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CAN PHOTOPLETHYSMOGRAPHY VARIABILITY SERVE AS AN ALTERNATIVE APPROACH TO OBTAIN HEART RATE VARIABILITY INFORMATION?

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Lu S, Zhao H, Ju K, Shin KS, Lee MH, Shelley K, Chon KH. Can photoplethysmography variability serve as an alternative approach to obtain heart rate variability information?
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ABSTRACT. Heart rate variability (HRV), extracted from an electrocardiogram, is known to be a noninvasive indicator reflecting the dynamic interplay between perturbations to cardiovascular function and the dynamic response of the cardiovascular regulatory system. Photoplethysmography (PPG) is a noninvasive method to monitor arterial oxygen saturation on a continuous basis. Given the rich cardiovascular information in the PPG signal, and the ubiquity and simplicity of pulse oximetry, we are investigating the feasibility of acquiring dynamics pertaining to the autonomic nervous system from PPG waveforms. To do this, we are quantifying PPG variability (PPGV). Detailed algorithmic approaches for extracting accurate PPGV signals are presented. We compare PPGV to HRV by computing time and frequency domain parameters often associated with HRV measurements, as well as approximate entropy calculations. Our results demonstrate that the parameters of PPGV are highly correlated with the parameters of HRV. Thus, our results indicate that PPGV could be used as an alternative measurement of HRV.

KEY WORDS. autonomic nervous system, heart rate variability, pulse oximeter.

INTRODUCTION

As a non-invasive means to monitor arterial oxygen saturation (SaO_2) on a continuous basis, pulse oximetry is a well-established technology based on photoplethysmography that has become one of the most commonly used patient monitoring devices during anesthesia and in intensive care units. Given the ubiquity and simplicity of pulse oximetry, it is desirable to maximize its potential by exploring additional measurements we can derive from the pulse oximeter. In the present study, our goal was to determine if variations in the PPG signal can be used in lieu of heart rate variability (HRV) to extract dynamics pertaining to the autonomic nervous system.

HRV reflects the dynamic interplay between perturbations to cardiovascular function and the dynamic response of cardiovascular regulatory systems. It is clear from a work by Akselrod et al. [2] in the early 1980s, as well as numerous publications since, that maintaining ANS balance is important for cardiovascular health. Numerous studies have shown that altered variability in

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the cardiovascular system is associated with a range of cardiovascular diseases and increased mortality [1, 9]. Cardiovascular variables such as heart rate, arterial blood pressure, and stroke volume, as well as lung volume, fluctuate on a beat-to-beat basis. The variability in cardiovascular signals reflects the homeostatic interplay between perturbations in cardiovascular functions and the dynamic responses of the cardiovascular regulatory systems [1, 6]. Thus, the normal heart rate is determined by many interacting systems, including the nervous system, baro- and chemoreceptors, local feedback loops in the heart, and several hormonal systems. These systems work on different time scales, and the complexity of this regulation is reflected in the apparently random fluctuations in heart rate [5]. There is considerable interest in these fluctuations because their simple statistical measures such as the standard deviation of the interbeat intervals (the *R–R*-intervals), have been shown to be some of the strongest independent predictors of mortality after myocardial infarction [10]. Moreover, other techniques such as spectral analysis and nonlinear analysis of the *R–R*-intervals of heart rate have been widely used in HRV studies, and on some occasions they have been shown to discriminate between subjects with different cardiac conditions as well as to predict mortality in some groups of patients [3, 9].

To date, only a few studies have demonstrated the use of PPG variability as a noninvasive measure of the dynamics pertaining to the autonomic nervous system, but none of these studies have provided detailed and direct quantitative comparison between the PPG and ECG signals [4, 11]. These studies were mainly based on the use of the pulse oximeter to examine specific cardiovascular problems that are associated with the autonomic nervous system. For example, one study has noted that in diabetic autonomic neuropathy patients, the rate of fall in percentage of oxygen saturation was significantly lower, less intense, and with delayed subsequent recovery compared to normal subjects [11]. In a separate study, recordings of the pulse oximeter waveforms during the Valsava maneuver were useful in rapid pre-operative identification of patients who have an autonomic neuropathy [4]. It is not surprising that only scant reports exist of using PPG variability as a noninvasive measure of the dynamics underlying the autonomic nervous system, since the rich information the pulse oximeter provides has only recently been appreciated. As the rise and fall of the PPG signal reflects the fluctuations of the heart beats, it is possible that PPG variability does reflect the dynamics of the autonomic nervous system. Our results show that this very hypothesis is feasible and that we can obtain similar information to that from HRV analysis. The significance of using the PPG instead of the ECG is that this allows multi-functionality of the pulse oximetry, which would simplify many facets of monitoring systems, reduce healthcare costs, provide a more compact system, and the home health care monitoring more attainable.

METHOD

Ten healthy subjects were involved in the study (26 ± 7.47 years). Twenty minutes (10 min in the upright position and 10 min in the supine position) of PPG waveform data (pulse oximeter module MP506, Nellcor Puritan Bennett) and ECG signal (HP 78354A patient monitor) were collected simultaneously and digitized with a sampling rate of 400 Hz (Powerlab 4SP, ADInstruments). HRV was obtained from ECG signals after R-wave peaks were detected, followed by cubic spline interpolation.

The PPG waveforms were denoised and detrended with empirical mode decomposition method (EMD) [12]. The EMD is based on a concept that any signal $x(t)$ can be decomposed into a finite number of ''intrinsic mode functions'' (IMFs):

$$x(t) = \sum_{i=1}^{n} IMF_i + r_n$$

where r_n is a residue. An IMF is a function that satisfies two conditions:

(1) The number of extrema and the number of zero crossings must either be equal or differ at most by one.
(2) At any point the mean value of the envelope defined by the local maxima and the envelope defined by the local minima is zero.

IMFs represent oscillatory modes embedded within data where each IMF involves only one mode of oscillation. The EMD algorithm has been widely applied [7, 8], and thus, we only briefly summarize the following four steps:

(1) Given the signal $x(t)$, identify the successive extrema of $x(t)$. Extract the upper and lower envelopes by interpolation and compute the average, and denote it as m_1:

$$m_1 = \frac{e_{\max}(t) + e_{\min}(t)}{2} \quad (1)$$

(2) Subtract the envelope mean signal from the signal

$$h_1(t) = x(t) - m_1 \quad (2)$$

Treat $h_1(t)$ as a new set of data, and repeat steps 1–2 until $h_1(t)$ is converged. Then set $C_1(t) = h_1(t)$. The process stops when the difference between two consecutive shifts is smaller than a selected threshold SD, defined by

$$SD = \sum_{t=0}^{T} \left[\frac{\left| h_{1(k-1)}(t) - h_{1k}(t) \right|^2}{h_{1(k-1)}^2(t)} \right] \tag{3}$$

(3) Calculate the residue $R_1(n) = x(n) - C_1(n)$; Treat $R_1(n)$ as a new set of data, and repeat steps 1–2 until the residue becomes a constant or a monotonic function.

(4) $x(n) = C_1(n) + C_2(n) + \cdots + C_N(n) + R_N(n)$. $C_i(n)$ is an intrinsic oscillatory mode and $R_N(n)$ is the residue. Thus, the signal can be reconstructed by summing up all intrinsic oscillatory modes.When all the IMFs are extracted, the cross-correlation between each IMF and $x(t)$ is calculated. The most correlated N number of IMFs whose dominant frequencies are larger than 0.5 Hz will be used to reconstruct the signal. In this way, most low frequency trends and high frequency noise can be removed. In our study, we used $N = 4$.

Once the low frequency trends and high frequency noise were removed via the EMD algorithm, the PPG variability series $\boldsymbol{p}$ was obtained by taking the first derivative of the down-slope phase of the PPG waveforms followed by selecting the resulting largest negative values. To ensure the robustness of the algorithm, two moving average processes were applied in the PPG variability detection procedure.

First, PPG waveforms are denoted as $\boldsymbol{a}(i)$, $i = 1, 2, 3, \pm, \ldots, N$ and the moving average of the signal a is performed:

$$b(i - M + 1) = \frac{1}{2M+1} \sum_{j=i-M}^{i+M} a(j) \tag{4}$$

where $i = M, M + 1, M + 2, \ldots, N - M$ with $M = \boldsymbol{fs}/8$. The fs refers to the sampling frequency. This ensures that the local minima of the PPG signals are accentuated when the derivative is taken in the proceeding step.

Second, define $\boldsymbol{c}$ as the successive difference (first derivative) series of $\boldsymbol{b}$:

$$c(i) = \Delta b = b(i+1) - b(i) \tag{5}$$

$$i = 1, 2, 3, \ldots, N - 2M$$

Third, perform a second moving average of the signal $\boldsymbol{c}$:

$$d(i - M + 1) = \frac{1}{2M+1} \sum_{j=i-M}^{i+M} c(j) \tag{6}$$

where $i = M, M + 1, M + 2, \ldots, N - 3M$ with $M = \boldsymbol{fs}/8$. Similar to the first moving average procedure, this facilitates choosing more accurate local minima.

Fourth, local minima and their positions are obtained by using an adaptive threshold (Th_a) and a moving window length, W. Local minima obtained on the boundary of a moving window are neglected. Local minima should be no larger than the set adaptive threshold value. The length of a window should not exceed half of the cardiac cycle to avoid including down-slope segments from different cardiac cycles. In this study, the moving window length, W, was selected as $\boldsymbol{fs}/4 = 100$. The adaptive threshold was obtained by setting $Th_a(i) = ((i-1\text{th})$ local minimum$)/3$, where $Th_a(1)$ is defined as the mean of the first 5 local minima, where $i = 1, 2, 3, \ldots, N$. The moving average parameter M was selected as $\boldsymbol{fs}/8$. Justification for this selection will be shown in the Results section.

To compare the similarity indices between PPGV and HRV, the following widely used time- and frequency-domain parameters are calculated and compared: the standard deviation of normal-to-normal R–R intervals (SDNN), the root-mean square of the difference of successive R–R intervals (RMSSD), the ratio of the low-to-high frequency spectra (LF/HF, LF: 0.04–0.15 Hz, HF: 0.15–0.4 Hz) and the approximate entropy (ApEn). ApEn is denoted as ApEn(m, r, N) where N is the length of the series to be analyzed and m determines the length of the sequences to be compared, which can be estimated by calculating the false nearest neighbor. The parameter r is the tolerance threshold for accepting similar patterns between two segments, and has been recommended to be within 0.1–0.2 times the standard deviation of the data [13]. ApEn(m, r, N) is the average of the logarithms of the conditional probabilities that sequences of m beats which are "close" (within $\pm r$) will remain "close" at the $(m + 1)$th beat:

$$ApEn = -\frac{\sum_{i=1}^{N-m} \ln \frac{C_i^{m+1}(r)}{C_i^m(r)}}{N - m} \tag{7}$$

where $C_r^m(i) = V^m(i)/(N - m + 1)$ where $V^m(i) = no.\ of\ d[X(i), X(j)] \le r$.

The student-t test was used to determine whether there is a statistical significance between PPGV and HRV. Correlation coefficients wewe used to measure the linear relation between PPGV and HRV. p-values less than 0.05 were considered to be statistically significant.

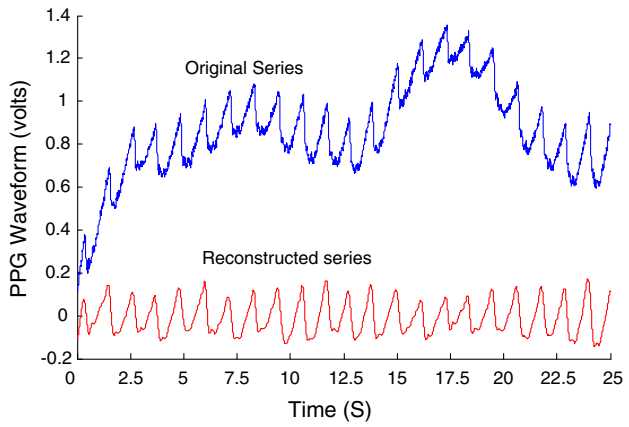

Fig. 1. Comparison of the original PPG and the reconstructed PPG waveforms based on the use of empirical mode decomposition.

RESULTS

A comparison between the original and the reconstructed PPG signal via the use of EMD is shown in Figure 1. The reconstruction was based on using the four most correlated IMFs whose dominant frequency components are higher than 0.5 Hz. We note that both high and low frequency trends and noise are removed in the reconstructed signal. The EMD procedure was successful in removing noise and low frequency trends in all of the signals analyzed, and this procedure facilitates down-slope peak detection of the PPG waveforms.

Figure 2 shows a representative result obtained using the procedure outlined in the Methods section for the detection of the largest negative peak of the PPG waveform. Panel (a) is the detrended PPG waveform, panel (b) represents the moving average of the signal in panel (a), panel (c) represents the first derivative of the signal in panel (b), and panel (d) represents the moving average of the signal in panel (c). Details regarding the moving average and the derivative parameters are provided in the Methods section. The circles in panel (d) represent the position of the largest negative values. Note that as compared to panel (a), the negative values are better defined in panel (d). Finally, the PPGV signal is obtained by measuring the distance between two consecutive PPG signals in panel (d).

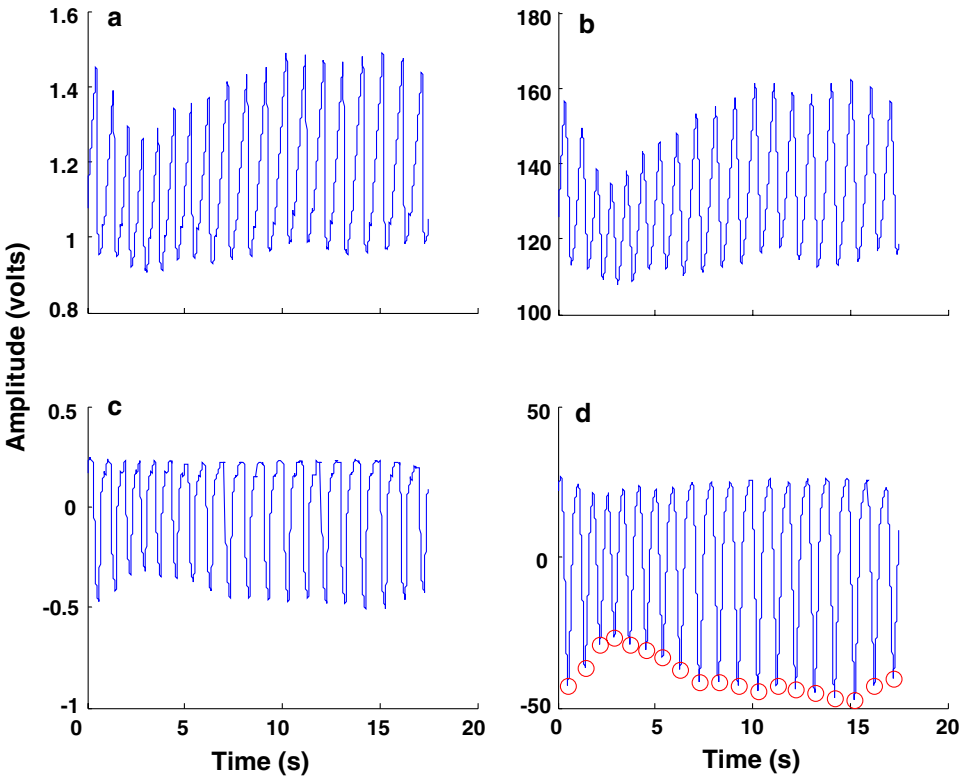

Fig. 2. Smoothing via moving average filter and the first derivative used to accentuate better detection of the local minima of the processed PPG signal. Panels a, b, c and d represent the PPG signal, moving average filter applied to the signal shown in panel a, derivative of the signal shown in panel b, and a second moving average filter on the signal shown in panel c, respectively.

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