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Predicting Arterial Stiffness from Physiological Characteristics of Photoplethysmography Signals Quantified Through Second Derivative

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Abstract

Objectives: Cardiovascular diseases arise mainly due to arterial stiffening leading to atherosclerosis and arteriosclerosis. Contour analysis of second Derivative Photoplethysmogram (SDPPG) reveals cardiovascular properties. In this paper, a novel SDPPG analysis algorithm is used for the assessment of arterial stiffness. **Methods/Statistical Analysis:** The proposed algorithm based on re-sampling technique is used for an accurate detection of significant points of interest (a, b and e wave) in SDPPG to evaluate desired parameters for the assessment of arterial stiffness. The parameters identified are PPL (PPG peak latency), PNL (PPG notch latency), PNRA (PPG notch relative amplitude), PTNL (peak to notch latency) and NI (Notch Index) and the correlation between these parameters are studied on the records obtained from the large-scale openly available database PhysioNet. **Findings:** The performance evaluation of the proposed SDPPG analysis algorithm is better than existing methods in terms of sensitivity and positive predictivity for a, b and e wave detection. Correlation analysis were examined for the PPG signals with low and varying amplitudes, regular and irregular heart rhythms and non-stationary signals that varies from healthy adults to unhealthy and aged patients. The positive linear correlation coefficient 'r' ranges from 0.7 to 0.9 for NI and PNL or PNL and PTNL, representing a significant relationship between them whereas PNL and PPL, NI and PTNL or NI and PPL, present a moderate correlation. However, a negative correlation with r=-0.66 is obtained for PNRA and PTNL. The parameters associated with dicrotic notch NI, PNL and PTNL considerably reflect the stiffness of the arteries, with smaller values of these parameters indicating stiffer arteries. Hence, the notch is the valuable characteristics of the PPG Waveform and plays a significant role in the diagnosis of arterial condition. Also, faithful association between arterial stiffness and Pulse Wave Velocity (PWV) can be acquired from PNRA and PNL, as they represent relative height of notch and position of notch with respect to time respectively, instead of Stiffness index (SI) and Reflection Index (RI) that relates stiffness of arteries. **Application/Improvement:** Although, the number of PPG records used for performance evaluation was self-effacing, a larger database is required to validate the findings of this study.

Keywords: Arterial Stiffness, Dicrotic Notch Detection, Digital Volume Pulse (DVP), Derivative of the Photoplethysmography Signal (SDPPG), Onsets, Second Systolic Peaks

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1. Introduction

Age, sex, hypertension, serum cholesterol and diabetes mellitus are the common risk factors for Cardiovascular Disease (CVD), the chief cause of mortality in the developed world. CVD arises mainly due to atherosclerosis and arteriosclerosis, an inflammatory and degenerative condition of the arterial wall. Arterial stiffness is one of the risk factor for cardiovascular morbidity and its measurement is a promising one. Stiffening of arteries increases with age and arteriosclerosis and atherosclerosis result in early stiffening. There has been always a concern in the improvement of novel non-invasive techniques and devices for the diagnosis of cardiovascular diseases[1,2]. An alternative and simpler technique yet broadly applicable would be of great benefit in screening CVD.

Arterial stiffness can be determined non-invasively with Photoplethysmography (PPG) through digital volume pulse analysis. It is inexpensive, simple, operator independent and suitable for clinical practice[3] unlike pressure pulse wave analysis obtained through tonometry which requires specialized operators resulting in lesser impact in clinical practice, though it benefits in predicting cardiovascular morbidity[4]. The PPG pulse can be easily obtained by computing absorption of infrared light across the finger that has a pulsatile component and a constant component. This varies with flow, volume, vessel wall movement of blood and the arrangement of red blood cells in the underlying tissue in the cardiac cycle[5]. The contour of PPG reveals the features of the heart and large arteries, though its amplitude depends on temperature and perfusion of the hand.

The widely used method to measure stiffness is the arterial Pulse Wave Velocity (PWV), the velocity of the pressure pulse that transmits through arterial tree. The PWV is correlated to age, arteriosclerosis and Blood Pressure (BP) and it is a better indicator than traditional risk markers in assessment of cardiovascular disease[6,7]. Arterial stiffness can be evaluated by Augmentation Index (AIx) i.e. the augmentation of the forward pulse wave curve due to the overlap of the reflected PW[8]. The forward PW travels more rapidly in the arteries, the reflected PW returns in advance to the point of measurement, and the reflected PW augments the forward PW at an increased arterial stiffness. AIx is affected by large artery stiffness and associated with cardiovascular risk.

Few researchers quantified the PPG wave with Stiffness Index (SI) and Reflection Index (RI) for arterial stiffness and vascular tone, respectively. SI derived from subject height and the duration between the systolic and diastolic peaks, the Peak-To-Peak Time (PPT) can be used as a surrogate measure of PWV indicating large artery stiffness[9]. RI has been revealed as a non-invasive indicator for vascular assessment[10] which is the ratio of amplitudes of second peak to that of first peak. The "ageing index" (AGI), determined from the second derivative Photoplethysmographic (SDPPG) waveform, has been used for evaluating arterial stiffness and cardiovascular ageing[11].

1.1 Estimating Arterial Stiffness by SDPPG Analysis

The pulsatile component of PPG pulse has anacrotic or early phase with systolic peak and dicrotic or late phase with diastolic peak, exhibiting a dicrotic notch between these peaks. It has been reported that PPG signals can be successfully used to derive heart rate signals. In particular, dicrotic notches and peaks provide important information about the cardiovascular system. The location of the notch can be used to examine cardiac function as it indicates the closure of the aortic valve and following retrograde blood flow. These peaks and the dicrotic notch likely to be less pronounced, due to the effects of diseases like diabetes, atherosclerosis etc., and aging. In elderly subjects and in subjects with early arterial stiffening, however, the systolic and diastolic peaks and the dicrotic notch in the PPG waveform become hard to identify and tracing these peaks with the absence of the dicrotic notch constituted a challenge.

PPG waveform characterisation has been easily quantified by the derivatives of PPG signal and the second derivative of the PPG signal (SDPPG) allowed easier interpretation of the original waveform. In SDPPG analysis, five distinctive waves have been identified as a, b, c and d situated in the systolic phase and e representing the dicrotic notch located in the diastolic phase of the heart cycle as illustrated in Figure 1

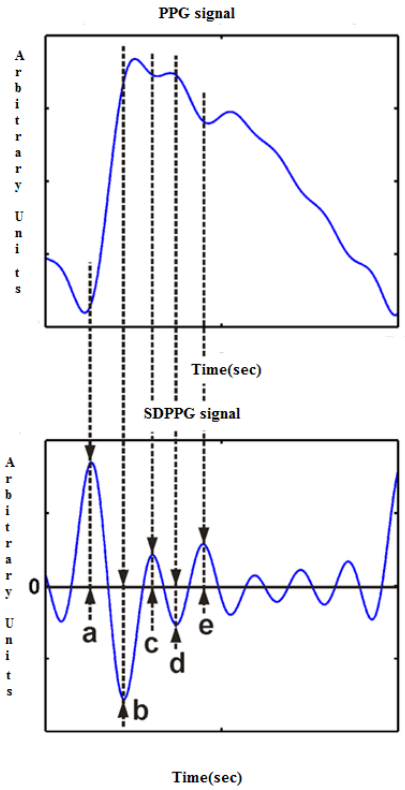

Figure 1. A schema of the photoplethysmogram (PPG, Top) and the second derivative of the Photoplethysmogram (SDPPG, Bottom).The SDPPG consists of 5 waves and each wave is consecutively named 'a','b', 'c', 'd' and 'e' wave respectively.

This paper clearly shows the possibility of arterial stiffness assessment and thus cardiovascular health of a subject simply and rapidly from the physiological characteristics of PPG quantified through its second derivative characterising PPG peaks and dicrotic notch.

2. Materials and Methods

2.1 Database Used

PPG waveforms have been obtained from the large-scale openly available database from PhysioNet (http://www.physionet.org). The PPG database of 20 records with a sampling frequency of 125 Hz and duration of 10 seconds for each signal are considered for analysis. PPG signals with different morphologies such as baseline fluctuations, low and varying amplitudes, irregular heart rhythms were experimented for arterial stiffness assessment.

2.2 Methodology

The parameters (or features) related with the physiological characteristics of the aorta and arteries can be obtained from the PPG waveform. We have exploited theoretic approaches to extract features and various combinations of these features are compared and experimented and found that five of these features provide the best measurement of arterial stiffness. The features were identified as PPL (PPG peak latency), PNL (PPG notch latency), PNRA (PPG notch relative amplitude), PTNL (peak to notch latency) and NI (Notch Index).These features have been referred in the literature[11] for cardiovascular pathology.

SI or RI could be same though they are estimated from individual waveforms, if their peak height and peak-to-peak time delay are same as shown in Figure 2. A qualitative association between arterial stiffness and PWV was obtained from PPG Notch Latency (PNL) i.e. Percentage of the time-to-notch to the pulse time and PPG Notch Relative Amplitude (PNRA) i.e. Percentage of the notch amplitude to the total pulse amplitude as these pulses exhibit dissimilar notch height and different notch time[12]. Therefore, these two parameters could be an equivalent for RI and SI while relating the stiffness of arteries.

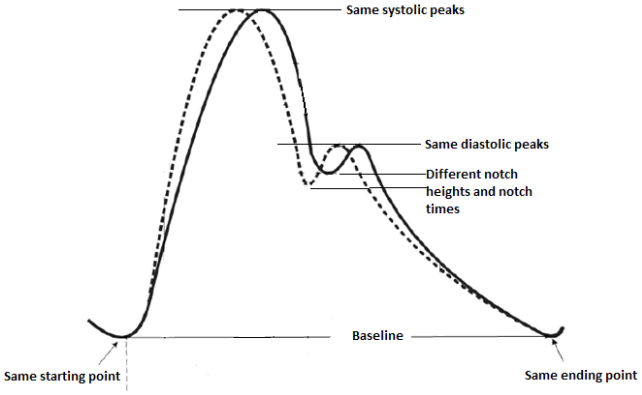

Figure 2. The two separate waveforms (solid line and the dashed line) have same peak heights and same peak to peak duration and hence same RI and SI but different PNL and PNRA as they have different notch points with respect to amplitude and time.

In this study, an adaptive delineator for PPG waveforms proposed by[13] to detect peaks and notch in PPG

signals has been utilised. The proposed algorithm is primarily based on vital point detection in the second derivative of PPG waveform, quantified by the zero crossing points.

2.2.1 Signal Pre-Processing (Bandpass Filtering and Second Derivative)

The raw PPG unprocessed waveforms are often distorted with various noises and artifacts thereby introducing aliasing points in their derivatives. Initially, signals were pre-processed taking into consideration the baseline drift as well as other low and high-frequency components. High-frequency noise that exist above 9 Hz and low-frequency noise which causes wandering of baseline that is present up to 0.5 Hz are eliminated by a band pass filter using Fast Fourier Transform (FFT) filtering with a pass band of 0.5Hz –9 Hz, as almost all the energy of the PPG signal is below 9 Hz. The second derivative has been applied to the filtered PPG signal for further analysis. The proposed pre-processing output is shown in Figure 3.

2.2.2 Contour Analysis of SDPPG Waveform

In SDPPG, *a* represents the onset of pulse i.e. initial point of arterial pulse wave, *b* wave point towards peak of percussion wave; *e* wave characterize the dicrotic notch and specifies the closure of aortic valve. Hence, a-a interval gives pulse Time, ratio b/a relates to the increasing systolic slope i.e. pulse Height, (b-a) on time domain relates peak Time, (e-a) on time domain relates Notch *Time and* ratio e/a relates to the Notch Height. Hence, these relevant features shown in Figure 4 and listed in Table 1were extracted using the delineator[13].

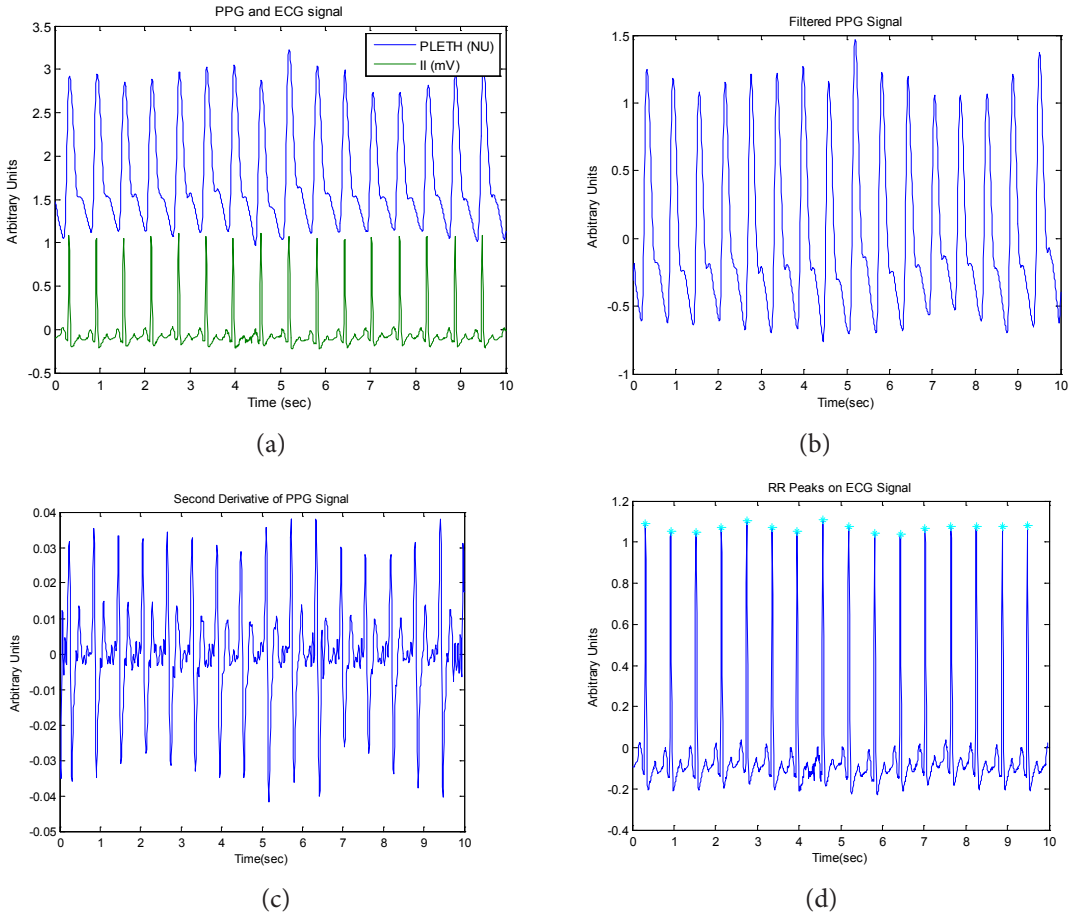

Figure 3. The proposed pre-processing output (A) Raw PPG unprocessed signal (B) Filtered PPG signal with baseline drift elimination (C) SDPPG signal(D) R peaks on ECG signal.

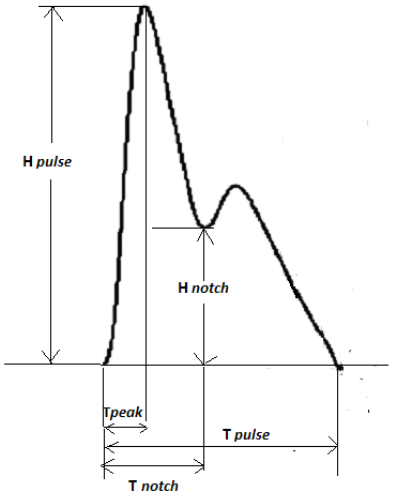

Figure 4. The schematic representation of PPG features.

Table 1. Descriptions of the PPG features

Features	Description	Parameters
PPG amplitude	Distance from the baseline to the maximum of the pulse	H_{pulse}
Peak duration	Elapsed time between onset and maximum of the pulse	T_{peak}
Pulse duration	Total pulse duration	T_{pulse}
PPG notch amplitude	Distance from the baseline to the notch minimum	H_{notch}
Notch duration	Elapsed time between onset and notch minimum of the pulse	T_{notch}
PPG peak latency **(PPL)**	Percentage of the time-to-peak to the total pulse duration	T_{peak} / T_{pulse}
Notch relative amplitude **(PNRA)**	Percentage of the notch amplitude to the total pulse amplitude	H_{notch}/ H_{pulse}
PPG notch latency **(PNL)**	Percentage of the time-to-notch to the pulse time	T_{notch}/ T_{pulse}
Peak-to-notch latency **(PTNL)**	-	[T_{notch}- T_{peak}] / T_{pulse}
Notch index**(NI)**	-	T_{notch}/ [T_{pulse}- T_{notch}]

The delineator is based on re-sampling technique[13] which normalizes the signal and ensures the presence of all significant points of interest in all its recurrences. The recurrences are considered to be the wave duration between two consecutive peaks of the signal. The filtering, re-sampling and aligning processes are carried out independently for every recurrence in PPG signal and the averaged waveform is obtained. It detects a, b and e waves in SDPPG based on the combined analysis of Photoplethysmography waveforms and their second derivatives, characterising them beat-by-beat evaluated by Electrocardiograph (ECG) signals. The recurrences are aligned and averaged to obtain the final mean of the original signal and its second derivative. The averaged original signal and averaged second derivative of the signal are mapped to acquire a, b and e points to estimate the required parameters. The system implementation is shown in Figure 5.

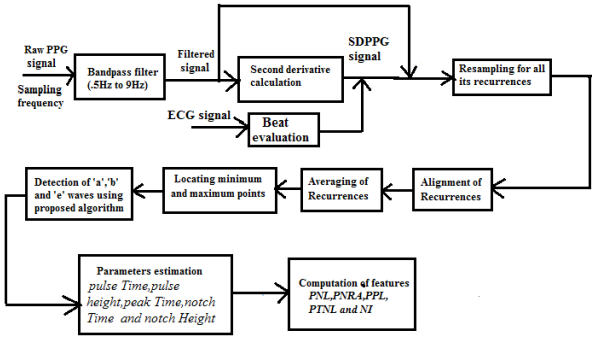

Figure 5. Flowchart of the proposed system implementation.

2.2.3 Statistical Analysis

The algorithm was tested on a large-scale openly accessible database from PhysioNet (http://www.physionet.org) for performance evaluation with different morphology such as signals exhibiting various pathophysiological complexities such as regular and irregular heart rhythms, low and varying amplitudes and found to be robust. The performance evaluation of the adaptive delineator[13] is better than existing methods in terms of sensitivity and positive predictivity for a, b and e wave detection. The averaged PPG and averaged SDPPG waveforms (red bold line) with filtered and normalized recurrences (thin lines) for one record are shown in Figure 6 and the averaged PPG and averaged SDPPG with distinct a, b and e points are shown in Figure 7

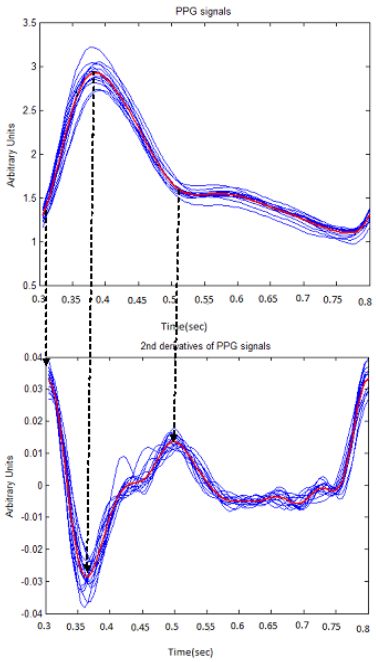

Figure 6. The averaged PPG and its second derivative waveforms (red bold line) with filtered and normalized recurrences (thin lines) for one record.

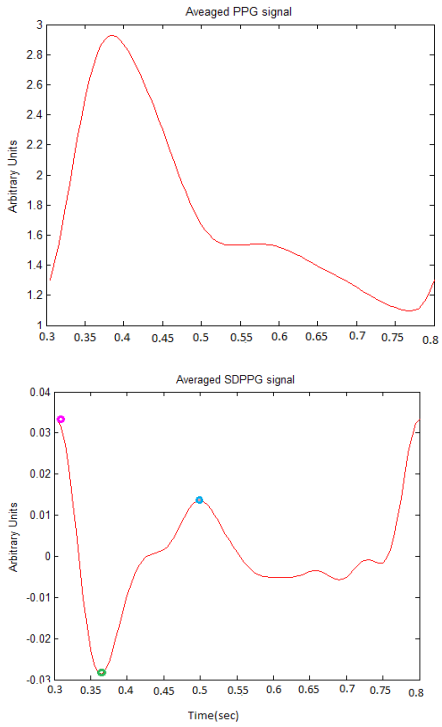

Figure 7. The averaged PPG and averaged SDPPG with distinct a, b and e waves. Here, the 'magenta circle' represents the detected a wave, the 'green circle' represents the detected *b* wave and the ` blue circle' represents the detected e wave.

3. Results and Discussion

In this study, stiffness of the arteries has been noninvasively investigated through SDPPG and its various features of interest Pulse Height, Peak Time, Pulse Time, Notch Height and Notch Time are extracted to assess PPL, PNL, PNRA, PTNL and NI. Table 2 shows arterial stiffness parameter estimation for 20 subjects.

Table 2. Waveform characteristics. The values are given as mean ±SD.

Features	Mean ±SD
PPL	0.1364±0.05
PNRA	0.36±0.08
PNL	0.3175±0.17
PTNL	0.1274±0.04
NI	0.572±0.5

The systolic and the diastolic component of the PPG pulse arises due to the pressure wave that traverses from the left ventricle to the finger and the reflected wave back to the finger that has navigated to the small arteries along the aorta respectively[2]. The stiffness of the arteries is normally accompanied by the occurrence of early wave reflection[14].The reflected wave arrives early with increased stiffness and hence it shifts from the diastolic to the systolic phase of the pulse. Consequently, the inflection point, i.e. notch height, on the contour of the pulse is elevated for the stiffer arteries compared to that in the less stiff arteries. PNRA, representing the relative height of the notch is the indicator of arterial aging. NI, PNL and PTNL signifies the notch generation time by the reflected wave and found to be considerably reflecting the stiffness of the arteries, with lesser values of these features indicating stiffer arteries. This clearly shows the significance of the notch in the diagnosis of arterial condition.

Correlation coefficient analysis was used to examine the association and strength of the two quantitative variables. The relationships between NI and PNL or PNL and PTNL, present a significant positive linear correlation, with 'r' ranging from0.7 to 0.9 whereas NI and PPL, NI and PTNL and PNL and PPL are moderately correlated. This signifies that the time at which the reflected wave occurs with respect to systolic peak has impact on these features. PNRA and PTNL is negatively correlated with r=-0.66 indicative of wave reflection and hence arterial condition. The correlation between these parameters is shown in Figure 8. [Figure 8]

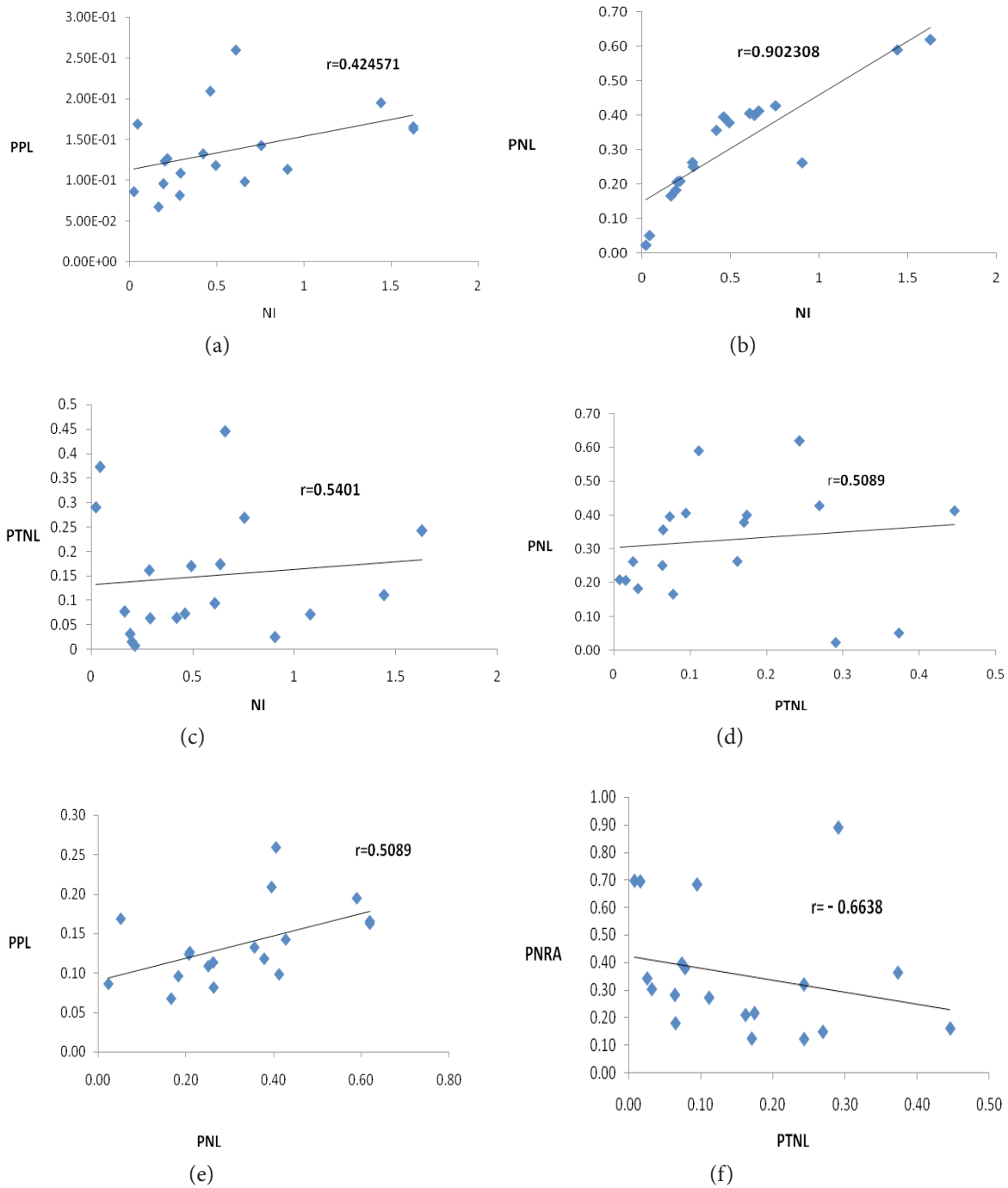

Figure 8. Linear correlation analysis between relevant parameters. Diamonds symbolize the values of these parameters. The relationships between (a) NI and PPL, (b) NI and PNL, (c) NI and PTNL, (d) PNL and PTNL (e) PNL and PPL and (f) PNRA and PTNL. NI and PNL exhibit a strong linear correlation (r=0.902308), NI and PTNL display a good linear correlation (r=0.7206) whereas PPL and PNL and PTNL and NI show a moderate correlation(r=0.5089 and r=0.5401 respectively) and PTNL and PNRA display a negative correlation (r= -0.6638).

4. Conclusion

PPG waveforms are rich in pathophysiological information of cardiovascular circulation system and the contour analysis of PPG signal has been used widely to screen CVD. PPG waveform characterisation has been easily quantified by the derivatives of PPG signal and the second derivative of the PPG signal (SDPPG) allowed easier interpretation of the original waveform. Presently, a complete perceptive of the diagnostic importance of the different features of the SDPPG signal is still lacking and further research is needed.

Results indicate that the proposed method has better performance for arterial stiffness prediction compared to SI or RI. A faithful association between arterial stiffness and PWV can be derived from PNRA and PNL, as they relate notch height and occurrence of notch with respect to time respectively. Arterial stiffness was evaluated[11] using PNRA and PNL only for young adults, whereas, in this study, arterial stiffness was evaluated for 20 records from PhysioNet (http://www.physionet.org) with different morphology such as signals exhibiting various pathophysiological complexities such as regular and irregular heart rhythms, low and varying amplitudes. These features can be extracted very simply and quickly, and we, therefore, conclude that this non-invasive technique is highly suitable for health professionals to assess stiffness of arteries.

5. References

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