The Investigation of the Effect of Aging through Photoplethysmogram Signal Analysis of Erectile Dysfunction Subjects

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Abstract: - This investigation presents the variations of photoplethysmogram (PPG) morphology with age. PPG measurement is done noninvasively at the index finger in both right and left hands of erectile dysfunction (ED) subjects. 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 arteriosclerosis.

Key-Words: - PPG, RI, SI, CIMT, Age, Contour analysis

1 Introduction

Erectile dysfunction is a sign of cardiovascular disease which can be a sign of increased risk [19]. The risk of cardiovascular diseases may damage the endothelium cells which may cause atherosclerosis (stiffening of arteries). Arterial stiffness is not only a marker of cardiovascular dysfunction but also an independent risk factor for cardiovascular disease [3] [4]. Pulse pressure, a surrogate marker of increased arterial stiffness, is a powerful predictor of cardiovascular events [5]. As large arteries stiffen with age or disease processes, the amplitude of the reflected wave increases [4].

Arterial stiffness can be measured noninvasively by the use of PPG technique, which reflects the changes in blood volume with each heart beat. Perhaps the most exciting application of PPG waveform analysis is the possibility of providing a rapid biophysical measure of diseases or ageing process [1]. PPG provides an estimation of cutaneous blood flow by measuring the dynamic attenuation of infrared light by the blood volume present in tissue [2]. 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 [6]. Arterial pulsations are the most significant portion of PPG [7]. PPG's oscillating component provides a pulsatile wave, whose contour may include content descriptive of vascular health [2, 8-9]. The PPG waveform comprises a pulsatile ('AC') physiological waveform attributed to cardiac synchronous changes in the blood volume with each heart beat [12]. PPG measurements done at index finger (both right and left hands) since finger PPG is a commonly used technique in medicine [10-11].

Derivations of quantitative measures characterizing pulse shape have proven useful in analyzing PPG signal [2]. The peripheral pulse is often used in the assessment of health and disease [10]. Figure 1 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.

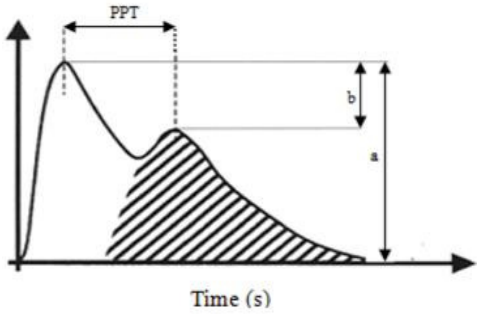

Figure 1: The characteristics of PPG

2 Methods

2.1 Data Acquisition

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).

2.2 Hardware and 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. 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. These filters did not introduce phase delays or distortion to the waveforms [18]. Utilizing PPG derivatives, those points of interest can be located and determined [13-15]. Figure 2 shows PPG signal, d1PPG, d2PPG and the process of peak detection.

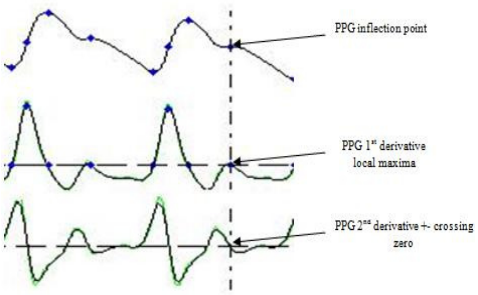

Figure 2: PPG signal, d1PPG, d2PPG and the process of peak detection.

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.

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.

The demonstration of correlations between parameters of peripheral pulse wave analysis and pulse wave velocity (*PWV*) measured both invasively and noninvasively, supports the revival of PPG as a simple and inexpensive technique for the assessment of vascular health [2, 15, 17]. 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 [2]. 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. 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.

2.3 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.

Table1: Medical data characteristics for each age group (median±SD)

Age (years)	*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).

Table 1 shows the medical data characteristics for each age group. 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.

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

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

2.4 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)

2.5 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

3 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. It is noteworthy that PPG time indices are equal; such observation shall be utilized in distinguish between normal and up normal signals.

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 [2] since age has no evidence to affect PPG indices in right and left hand fingers (our study was in the index finger while [2] study was in the middle finger).

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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 lose 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 3. 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.

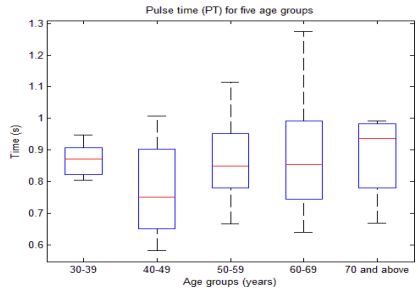

Figure 3: PPG pulse timing for five age groups

The maximum amplitude of PPG's single pulse (*PM*) contributes to the compliance of arteries which tends to be declined with age (figure 4). 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. Thereby, affecting the amplitude of PPG pulsations to be reduced.

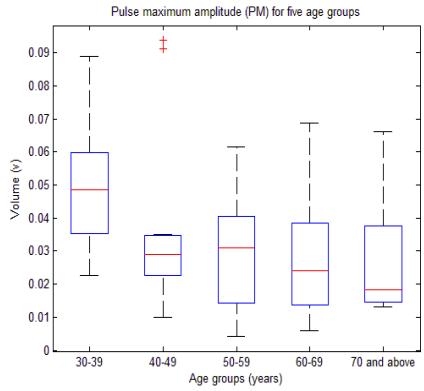

Figure 4: Boxplot for PM of five age groups

RI is derived as a measure of PPG amplitude changes based on the detection of systole and inflection point. Figure 5 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.

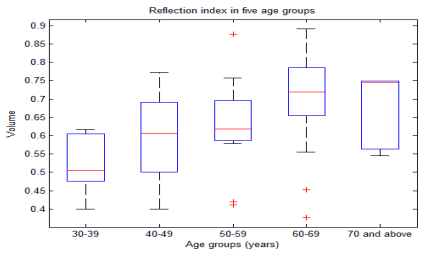

Figure 5: RI among five age groups

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.

PPG augmentation index has shown to be a noninvasive indicator for vascular assessments [16]. Figure 6 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 [14], (AI and RI calculated from 2 PPG sites (middle finger and ear)).

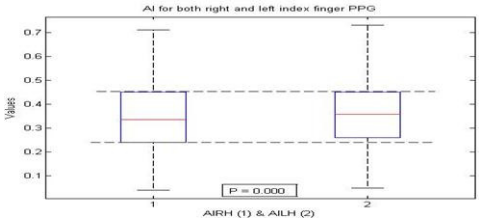

Figure 6: Boxplot for AI right-hand & AI left-hand

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 the gold standard test for arteriosclerosis found to be associated with SI and ΔT. The observation is that, an increment in 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

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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 [2].

4 Conclusion

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. 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.

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