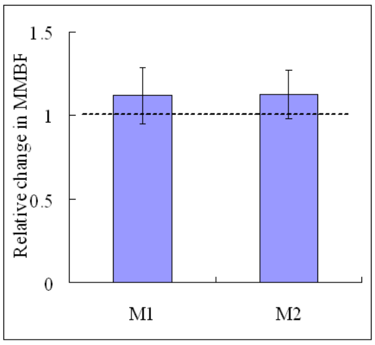

Fig. 3. Relative changes (defined as [$M1$ or $M2$ values] / [$M0$ value]) of MMBF following LH. Both $p<0.05$ compared with the baseline ($M0$) value by two-tailed t-test

(DBP) using a sphygmomanometer (MediGuard 150i, Rossmax). One thermistor was attached to monitor the contact temperature between the skin surface and the waterbag. The acceptable range for the temperature stability during the baseline period was a temperature variation of less than 1.0 ℃.

B. Signal Analysis

For the LDF signals, the mean MBF (MMBF) was defined as their average values during each 3-minute data sequence. The PPG and BP signals were first passed through a digital 11th-order high-pass Chebyshev filter with a cut-off frequency of 0.01 Hz to eliminate the baseline drift. To determine each beat-to-beat waveform, the two neighboring minima of a signal helped to identify the cut points to define the pulse [2].

In harmonic analysis, the acquired BPW or PPG pulse [$x(t)$] can be represented by the following finite series:

$$x(t)=\frac{A_0}{2}+\{\sum_{n=1}^{k/2}A_n\cos n\omega t_s+\sum_{n=1}^{k/2}B_n\sin n\omega t_s\}$$

The Fourier coefficients (A_n and B_n) of the BPW pulse can be calculated by

$$A_n=\frac{2}{k}\sum_{s=0}^{k}x_s\cos n\omega t_s\quad(\text{for } n=0,1,...,\frac{k}{2})$$

$$B_n=\frac{2}{k}\sum_{s=0}^{k}x_s\sin n\omega t_s\quad(\text{for } n=0,1,...,\frac{k}{2})$$

where ω is the angular frequency and t_s is the sampling time interval. The amplitude (Amp_n) and phase angle (P_n) of each harmonic can then be calculated by $Amp_n=\sqrt{A_n^2+B_n^2}$ and $P_n=\tan^{-1}(B/A)$, respectively.

BPW and PPG spectra were calculated from the averages of all of the pulses during the entire measurement period for the amplitude proportion (C_n) of the nth harmonic according to Amp_n/Amp_0 × 100% for n=1 to 10, where Amp_n is the amplitude of the nth harmonic of the BPW and Amp_0 is the DC component of the pulse spectrum. Signal processing was performed with MATLAB. Differences were considered significant when $p<0.05$. Linear regression was applied onto the harmonic components between the BPW and PPG waveforms to study the correlation between them.

III. Results

The fundamental physiological parameters did not change significantly between before and after the LH ($p>0.2$ by two-tailed paired t-test). As shown in Fig. 3, MMBF was significantly increased following LH, which illustrated prominent influences on local MBF supply.

TABLE I: Baseline Values ($M0$) of C_n (in %) of the BPW and PPG Waveforms.

Harmonic number	BPW		PPG	
	mean	SD	mean	SD
1	18.59	1.44	20.29	1.53
2	12.94	2.24	11.59	2.28
3	10.59	1.53	8.32	1.47
4	4.98	0.80	4.07	0.81
5	3.63	0.65	2.90	0.43
6	2.18	0.64	1.83	0.35
7	1.09	0.34	1.09	0.21
8	0.70	0.17	0.78	0.16
9	0.53	0.15	0.59	0.13
10	0.35	0.12	0.43	0.11

TABLE II: Baseline Values ($M0$) of P_n (in Degrees) of the BPW and PPG Waveforms.

Harmonic number	BPW		PPG	
	mean	SD	mean	SD
1	259.22	5.22	239.35	6.31
2	243.33	11.02	213.53	13.95
3	179.14	21.05	167.32	20.59
4	141.34	21.27	146.08	25.95
5	113.02	29.96	138.08	31.66
6	69.79	35.98	159.28	25.44
7	45.39	38.24	162.09	15.80
8	45.71	66.29	160.48	10.45
9	26.01	71.57	157.34	7.90
10	34.94	85.42	154.88	5.81

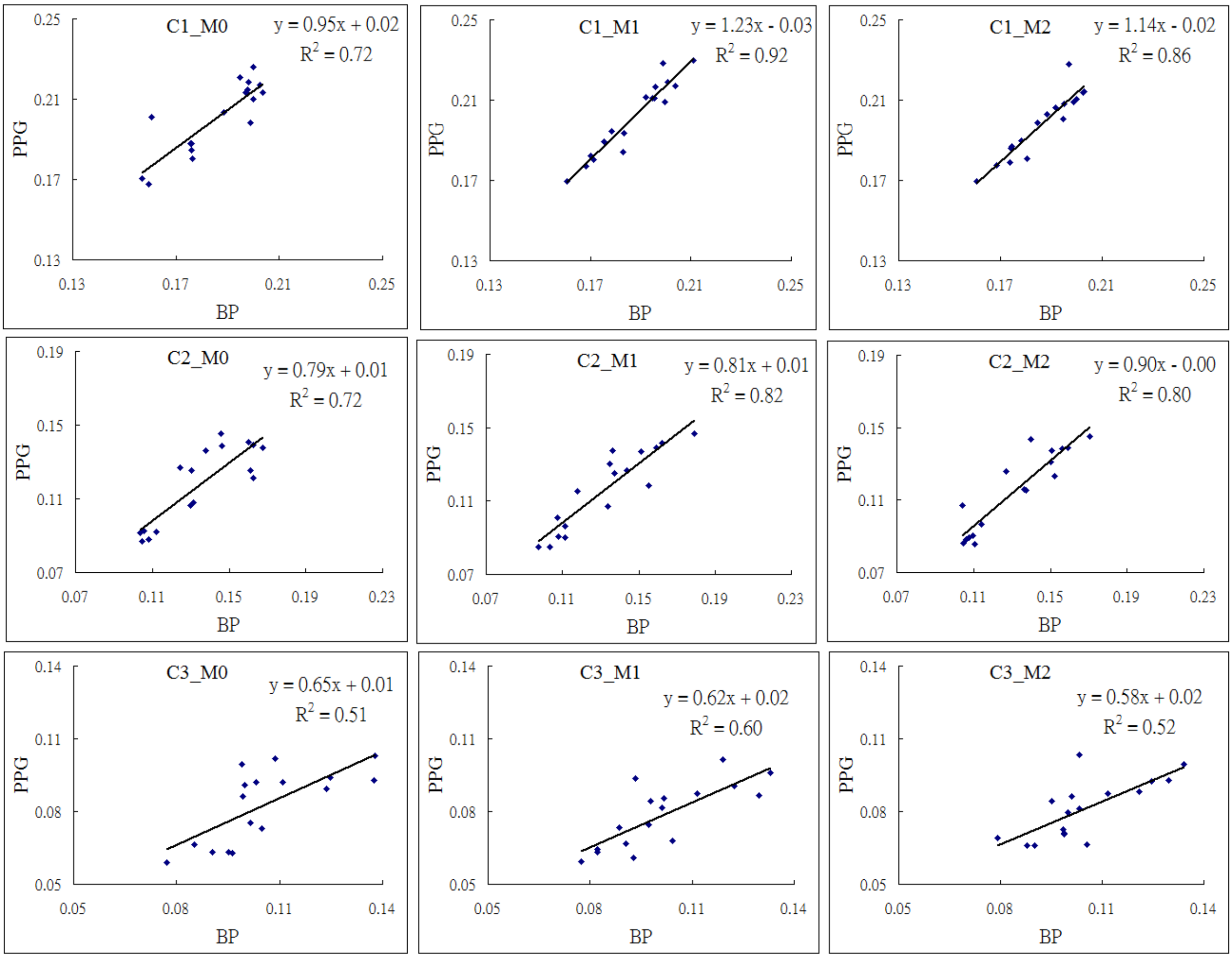

Fig. 4. Linear regression of the first three harmonic components (C_n, the amplitude rations) between BPW and PPG waveforms following LH.

TABLE III: CORRELATION COEFFICIENTS (R^2) OF THE REGRESSION LINE OF HARMONIC COMPONENT (C_n) BETWEEN BPW AND PPG WAVEFORMS.

	*M*0	*M*1	*M*2
*C*1	0.72	0.92	0.86
*C*2	0.72	0.82	0.83
*C*3	0.51	0.60	0.52
*C*4	0.0049	0.02	0.0067
*C*5	0.14	0.0064	0.0232
*C*6	0.0087	0.2398	0.0657
*C*7	0.0003	0.2304	0.0017
*C*8	0.0672	0.4672	0.0794
*C*9	0.0378	0.2282	0.1326
*C*10	0.0917	0.2608	0.1281

As listed in Table III and shown in Fig. 4, the correlation coefficients of the regression line of the first three harmonic component (C_n, the amplitude ratios) between BPW and PPG waveforms were improved (increased) following the present mild LH.

TABLE IV: CORRELATION COEFFICIENTS (R^2) OF THE REGRESSION LINES OF THE PHASE ANGLE OF EACH HARMONIC COMPONENT (P_n) BETWEEN BPW AND PPG WAVEFORMS.

	*M*0	*M*1	*M*2
*P*1	0.15	0.24	0.21
*P*2	0.54	0.49	0.52
*P*3	0.56	0.55	0.64
*P*4	0.33	0.11	0.27
*P*5	0.17	0.00	0.18
*P*6	0.02	0.05	0.00
*P*7	0.04	0.03	0.01
*P*8	0.00	0.04	0.23
*P*9	0.00	0.01	0.09
*P*10	0.04	0.03	0.10

As listed in Table IV and shown in Fig. 5, following the present mild LH, there were no such prominent baseline-effect differences of correlation coefficients in P_n (phase angle) as in those of C_n. However as revealed in Table 5, the sum of the squared residuals between BPW and PPG waveforms were improved (decreased) in most of the harmonics, either during M1 or *M*2.

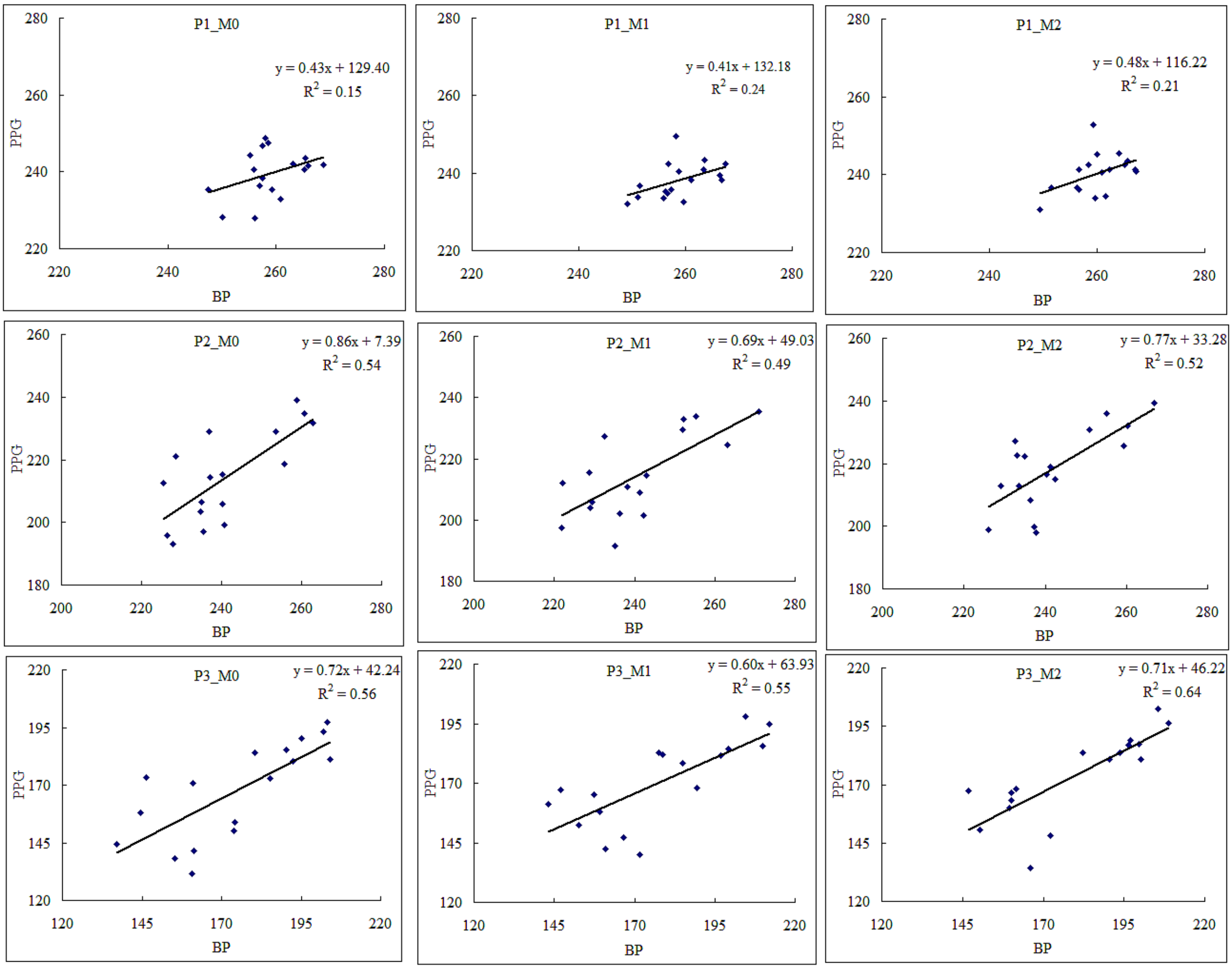

Fig. 5. Linear regression of the first three harmonic components (P_n, the phase angles) between BPW and PPG waveforms following LH.

TABLE V: SUM OF THE SQUARED RESIDUALS (SSRESID) OF THE REGRESSION LINES OF THE PHASE ANGLE OF EACH HARMONIC COMPONENT (P_n) BETWEEN BPW AND PPG WAVEFORMS.

	*M*0	*M*1	*M*2
*P*1	522	261	347
*P*2	1571	1534	1231
*P*3	3085	2295	1927
*P*4	8182	5921	5502
*P*5	17968	13064	15415
*P*6	11899	20467	11863
*P*7	4427	3712	2574
*P*8	2147	1149	709
*P*9	851	554	302
*P*10	285	274	195

IV. DISCUSSION

Based on the present result, we have demonstrated that although the present LH was mild (in order to minimize interference of other physiological mechanisms to focus the discussion), harmonic-analysis index of BP and PPG waveforms, possible indicators of wave transmission, were significantly changed. In performing linear regression, the correlation coefficient is suggested to correspond to the explain ability for the parameter variations, whereas the Sum of the squared residuals can be used to correspond to the dispersion condition from the regression line of the data points. Applying LH to the skin surface of the PPG measurement site had a prominent effect on the PPG waveform. The regression between the radial-artery BP and finger PPG waveforms was improved either in the amplitude or in the phase angle, which implies that using an appropriate applied LH could improve the reconstruction of the BP waveform from noninvasive PPG measurements. Significant differences in MMBF of LDF signals were noted, whereas absence of significant difference in fundamental physiological parameters illustrated no prominent induced whole-body effect following the present mild LH, which ensured local response and minimized the interference of other sensational effect induced by LH.

It is possible that the temperature rising can increase the blood flow supply in the underlying vascular beds of the finger. The pulsation of the local arteries was increased, and therefore the index of the PPG waveform can aid the monitoring of the change in the local microcirculatory condition. As blood fills the microvascular beds, it might enhance the resistance ability for the vessels against various external interfering factors on the coupling between the radial artery and the finger vessels, and hence produce a reliable transfer relation between finger PPG and radial-artery BP waveforms.

BP waveform is an important and widely-used factor to aid the prediction or diagnosis of circulation diseases. For example, arterial pulse-wave analysis has been employed widely in clinical practice, such as in hypertension, cardiac failure, and aging [7]. The time-domain augmentation index describes characteristic changes in the pulse waveform induced by aging [7], [8] diseases [9], and also cardiovascular events in coronary and end-stage renal disease patients [10]. In frequency-domain BPW analysis, it has been suggested that individual vascular beds exert independent, frequency-specific, and linearly additive effects on the peripheral pressure wave, and hence that harmonic analysis of the BPW could elucidate the physical status of specific vascular beds [11]. This illustrates the possible relation between harmonic components within BPW and the peripheral blood supply [2], [12]-[14].

In our previous works, we try to build up a novel PPG measurement system. Two features of our PPG system are an appropriate contacting pressure imposed on the measured finger and a hand-shape mold used to fix the position of the palm and the finger. It has been revealed that not only the user-friendliness of the PPG measurement is improved; the waveform reproducibility between repeated measurement is also small enough, with the potential to discriminate human circulatory condition [1], [2]. Based on the stability of the acquired PPG waveform parameter by using our self-made system, we can further study the correlation of frequency components between BP and PPG waveforms with higher reliability. The frequency-domain analysis may help to overcome the problem that the time-domain BPW can often be easily distorted by various forms of interferences or noises, and thus may aid the improvement of physiological discriminating ability of BPW analysis.

The finding of the present preliminary study suggests that the responses of harmonic index of BP and PPG waveforms can be used to quantify the microcirculatory to LH, possibly due to providing more detailed information about the pulse transmission of each frequency components. Since blood supply is essential to the physiological function of local tissue, the present finding provides new insight into the cardiovascular responses to LH, and could have meanings in developing index to improve the resolving ability for the arterial elastic properties induced by LH, other forms of stimulation, or pathological factors.

The pulse waveform can vary between different sites along the arterial transmission. The BP pulse contour is often difficult to assess noninvasively, except for some specific sites such as the skin surface of the radial artery or the carotid artery. Compared with BP measurement, assessing PPG waveform is easier on many sites, such as the downstream site (the finger) of the radial artery. This advantage of PPG measurement may facilitate an easier and more user-friendly method to noninvasively evaluate the condition of arterial pulse transmission [2]. More researches can be devoted to further simplify user's operation, to improve the measurement reliability, and to study the parameter responses under various physiological or pathological stimulations. The present finding could provide a new solution for the practical application of PPG measurement, and may be pertinent to monitoring of disease progression, evaluation of treatment efficacy, and to the medical-device development for application in point-of-care system, home-care device, or in telemedicine.

REFERENCES

[1] H. Hsiu, C. L. Hsu, and T. L. Wu, "Effects of different contacting pressure on the transfer function between finger photoplethysmographic and radial blood pressure waveforms," *P. I. Mech. Eng. H.*, vol. 225, no. H6, pp. 575-584, 2011.

[2] H. Hsiu, S. M. Huang, C. L. Hsu, S. F. Hu, and H. W. Lin, "Effects of cold stimulation on the harmonic structure of the blood pressure and photoplethysmography waveforms," *Photomed. Laser Surg.*, vol. 30, no. 2, pp.77-84, 2012.

[3] M. F. O'Rourke, A. Pauca, and X. J. Jiang, "Pulse wave analysis," *Br. J. Clin. Pharmacol.*, vol. 51, pp.507–522, 2001.

[4] M. G. Taylor, "Use of random excitation and spectral analysis in the study of frequency dependent parameters of the cardiovascular system," *Circ. Res*., vol. 18, pp. 585-595, 1966.

[5] L.Y. Wei and P. Chow, "Frequency distribution of human pulse spectra," *IEEE. Trans. Biomed. Eng.*, vol. 32, pp. 245-246, 1985.

[6] M. Nitzan, A. Babchenko, and B. Khanokh, "Very low frequency variability in arterial blood pressure and blood volume pulse," *Med. Biol. Eng. Comput.*, vol. 37, no. 1, pp. 54-58, 1999.

[7] K. Kohara, Y. Tabara, A. Oshiumi, Y. Miyawaki, T. Kobayashi, and T. Miki, "Radial augmentation index: A useful and easily obtainable parameter for vascular aging," *Am. J. Hypertens*, vol. 18, pp. 11S–14S, 2005.

[8] R. Kelly, C. Hayward, A. Avolio, and M. F. O'Rourke, "Nonivasive determination of age-related changes in the human arterial pulse," *Circulation* vol. 80, pp. 1652–1659, 1989.

[9] G. M. London, J. Blacher, B. Pannier, A. P. Guerin, S. J. Marchais, and M. E. Safa, "Arterial wave reflections and survival in end stage renal failure," *Hypertension* vol. 38, pp. 434–438, 2001.

[10] S. Zoungas and R. P. Asmar, "Arterial stiffness and cardiovascular outcome," *Clin. Exp. Pharmacol. Physiol.* vol. 34, no. 7, pp. 647-651, 2007.

[11] Y. Y. Wang Lin, T. L. Hsu, M. Y. Jan, and W. K. Wang, "Theory and applications of the harmonic analysis of arterial pressure pulse waves," *J. Med. Biol. Eng*., vol. 30, no. 3, pp. 125-131, 2010.

[12] C. T. Chen, S. M. Huang, H. Hsiu, W. C. Hsu, F. C. Lin, and H. W. Lin, "Using a blood pressure harmonic variability index to monitor the cerebral blood flow condition in stroke patients," *Biorheology*, vol. 48, no. 3, pp. 219-228, 2011.

[13] H. Hsiu, P. T. Chao, W. C. Hsu, M. Y. Jan, Y. Y. Wang Lin, and W. K. Wang, "The possible role of arterial radial vibration in heart rate and blood pressure matching," *P I Mech Eng H*, vol. 222, no. H5, pp. 773-779, 2008.

[14] H. Hsiu, S. M. Huang, and T. L. Hsu, "Evaluation of the function of arteriolar opening by variability in microcirculatory blood flow following angiotensin II administration in rats," *Biorheology*, vol. 47, no. 3, pp. 239-253, 2010.