The analysis of PPG contour in the assessment of atherosclerosis for erectile dysfunction subjects

Y. K. Qawqzeh, M. B. I. Reaz, M. A. M. Ali

***Abstract*—** The risk of cardiovascular diseases may damage the endothelium cells which may cause atherosclerosis. Arterial stiffness can be measured noninvasively by the use of photoplethysmogram (PPG) technique. This research presents the variations of PPG morphology with age. Based on a sample of 65 subjects whom having established erectile dysfunction (ED), the study proposed to assess the variations of PPG contour at two sites of measurements (right and left index finger). The study concluded that PPG timing indices are equal in both right and left hand. Parameters derived from the analysis of PPG contour showed an association with age. The age is found to be an important factor that affecting the contour of PPG signals, which accelerates the disappearance of PPG dicrotic notch and PPG inflection point as well. Arterial compliance found to be decreased with age due to the fall of arterial elasticity. This study approaches the establishment of the usefulness of PPG contour analysis in investigating the changes in the elastic properties of the vascular system with age and the detection of early atherosclerosis. The study approaches the establishment of the differences between PPG's time indices and PPG's amplitude indices.

***Keywords*—**PPG, RI, SI, CIMT, Age, Arterial Stiffness, Endothelial Dysfunction, Contour analysis.

I. Introduction

ERECTILE dysfunction (ED) is a sign of cardiovascular disease which can be a sign of increased risk [1]. The main cause of ED is still unknown. The researchers from Medical side thought of atherosclerosis (stiffening of arteries) and arteriosclerosis to be the significant harmful cause of ED. Such hypothesis might be drawn due to the effects of arteriosclerosis and atherosclerosis on arterial walls, therefore, affecting the endothelial cells badly. There has been much recent interest in the relationship between arterial stiffness and cardiovascular disease [2]. Pulse pressure and pulse wave velocity, surrogate measures of arterial stiffness, indicate that arterial stiffness increases both with age and in certain disease states that are themselves associated with increased cardiovascular risk, including hypertension, diabetes mellitus, hypercholesterolaemia and end-stage renal failure [3]. The risk of cardiovascular diseases may damage the endothelium cells which may cause atherosclerosis. Endothelial dysfunction is characterized by a shift of the actions of the endothelium toward reduced vasodilation, a proinflammatory state, and prothrombic properties. Endothelial function is often assessed non-invasively by ultrasound brachial artery diameter measurement before and after several minutes of blood flow occlusion to the arm [4]. Endothelial dysfunction is the initial step of the atherosclerotic process involving many vascular districts, including penile and coronary circulation [5]. Endothelial dysfunction is associated with cardiovascular disease risk factors [6-7]. Endothelial dysfunction has been proposed to be an early event of patho-physiologic importance in the atherosclerotic process [4, 8] and provides an important link between diseases such as hypertension, chronic renal failure, or diabetes and the high risk of cardiovascular events in patients exhibiting these conditions [9]. Both endothelial dysfunction and increased arterial stiffness commonly coexist in patients at increased risk of cardiovascular disease [10-15]. Researchers had thought that atherosclerosis erodes the natural suppleness of the protein elastin, therefore hardening arteries. Figure 1 represents the risk of atherosclerosis measured at carotid intima-media arteries. Atherosclerosis can lead to clogged arteries in any part of the body. When the arteries to the heart are affected, angina (chest pain) or a heart attack may result. It is accepted that older subjects have increasing arterial stiffness, which results in increasingly faster pulse transmission to the periphery [16]. Evidence regarding the associations of adult coronary artery disease risk factors with atherosclerosis in young persons has been described [17-18]. Age considered as powerful predictor of cardiovascular morbidity, mortality, and disability. Age has traditionally been ignored as a risk factor for cardiovascular disease because it is considered a non-modifiable risk. Risk factors, including intimal medial thickness, vascular stiffness, and endothelial dysfunction, alter the substrate upon which the cardiovascular diseases are superimposed; which in turn affect the development, manifestation, severity, and prognosis of these diseases. Aging is accompanied by increased stiffness of large elastic arteries, leading to an increase in pulse wave velocity (PWV) [19-22]. PWV is the speed at which the forward pressure wave is transmitted from the aorta through the vascular tree. In addition increased vascular stiffness has important haemodynamic consequences. Large arteries are normally compliant structures, capable of buffering pressure

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changes that occur during the cardiac cycle to maintain constant tissue blood flow [23]. Arterial stiffness is not only a marker of cardiovascular dysfunction but also an independent risk factor for cardiovascular disease [23-27]. Pulse pressure, a surrogate marker of increased arterial stiffness, is a powerful predictor of cardiovascular events [28-30]. As large arteries stiffen with age or disease processes, the amplitude of the reflected wave increases [23]. Arterial stiffness may be measured using a variety of different techniques, although at present the majority of measurements are made for experimental and physiological studies rather than in clinical practice [2].

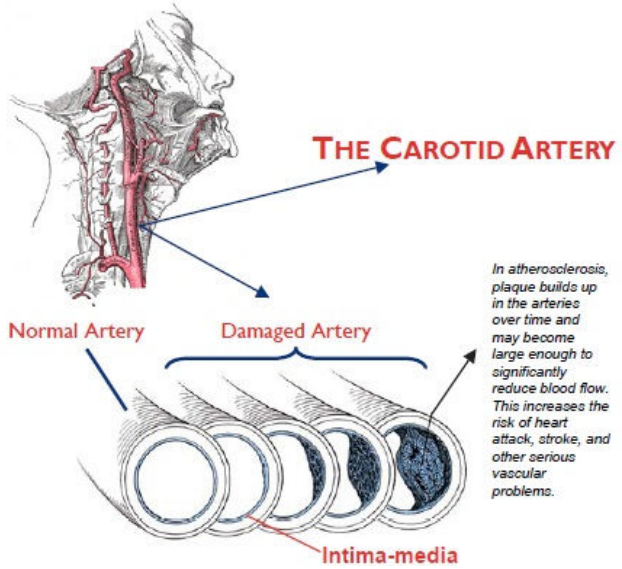


Fig1. Atherosclerosis risk at carotid intima-media arteries
Source: [31]

Arterial thickening provides the earliest evidence of atherosclerosis, or hardening of the arteries, the beginning stage of a disease process that leads to heart disease and stroke [32]. Arterial stiffness can be measured noninvasively by the use of PPG technique, which reflects the changes in blood volume with each heart beat. The PPG signals can be acquired more conveniently than other signals, such as ECG, EEG signals [33]. Developments in arterial hemodynamics have indicated that the human arterial pressure waveform contains more information than is available from sphygmomanometry or PPG. This information includes indices describing left ventricular systolic function, arterial stiffness and the character of the wave reflections in peripheral arterial branches [34]. PPG is characterized by an inflection point, or notch, and the height of this has been suggested as a measure of peripheral pressure wave reflection [35-36].The arterial pressure waveform is a composite of the forward pressure wave created by ventricular contraction and a reflected wave [19, 37-38]. Waves are reflected from the periphery mainly at branch points [34]. The pulse is frequently used by clinicians in the assessment of vascular diseases, where a weak, delayed or damped pulse is often a sign of occlusive arterial disease [16]. PPG has widespread clinical application, with the technology utilized in commercially available medical devices (e.g. in pulse oximeters, vascular diagnostics and digital beat-to-beat blood pressure measurement systems) [39]. The introduction of pulse oximeter was the the major advance in the clinical use of a PPG-based technology which is used as a non-invasive method for monitoring patients' arterial oxygen saturation [40-41].

PPG signal is hypothesized to detect alterations on arterial system due to its ability of reflecting changes of blood volume. Blood volume changes and blood streaming variations might reflect the underlying diseases or/ and disorders of human arteries. It's noteworthy that, ED as hypothesized to be caused by atherosclerosis and arteriosclerosis might be diagnosed by the use of PPG waveform. Perhaps the most exciting application of PPG waveform analysis is the possibility of providing a rapid biophysical measure of diseases or ageing process [42]. Generally, PPG is formed by a direct pressure wave that propagates from the heart to the peripheral, and a delayed component that is reflected backward from peripheral arteries, mainly in the lower body. PPG provides an estimation of coetaneous blood flow by measuring the dynamic attenuation of infrared light by the blood volume present in tissue [43].

Analysis of the PPG pulse volume contour in terms of crest time revealed age dependence and clinically significant variations between health and disease, including arteriosclerosis, hypertension and various dermatoses [44]. Arterial pulsations are the most significant portion of PPG [45]. PPG's oscillating component provides a pulsatile wave, whose contour may include content descriptive of vascular health [19, 43, 46]. The PPG waveform comprises a pulsatile ('AC') physiological waveform attributed to cardiac synchronous changes in the blood volume with each heart beat [47]. PPG's 'AC' components (its fundamental frequency, typically around 1 Hz, depending on heart rate [39]) are the actual measure of PPG signals. The variations of 'AC' waveform due to aging and diseases should be highly investigated. Figure 2 demonstrates the pulsatile components of PPG waveform. PPG measurements done at index finger (both right and left hands) since finger PPG is a commonly used technique in medicine [39, 48] and due to the simplicity of probes attachment.

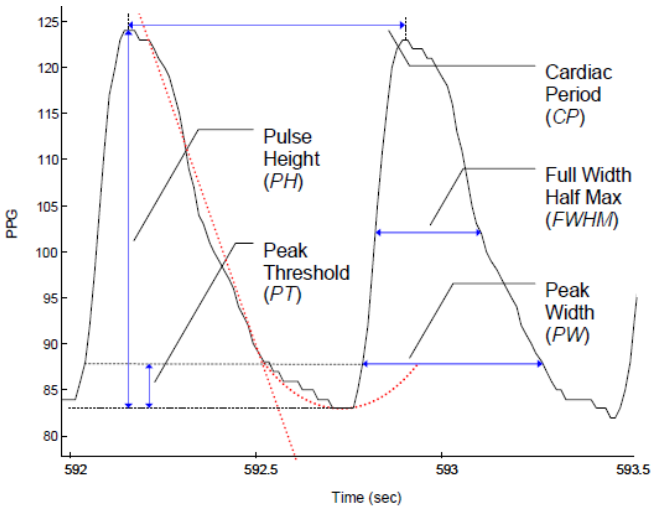


Fig2. The features of PPG's pulsatile components

Derivations of quantitative measures characterizing pulse shape have proven useful in analyzing PPG signal [43]. The peripheral pulse is often used in the assessment of health and disease [48]. Figure 3 shows the characteristics of PPG, the peaks position and timing are utilized in calculating PPG indices. Reflection index (RI) is derived as a ratio of pulse inflection point amplitude (second peak) over the pulse max amplitude. RI can provide a window to vascular age and arterial compliance. RI is mainly depends on the detection of PPG second peak which tends to be less pronounced with aging. The systole, diastole and dicrotic notch points over PPG contour were located and calculated by an optimized algorithm developed in Matlab.

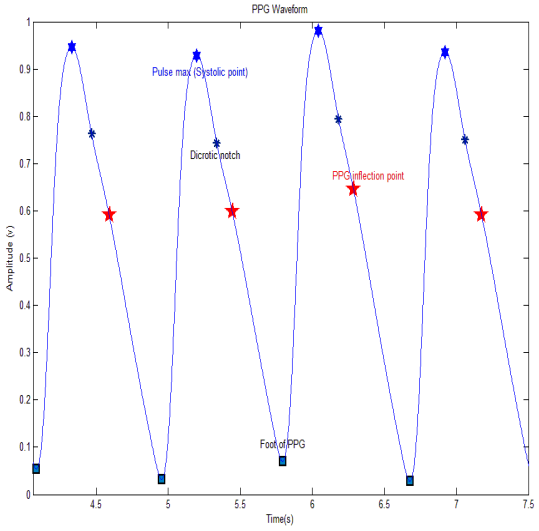


Fig. 3 The characteristics of PPG

The aim of this study was to study and investigate the correlation between PPG's indices at different site of measurements and the correlation between PPG's parameters and age. Therefore, extraction and evaluation of PPG's indices based on its morphological changes took place in order to get insight such associations.

II. Methodology

A. Data Acquisition for PPG Analysis

PPG pulse measurements collected simultaneously from the right and left index fingers to study and analyze arterial conditions. All patients are having established erectile dysfunction which differs on the amount of experiencing from one patient to another. After subject being rested for four minutes, PPG recordings carried out for duration of 90 seconds in both right and left finger index. During the measurements, subjects were keeping quiet, and breathe normally while resting in a supine position. PPG measurements were performed in hospital conditions at room temperature (24±1 °C).

B. Hardware Setup for Signal Processing

A special National Instruments with data acquisition board (NI cDAQ-9172) was used to digitize the signals locally and transmit the digital data to the personal computer with sampling rate of 5500 Hz. Figure 4 shows the experimental setup including PPG instrumentation unit, probes, and the used laptop. The recorded signals were analyzed off-line using customized algorithms developed in MATLAB (The MathWorks, Inc). PPG signals were down-sampled (275 Hz), de-trended for removing outliers, drifts, offset and any movement artifacts. Next PPG signals were band-pass filtered (0.6–15 Hz) for removing the effect of the respiratory rhythm and higher frequency disturbances [49]. These filters did not introduce phase delays or distortion to the waveforms [50]. Utilizing PPG derivatives, those points of interest can be located and determined [50-53].

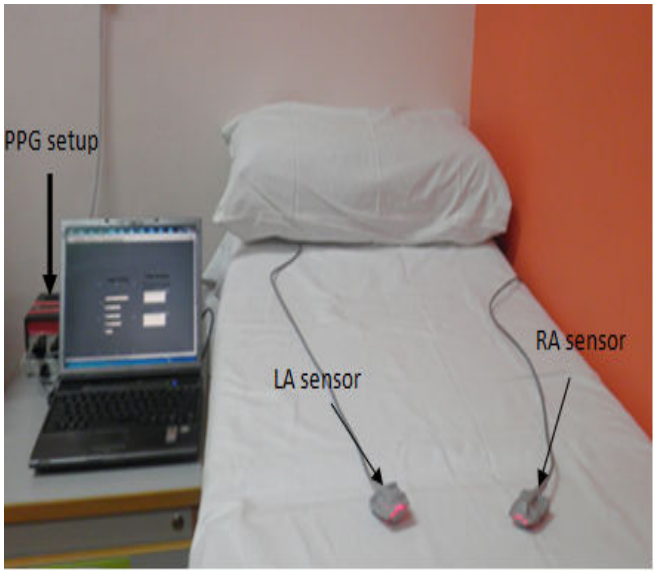


Fig. 4 PPG instrumentation unit, probes, and the used laptop

Basically, seeking certain information from PPG signals was the essence of the analysis of its morphology variations. The morphology of the pulsatile component of the PPG has been shown to vary with physiology [54]. However, PPG consists of three main points of interest: Systolic point (AC peak); dicrotic notch (valley); and inflection point (diastolic point (peak)). These points seem to be clearly pronounced in adult subjects since the discrimination between them can be simply visualized by eye. However, because of the smooth appearance of the PPG signal due to damping, other features, such as early and late systolic inflections, cannot be readily detected [55]. In fact, those points tend to be less pronounced in most of the PPG signals due to the effects of aging, diabetes, atherosclerosis, arterial stiffness …etc. Moreover, locating these points with the absence of the dicrotic notch and/ or the inflection point constituted a challenge.

The analysis of the morphology of PPG has become important because it contains much information about cardiovascular activity. Traditionally, pulse contour analysis

requires 1st or higher derivatives to be calculated [34]. There are two main approaches that have been developed to describe the characteristics of the PPG waveform. The first method is the analysis of PPG 2nd derivatives [56-59]. The 2nd dPPG represents the double differentiation of the original PPG waveform. It also known as acceleration PPG. The 2nd dPPG consists of 5 consequent waves (a, b, c, and d) waves in systolic part and (e) wave in diastolic part. While PPG signals reflect a combination of volume and flow change in skin microcirculation [46, 60], these consequent waves' help in the analysis of the original waveform and therefore help in recognizing points of interest on PPG morphology. Moreover, 2nd dPPG provides an extremely useful measurement of the "biological age" of the patient's cardiovascular system [15, 68]. The peak positions of the 2nd dPPG give information about the PPG and give pulse parameters [34]. The first present of 2nd dPPG was by Ozawa 1972, in which he reported that, the 2nd dPPG had characteristic contours that facilitated the interpretation of the original PPG. The positions of the peaks and valleys of the 2nd derivative give information about the PPG and its pulse parameters. The second method involves extracting the pulse parameters from the peaks of the PPG directly, using the 1st [19, 61] or 3rd derivatives of the PPG [51]. In fact, PPG derivatives facilitate the understanding of the morphological variations of the PPG signal. Figure 5 represents PPG signal, 1st dPPG, 2nd dPPG and the process of peak detection.

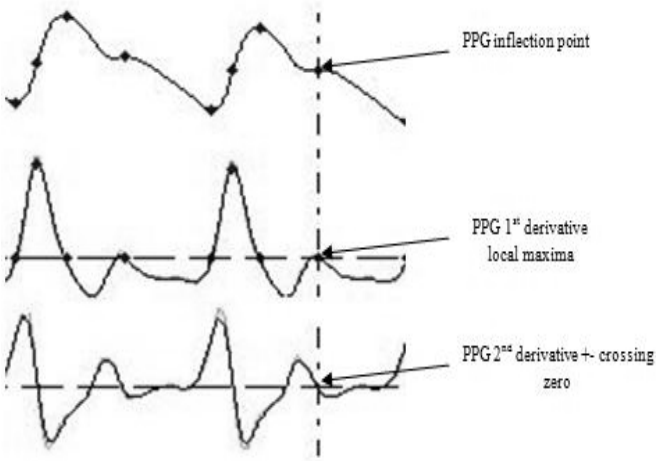


Fig. 5 PPG signal, 1st dPPG, 2nd dPPG and the process of peak detection.

As we age, PPG amplitude is subject to reduction because of the accumulated atherosclerosis, which in turn increases the resistance of arteries and reduces arterial compliance. It is noteworthy that, atherosclerosis affects the elastic properties of the arterial wall, making it stiffen. As arteries become stiffer, blood propagation becomes faster and pulse amplitude becomes lower as well.

The extracted indices of the PPG signal represented the analysis of the time domain (the AC components). Since the most obvious feature of blood flow in arteries is that it is pulsatile [62], the derived indices were classified into time indices and amplitude (volume) indices. Time indices represent the time between two consequence points on the PPG waveform; while PPG amplitude indices represent the difference in amplitude between any point of a PPG waveform and the baseline.

RI has shown to be a noninvasive indicator for vascular assessment. RI can be calculated based on equation 1:

$$RI = \frac{b}{a} * 100\% \quad (1)$$

Where *b or DM* is the amplitude of inflection point (second peak), and, *a* or *PM* is the maximum amplitude of the pulse. RI and SI indices were used to quantify PPG's figure pulse shape [19] to give information representing arterial stiffness and vascular tone.

Basically, PPG signals which experience a clearly seen second peak, seems to be visualized in healthy young subjects. While in old subjects, the second peak tends to be less pronounced or unseen. These observations are not applicable for all cases, since we still have the opposite situation in some other cases for each observation. However, RI remains a good measure for arterial compliance. In addition, augmentation index (*AI*) was derived in terms of pulse maximum peak and PPG second peak as well. AI can be used as a measure of arterial stiffness.

Both *RI* and *AI* depend completely on *PM* and *DM* parameters. *PM* appears to be correlates negatively with age which reflects arterial compliance and can provide a window to arterial elasticity. Healthy artery shall be less in resistance which in turn increases the compliance. While aging artery is high in resistance which decreases the compliance. Thereby, *PM* can be used as a measure of arterial compliance since it is going to be reduced with age.

Pulse wave velocity (PWV) is known to be an indicator of arterial stiffness, and has been regarded as a marker reflecting vascular damages [63]. The demonstration of correlations between parameters of peripheral pulse wave analysis and *PWV* measured both invasively and noninvasively, supports the revival of PPG as a simple and inexpensive technique for the assessment of vascular health [34, 52, 64]. Stiffness index (*SI*) is a measure of larger arteries stiffness, can be used as a surrogate measure of *PWV*, correlates negatively with age. *SI* is calculated (equation2) in terms of subject's height divided by pulse transit time (*PTT* or ΔT). The peripheral pulse wave at the finger characteristically exhibits a systolic peak resulting from the direct pressure wave traveling from the left ventricle to the digit, and a diastolic peak or inflection resulting from reflections of the pressure wave by arteries of the lower body back to the finger [43]. During advancing in age, diastolic peak tends to be closer to systolic peak which in turn, reduces *PTT* and increased *SI*.

$$SI = \frac{H}{\Delta T} \quad (2)$$

Where, H is subject's height.

This paper aims to investigate the effects of aging on arterial elastic properties and in the variations of PPG contour as well. In addition, it aims to study the associations between PPG parameters at one or two sites of measurements. This paper reports the usefulness of PPG contour analysis in investigating and studying cardiovascular activities. The effect of age in PPG's contour, data pre-processing and the differences between the left and right index finger hands, were also examined.

C. Erectile Dysfunction Subjects

PPG measurements were collected from the right and left index fingers of 65 participants with ages ranging from 30 to 78 years and median age 56 years (all men). Eleven subjects were excluded due to missing information (age or height), unacceptable pulse volume data and/or noisy signal at either right or left index finger PPG. A written consent is taken from each participant. The data were recorded from a longitudinal study initially undertaken for the assessment of endothelium dysfunction in subjects presenting with erectile dysfunction. Table 1 shows the medical data characteristics for each age group.

Table 1 Medical data characteristics for each age group (median±SD)

Age	*CIMT*	*BMI*	*SP*	*DP*	*PP*	*MAP*
30-40	0.467±0.115	23.4±0.35	130±10	80±10	50±0	96±10
41-50	0.63±0.22	26.3±4.7	135.5±10.5	82±6	53.5±6.7	100±7
51-60	0.92±0.37	26.8±5.4	138±11	81.6±6.2	56±12	100±6
>60	0.90±0.38	26.7±3.5	141±9	85±8.2	56±7.2	103±8

CIMT, carotid intima-media thickness (mm); BMI, body mass index (kg/m2); SP, systole blood pressure (mmHg); DP, diastole blood pressure (mmHg); PP, pulse pressure (mmHg); MAP, main arterial pressure (mmHg).

Carotid intima-media thickness (*CIMT*) test, body mass index (BMI), systolic pressure (SP), diastolic pressure (DP), pulse pressure (PP) and main arterial pressure (MAP) were taken in the same stage of data collection. The subjects are from three different races in Malaysia (Malay, Chinese and Indian). Main arterial pressure (MAP) and pulse pressure (PP) are calculated based on equation 3 and 4 respectively.

$$MAP \cong \frac{1}{3} * SBP + \frac{2}{3} DBP \quad (3)$$

$$PP = SP - DP \quad (4)$$

D. Protocol

The study is conducted in Urology Clinic in the National University of Malaysia Medical Centre (PPUKM). PPUKM is a teaching medical centre with 750 beds. The medical centre provides health services to most of the population around Kuala Lumpur as well Selangor state. The study was approved by the PPUKM ethics community review. Each patient was informed about the details of the study and their written consent was taken before the recordings were made.

The base-line examination included a medical history taking, physical examination, laboratory testing, and assessment of cardiovascular disease status and blood-pressure measurement have been investigated and recorded. Subjects are obeyed to some inclusion criteria (Hypertension, Diabetes mellitus, Dyslipidaemia, Obesity, Smoking, and Significant family history) and no cardiovascular disease or risks at all) and to some exclusion criteria as well (establish cardiovascular disease, liver cirrhosis, Renal failure, Thyroid disease and Spinal cord injuries and finger or having Raynauld's).

E. Statistical Analysis

The data are quantitative variables which summarized by means and standard deviations. Pearson correlation was used to characterize the relationship between continues variables (SPSS. Release 11.5.0). Box plot and scatter plot are performed using Matlab (R2008a). Table 2 demonstrates the correlation between some PPG indices for both right and left hand PPG.

The result reveals a strong correlation between amplitude PPG indices, while it also reveals an exact result for timing PPG indices. By observing Table 2, RI, AI, PM and DM are highly correlated (their calculation based on volume changes). While SI, PT, DiT and ΔT are exactly equal.

Table 2: Paired samples correlations

Parameter	*Correlation*	*Significant (p)*
RIR & RIL	0.703	0.000
SIR & SIL	1.000	0.000
AIR & AIL	0.892	0.000
PMR & PML	0.565	0.000
DMR & DML	0.753	0.000
PTR & PTL	1.000	0.000
DiTR & DiTL	0.999	0.000
ΔTR & ΔTL	1.000	0.000

III. Results and Discussion

The investigated PPG parameters of contour analysis are derived from measures of locating points of interest on the contour of PPG and calculate those indices in terms of timing and amplitude changes. Our results indicate that these parameters significantly correlate with one another. However, up to our knowledge, this is the first time that the correlation between PPG indices and age in erectile dysfunction subjects have been demonstrated and correlated with CIMT test. Increased CIMT is considered as an early phase of atherosclerosis and might be seen even in patients with mild hypertension and normal serum cholesterol [69-70]. It is noteworthy that PPG time indices are equal; such observation shall be utilized in distinguish between normal and up normal signals. Table 3 illustrates the characteristics of PPG's time indices, while Table 4 demonstrates the characteristics of PPG's amplitude indices.

Table 3: PPG time indices characteristics

Index	Mean	Median	S.E.	Range	Variance
TP	.8500	.8500	.1500	.69	.024
MET	.0900	.0900	.0080	.04	.000
ST	.2200	.2300	.0450	.17	.002
DT	.4100	.4200	.0400	.25	.002
PPT	.1800	.1850	.0400	.18	.002
SI	9.500	9.000	2.800	17	8.20
MEV	.0002	.0002	.0002	.00	.000

Note: The median values were used for further calculations…

Table 4: PPG amplitude indices characteristics

Index	Mean	Median	S.E.	Range	Variance
RI	.69	.700	.100	.60	.017
DM	.02	.0160	.016	.07	.000
PM	.03	.020	.020	.10	.001
b/a	.79	.770	.150	.75	.020
c/a	.73	.730	.060	.30	.004

Note: The median values were used for further calculations…

Since CIMT is used to measure atherosclerosis, the association between CIMT data and PPG parameters were explored. As can be noticed in Figure 6, RI tends to be increased as CIMT increased.

PPG parameters were found to be affected by age even the relationship is not linear. The contour of PPG pulse changed clearly with age. *SI* noticed to be increased with age due to the observation that ΔT tends to be decreased with age. The result supports the findings of [43] since age has no evidence to affect PPG indices in right and left hand fingers (our study was in the index finger while [43] study was in the middle finger).

The analysis of PPG amplitude (AC pulsations) is very important. The changes in blood volume (measured by PPG) provide abundant information about arterial compliance and arterial elastic properties. As arteries loss their elastic properties with age, PPG volume tends to be de declined reflecting the effect of arteriosclerosis on the propagation of blood stream. Indices utilizing the variations on PPG amplitude can provide a window to detect early arteriosclerosis in individuals experiencing one or more CVDs. The time for each pulse period of PPG signal (PT) can be calculated as the difference in time between each two sequential pulses. The relation between *PT* and age is illustrated in Figure 8. The result reveals the trend of PT to be increased with aging. Such observations relate PPG's contour to be altered with age which reflects the changes of arterial characteristics due to aging.

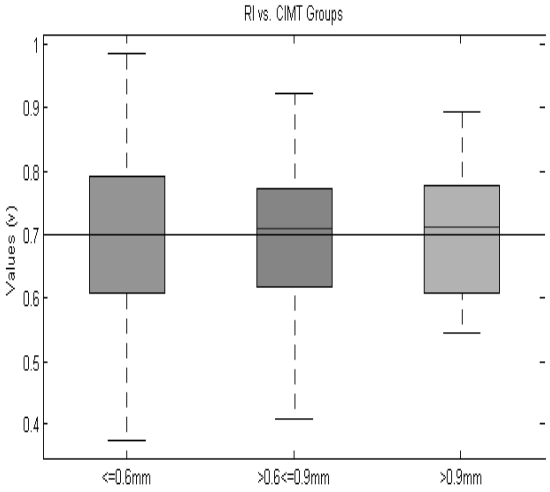


Fig. 6 Variations of RI based on CIMT groups

The process of atherosclerosis as measured by CIMT is chronic operation which thought to be a sign of CVD and an accompaniment to many underlined diseases. In fact, the inciting event of atherosclerosis is likely an inflammatory insult that occurs decades before the disease becomes clinically apparent [65]. The correlation between RI and SI is shown in Figure 7.

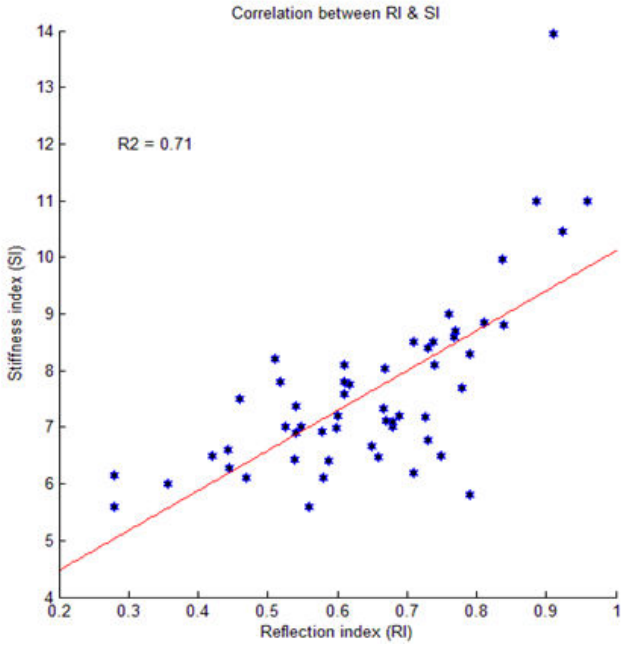


Fig.7 Correlation between RI and SI indices

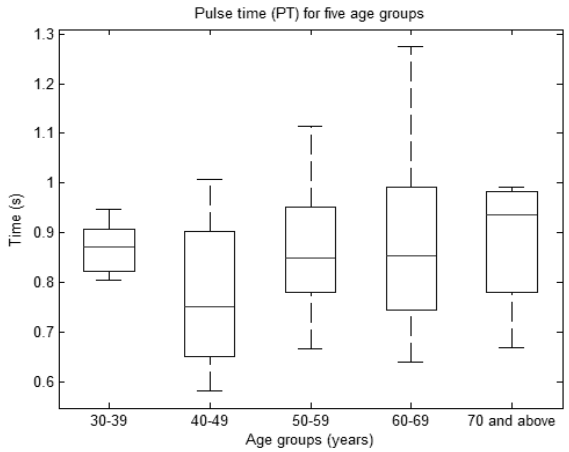


Fig. 8 Association between PT and age groups

However, since PPG signals are affected by the effects of atherosclerosis, PT tends to be altered due to the accumulation of atherosclerosis. In addition to the alterations of PT by atherosclerosis, PT is age-related. The analysis showed a trend of PT being increased as CIMT values increased. This strengthens the hypothesis of relating atherosclerosis to aging. Its noteworthy that, age is the dominant influence of atherosclerosis, PT showed a tendency to increase as we age.

The maximum amplitude of PPG's single pulse (*PM*) contributes to the compliance of arteries which tends to be declined with age (Figure 9). This phenomenon represents the response of arterial wall to blood pressure. In healthy (no or less arteriosclerosis) arteries, the resistance of artery wall to that pressure is low and the capacitance is high. If the process of arteriosclerosis is started, then the resistance will be higher and the capacitance will be declined, therefore, affecting the amplitude of PPG pulsations to be reduced.

While the PPG signal reflects blood volume changes, it also reflects the response of the arterial wall to the pressure initiated by blood propagation. The PM index represents the maximum point of the PPG waveform (the maximum systolic point), which can be used as a measure of arterial distensibility. Vascular impedance [66] relies on consideration of the circulation as an electrical circuit. Impedance describes the relation of forces acting in the circulation to the motion of blood [2]. Accumulated atherosclerosis results upon the decrease of PM values, due to the increase of arterial stiffness and the acceleration of pulse wave velocity. In normal arteries the compliance is high; therefore they can respond to the force of blood pressure making them more distensible. It follows that a loss of the arteries' elastic properties might result in a reduction of PM values. The analysis of PPG's amplitude changes might reveal lot of information representing vascular activities, which in turn might help in quantifying some indices to be used clinical settings. Therefore, the analysis of PPG's PM and RI indices could be a fruitful outcome.

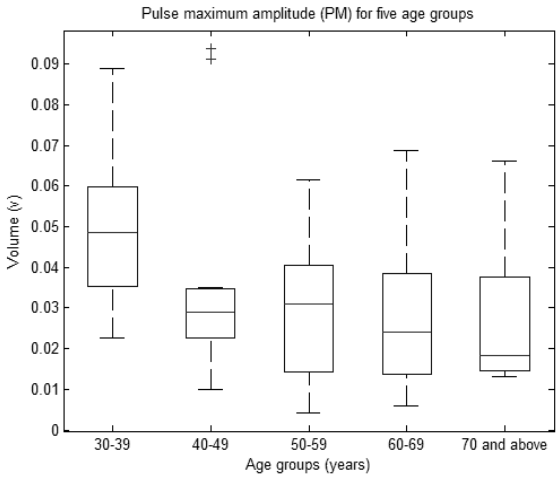
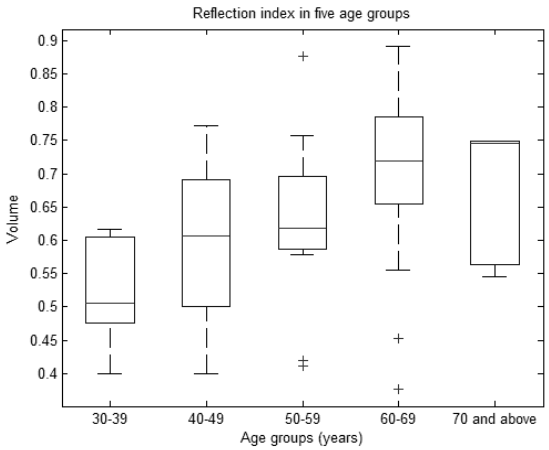


Fig. 9 Boxplot for PM of five age groups

PPG has been used to develop a stiffness index and a reflection index that are thought to reflect systemic arterial stiffness, and is now commercially available [2]. Problems include the damping of the peripheral pulse, and temperature-



dependant changes in the peripheral circulation. RI is derived as a measure of PPG amplitude changes based on the detection of systole and inflection point. Figure 10 represents Boxplot for *RI* based on five age groups. It is clearly seen that age is affecting the variations of *RI* parameter. By observing the changes among each age group, RI seems to be increased from one age group to the next, which in turn strengthen the effects of aging on PPG contour variations.

Fig. 10 RI among five age groups

RI is subjected to be increased with age due to the reduction in PM amplitude and to the increment of DM amplitude due to the augmentation of diastole in systole part with age. This phenomenon is the reason behind being inflection point close to systole point. Observing the variations of PPG signal in different age groups strengthen these findings. With age, PPG contour become more rounded which is observed by less in pronouncing of dicrotic notch and inflection point.

The positions of the DM points reflect the amount of the augmented diastolic blood into the systolic side. With age, the inflection point (diastolic point) becomes closer to the systolic point (PM). This phenomenon can be noticed through the reduction of peak-to-peak time (PPT or ΔT) (the time between the systolic and diastolic points). The DM can be used as a measure of small and medium arterial stiffness due to it is ability to reflect the response of PPG to the loss of arterial elastic properties. Moreover, the DM tends to be increased slightly with age and atherosclerosis. PPG augmentation index has shown to be a noninvasive indicator for vascular assessments [26]. Figure 11 shows that AI differs slightly from right to left hand. However, the correlation between AIR & AIL is (0.892, P <0.000). The findings for RI and AI are with agreement with the findings of [34], (AI and RI calculated from 2 PPG sites (middle finger and ear)).

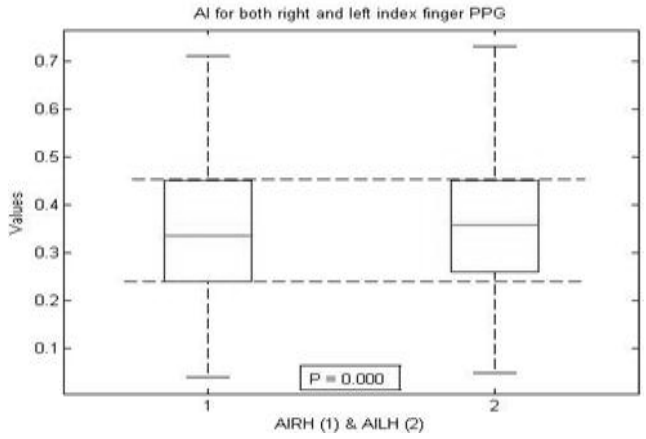


Fig. 11 Boxplot for AI right-hand & AI left-hand

With Age, the time to reach inflection point (DiT) tends to be increased. Statistics showed a good correlation between age and DiT since age correlates with DiTR (.295, P = 0.03) and with DiTL (.301, P = 0.03). CIMT test, which is an established measure for atherosclerosis found to be associated with SI and ΔT. The observation is that, an increment in CIMT measured by ultrasound represents a marker of structural atherosclerosis [70]. CIMT value will result in a reduction of ΔT which in turn affects SI to be increased as CIMT increased. Arteriosclerosis is affecting arterial elasticity thereby increasing arterial stiffness with age. PPG measurements were made using both the right and left index finger hands, hypothesizing that there would be little or no difference between the two sites of measurements. However, looking for the association between age and PPG is a great thinking, but one should realize that such a relation is not linear. Researchers thought that, in looking for the age affects on PPG, PPG better off to be considered as a whole pulse not as a single region or single parameter. Investigation and studying of age-related changes to the peripheral pulse contour using a much larger and diverse population is necessary for the establishment of important ageing indices [43]. The multi-site PPG measurements analysis has shown promise for the assessment of the normality of PPG's indices in ED patients among several age groups. Due to the differences of using several hardware instruments for PPG acquisition, several pre-processing and analyzing techniques, PPG shall be quantified by researchers in order to make a comparison between their results. Such comparison will contribute a lot in forming the quantified and drawing the general framework of this signal [67].

IV. Conclusion

Arterial stiffness was recognized as important in predicting cardiovascular disease. PPG contour analysis is great method which might be used to estimate arterial stiffness non-invasively. The analysis of PPG signals can provide a simple, inexpensive and non-invasive means for studying vascular function. Moreover, the PPG technique potentially has the advantage of being able to predict alterations in the vascular structure and function before the onset of clinical disease and before the clinical symptoms are detectable. Therefore, PPG contour analysis provides a window to the cardiovascular activities. This study proposed to assess PPG contour variations based on PPG data recording from right and left index finger. The study concluded that PPG timing indices are equal in both right and left hand. In addition, it concluded that, PPG amplitude indices differ slightly for right and left hand but still have a strong correlation with each other. A beat-to-beat change of the PPG amplitude is often the first clue that the patient has developed an irregular heart rhythm. The amplitude variations shall be giving more efforts and attention in order to ride the challenge in developing some means of pulse contour, which can be used to assist in health and disease and to be applied into clinical sittings. Age is an important factor in arterial stiffness since as you age; arteriosclerosis will be increased. In older subjects, the arteries are less distensible, leading to high SI and High RI, thereby resulting in a more rounded PPG with a lack of the dicrotic notch which in turn decreases arterial compliance. PPG has two main influences on vascular compliance, namely age and atherosclerosis. If PPG were to be validated, it would have potential uses in clinical settings. Analysis of PPG contour

might have important clinical implications which in turn strengthen the suggestion that PPG offers a fruitful avenue for new technologic developments in noninvasive circulatory monitoring. The major limitation of the study was definitely the small sample size. Our study was the first study investigating the correlation and association between CIMT, age, and PPG's indices in erectile dysfunction subjects.

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