

Extracting clinically relevant information from pulse oximetry traces.

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Cardiovascular assessment is necessary obtained from standard oximeters can provide reliable estimates for transit time, a measure associated to vascular stiffness, yet unaffordable for large population groups worldwide. Here we illustrate how signals, as well as complexity measures derived from Recursive plot analysis. The salient features of our research were: 1) The possibility to use of photoplethysmographic (PPG) signals as a surrogate for transit time estimation; 2)The use of PPG signals for HRV analysis; 3)The possibility to use 2-min PPG recordings for cardiovascular estimation; 4)The proposal of a new vascular age estimator. An automated algorithm for estimating transit time from the PPG waveform yielded a strong association with age ($r=0.80$). All indices obtained from Recurrent Plot analysis of tachograms with PPG signals exhibited a high correlation with subject's age. On the basis of the estimated indices a new estimator for cardiovascular age has been introduced, which exhibited a high correlation with age ($r=0.97$). Thus we concluded that PPG signals do retain information about cardiovascular age. This is evidenced from changes with age of different indices obtained from 2-min duration PPG traces. These results might be relevant for boosting cardiovascular diagnosis in settings with limited resources.

Keywords: Pulse Oximetry, Heart Rate Variability, Transit Time Estimation, Recurrent Plot Analysis, Cardio Vascular Age.

1 Introduction

One of the strategies in present-day medicine is to increase the diagnostic capacity of available methods and devices [1].

This is in line with the goal of reducing health care expenses, increase health care delivery efficiency and offer the best care possible without threatening the wellbeing of the patient.

Among markers of arterial disease, arterial stiffness has proven to be an important aspect in the assessment of cardiovascular risk [2]. From the different options to evaluate arterial stiffness, carotid to femoral pulse wave velocity (PWV) has emerged as the gold standard method because of growing evidence demonstrating its association with cardiovascular disease in various populations [3].

Arterial stiffness measures and PWV in particular, are being increasingly recommended for routine clinical assessment of patients as well as part of large-scale clinical studies. Thus PWV has been included in the 2007 guidelines from the European Society of Hypertension (ESH) and the European Society of Cardiology (ESC) for the management of hypertension [4].

On the other hand, togetherwith specific indices that measure a specific process (e. g. expression level for a living gene or visual acuity), we need indices for the state of the organism as a whole. In this sense, heart rhythm reflects the state of cardiac rhythm intrinsic mechanisms as well as its regulation by feedback from vasculature, autonomic function, respiration, as well as central nervous system. This explains the importance of heart rate variability (HRV) as a tool for accessing human body's complexity.

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Thus far, PWV and heart rate variability studies are performed almost exclusively in advanced laboratories in developed countries.

Here we illustrate how it is possible to perform high quality studies about cardiovascular system using affordable techniques for recordings and processing them with freely available software.

Our analysis will be based on the use of the photoplethysmographic (PPG) signal, which can be obtained through standard oximeters.

In particular we will show that a reliable estimate of PWV can be obtained from the study of PPG signals.

At the same time, the PPG signal has been proven as an excellent surrogate for electrocardiogram in heart rate variability studies. In this research we are estimating cardiovascular age on the basis of recurrent plot analysis of HRV signals obtained from photoplethysmograms.

As a matter of comparison, a commercially available SphygmoCor system for PWV analysis costs more than 10 000 US dollars, compared to less than 40 US dollars for a portable oximeter.

Attempts to obtain surrogates for PWV from PPG signals are not new [5]. This possibility arises from assuming that the PPG signal can be the result of a superposition of at least two waves: a direct pressure wave coming from the heart and a second, reflected wave coming from abdominal aorta bifurcation [6-7]. However, the diversity in PPG waveforms suggest that special algorithms are required for PWV estimation from PPG signals. Here we are introducing an automatic algorithm based on first derivative analysis.

The use of HRV for estimating cardiovascular age has been proposed by Giuliani et al in 1998 [8]. For that, these authors used 7 minutes of ECG recording both in supine and tilt positions.

Here we are showing that good estimates for cardiovascular age can be obtained from 2' minutes PPG signals recorded on supine position only.

Overall, our results point to a high potentiality of the PPG signal for cardiovascular assessment of individuals in rural communities worldwide.

2 Methods

2.1 Subjects

We studied 230 recordings from healthy subjects with their ages ranging from 8 to 89 years (34 subjects were male). The demographic data of the subjects are as summarized in Table I. Recordings were obtained in Orense, Spain, and more than 95% of subjects were original from Galicia.

The inclusion criteria were: no clinically apparent arterial disease or physical abnormality and not observantly obese or on any medication. Approval was obtained from the local research ethics committee, and each subject's verbal consent was taken before the recordings were made. Peripheral (pointer finger of the right arm) pulse measurements were recorded for 5 min, using a validated oximeter (Nellcor 395, USA), with the subject sitting on a chair and the arm positioned at heart level with the forearm resting on a table in a temperature controlled room ($24 \pm 1.5^\circ\text{C}$).

Table I. Demographic data of the subjects included in present study

Age range (years)	Female	Male	Total
6 to 20	7	11	18
21 to 30	17	23	40
31 to 40	24	25	49
41 to 50	12	30	42
51 to 60	11	18	29
61 to 70	12	12	24
71 to 80	10	14	24
81 to 89	3	1	4
	96	134	230

Care was taken to see that the effect of motion artifact was the lowest possible. The subjects were also asked not to undergo strenuous exercise, avoid consuming hot drinks or those containing caffeine, and

refrain from smoking for 2 hours prior to recording. It was also ensured that the subjects were relaxed and breathing regularly and gently. Signals were digitized at 1000 Hz and saved as ASCII files.

2.2 Transit Time estimation.

Two-min PPG recordings were used for this analysis. PPG peaks were automatically detected and an average trace of all waves present in a two-min PPG trace was obtained. The average signal was differentiated via obtaining the differences between successive peaks in the time series. A special algorithm was implemented in SciLab for detecting the position of local minima and inflexion points at the derivative signal. A Transmission Time estimator (TTW) was introduced as the difference between the first local minimum and the subsequent local maximum (or inflexion point) of the averaged signal's first derivative (see figure 1).

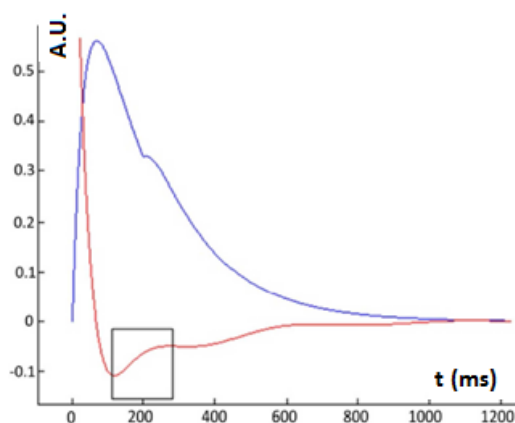


Figure 1. PPG averaged signal (blue) and its derivative (red). Here, TTW appears as the width of the black rectangle (170 ms).

2.3 Recurrent Plot Analysis

Cardiac tachograms were obtained as the differences between maxima positions in the PPG time series. Recurrent plot analysis [9] was performed using the Kubios 2.2 platform for HRV analysis [10].

The RQA is based on the computation of a distance matrix between the rows (epoch) of an embedding matrix of the tachogram. This distance matrix is computed making use of Euclidean metrics; after this first step, the distance matrix, having as rows and columns the subsequent epochs of the series of length equal to the chosen embedding dimension, is transformed into binarian data with values of zero for distances below a pre-established threshold. Here we used default data as proposed in the Kubios HRV package [10]. The following indices were studied:

- Recurrent Rate (Rec)
- Maximal Line length (Maxline)
- Percent of determinism (Det)
- Shannon entropy (Ent)

2.4 Statistical processing.

Procedures included regression and correlation analysis.

2.5 Limitations of Present Study

Studied subjects belong to a relatively large sample and are presumably healthy; however there are no clinical confirming data for cardiovascular health (e. g. ECG, blood pressure, lipid profile, etc.).

Another limitation is related to sample size. This study uses a much smaller sample than published PWV reports. However, it is larger compared to most PPG transit time publications thus far. Our data set is comparable to that of Giuliani et al, who applied recurrent plot analysis to HRV data.

3 Results

3.1 Estimation of transit time from PPG signals.

The relationship between TTW and age is presented in figure 2.

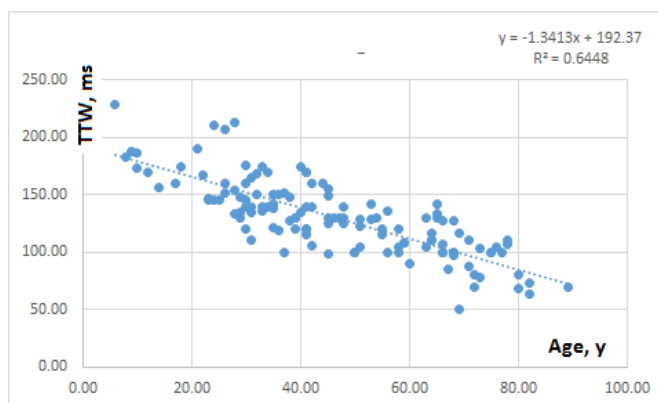


Figure 2. TTW age dependence for the whole sample.

The obtained correlation coefficient is $r=0.80$, similar to the value obtained by Hernandez Cáceres and Syed using a manual version of TTW [11].

3.2 Recurrent Plot Analysis

All studied RPA exhibited significant correlations with age (Table II). The strongest correlation corresponded to percentage of determinism ('Det'; Figure 3).

Table II. Correlation of Recurrent plot analysis variables respect to age.

Rec	Det	Ent	Maxline
-0.63	-0.71	-0.63	-0.54

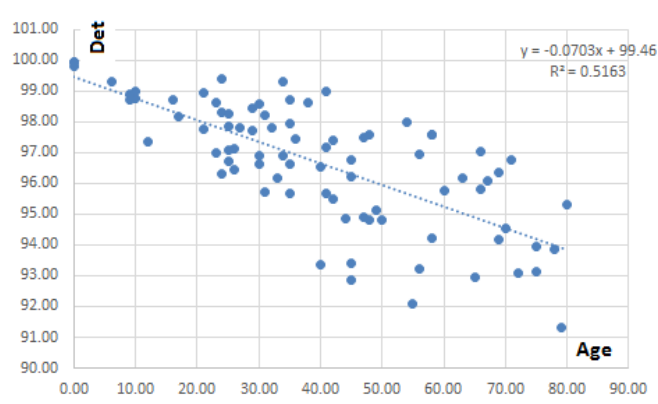


Figure 3. TTW age dependence for the whole sample. Points corresponding to age “Zero” represent three fetal tachograms downloaded from physionet.org

3.3 Towards a cardiovascular age estimator.

Based on our results, we introduced a cardiovascular age estimator. The proposed index is defined as the best candidate, for a given subject, among individual regression with age for each of the five variables obtained. As expected, the obtained correlation coefficient is very high, with a regression function very close to the identity line ($CVAge=0.98*ChronologicalAge$; $r=0.97$; figure 4)

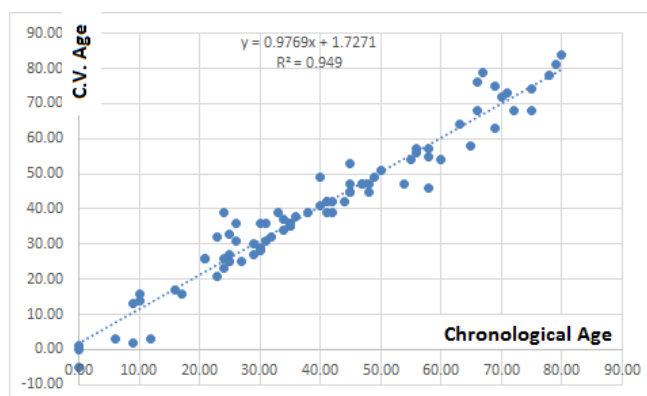


Figure 4. Estimated cardiovascular age as a function of observed chronological age

4 Discussion

The salient features of present research are

- The use of PPG signals as a surrogate for transit time estimation.
- The use of PPG signals for HRV analysis
- The possibility to use 2-min PPG recordings for cardiovascular estimation
- The proposal of a new vascular age estimator.

Theoretical research supports the idea of a PPG signal as a surrogate for pulse pressure recordings [11]. Here, we showed that it is possible to obtain a high correlation with age using an automatic algorithm for transit time estimation. This can avoid any bias related to subjective appreciation.

ECG-based tachograms can be a problem in certain settings. A pulse oximeter is much cheaper and easier to handle than an ECG-machine. This potentiates the value of the pulse oximeter as a means for assessing cardiovascular function.

The optimal duration of HRV recordings have been discussed in literature. Giuliani et al used traces with 7-min duration recorded both in supine and tilt position. The possibility to use traces with 2 min duration in supine position only increases the potential of PPG studies.

Finally, given the fact that 5 variables are exhibiting high correlation with age allowed us to propose a Cardio Vascular Age estimator based on the information provided by each of these variables. We do realize that this estimate does not take into consideration the structure of the covariance matrix, and further studies are required to determine the behavior of the estimated Cardio Vascular Age under different conditions.

Taken overall, our results illustrate that data obtained with a pulse oximeter do retain important information about cardiovascular function. This can contribute to both prevention and treatment of population at risk in remote settings.

5 Conclusion

PPG signals do retain information about cardiovascular age. This is evidenced from changes with age of different indices obtained from 2-min duration PPG traces. These results might be relevant for boosting cardiovascular diagnosis in settings with limited resources.

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