Artificial Intelligence-based Method for Carotid-to-Femoral Pulse Wave Velocity Estimation from Photoplethysmogram Signal

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***Abstract*—Cardiovascular diseases (CVDs) are the primary cause of death in the world. The development of easy-to-use and non-invasive monitoring and predicting CVDs' diagnosis methods is crucial. Among the key parameters in the cardiovascular system is the arterial stiffness. An increase in arterial stiffness is considered a primary risk factor for CVDs. Although arterial stiffness can be assessed non-invasively by measuring the carotid-to-femoral pulse wave velocity (cf–PWV), which is considered as a gold standard for arterial stiffness measurement, the clinical process of assessing this parameter is very intrusive and complicated. In this work, we propose an artificial intelligence-based method for the prediction of (cf–PWV) non-invasively using distal photoplethysmogram (PPG) waveforms. Functionally, PPG offers a simple, reliable, low-cost technique to measure blood volume change and hence assess the cardiovascular function. Here, we identify features from the timings of fiducial points that are extracted from the PPG, its first, second, and third derivative waveforms. The results based on virtual data-set show an acceptable estimation of the arterial stiffness index, carotid-to-femoral pulse wave velocity with mean absolute percentage error less than 2.5%.**

***Keywords*—Photoplethysmogram, Carotid to Femoral Pulse Wave Velocity, Deep learning, Estimation, fiducial points**

I. Introduction

Arterial stiffness is a crucial factor in several CVDs such as systolic hypertension, stroke, coronary artery disease, and heart failure. These diseases are among the significant causes of mortality in the world [1]. Therefore, assessment of the arterial stiffness is essential in cardiovascular research as well as in clinical routine [2]. The carotid to femoral pulse wave velocity (cf–PWV) is deemed the gold standard of the arterial stiffness measurement. This parameter evaluates the rate at which the pressure waveform moves down the central arteries, being a surrogate of the arterial stiffness, generally, as the cf–PWV increases, the arterial stiffness increases too [3]. Accordingly, several experimental and theoretical studies have shown a strong correlation between cf–PWV and the presence of CVDs [4]. Although measuring cf–PWV is currently considered the most reliable non-invasive method for evaluating arterial stiffness, its clinical assessment process is found to be complicated and intrusive. The calculation of cf–PWV requires the recording of blood pressure waveforms from inguinal sites (carotid and femoral sites) that needs an expert staff with a sophisticated setting. Additionally, it requires a precise measurement of the distance between the carotid and femoral sites that is usually not very accurate [5]. Thus, an easy-to-use, non-invasive, and novel measurement tool of cf–PWV would be very worthwhile and valuable for the medical and research community. Over the past few years, artificial intelligence techniques, including machine learning methods and recently deep learning approaches, have attracted the research community interest and especially in healthcare applications [6]. At the same time, photoplethysmogram (PPG), usually known as PPG, has been introduced as a low-cost and straightforward technique, which can sense blood volume variations in the microvascular bed of tissue. PPG is considered as a convenient and potentially useful method for assessing cardiac event since it contains valuable physiological information influenced by the vascular system [7]. Furthermore, PPG waveform is easy to acquire using a wide range of ubiquitous sensors that are usually integrated into fitness devices as well as smartphones or tablets [8], [9]. Therefore, the estimation of the cf–PWV from the PPG signal, if possible, will be a breakthrough in the CVDs monitoring [10].

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In this work, we introduce an easy-to-use and non-invasive artificial intelligence-based method to estimate the cf–PWV from a single PPG waveform measured at distal locations, such as radial, brachial or digital arteries. The signal processing inputs to the artificial intelligence algorithm are features extracted from PPG pulse waves by detecting fiducial points on the pulse wave and its derivatives and computing a range of features from the fiducial points. Moreover, some routine clinical variables such as age, heart rate and brachial systolic, and diastolic pressure values have been added to increase the accuracy. The results show that the proposed method is a reliable surrogate of cf–PWV. The rest of the paper is organized as follows. Section II describes the used data-set and the PPG pulse-based features extraction technique. In addition, we present the artificial intelligence based regres-

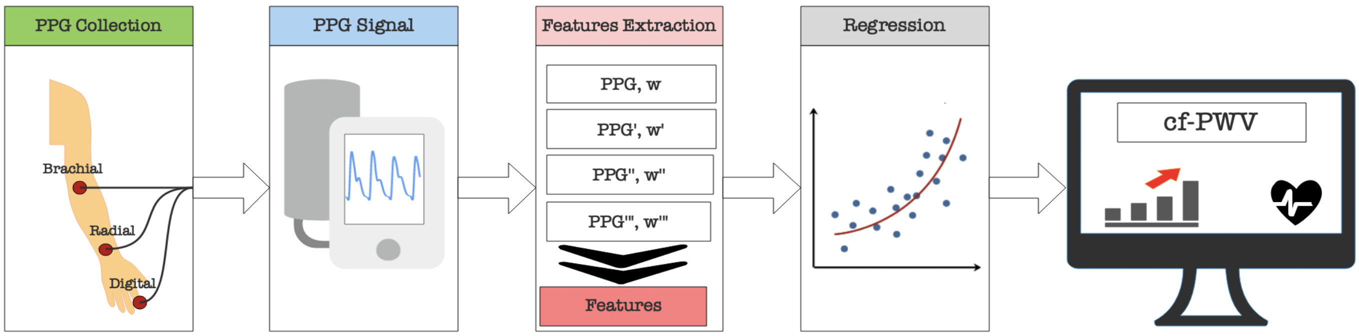

Fig. 1: A Framework for central arterial stiffness, carotid-to-femoral pulse wave velocity, estimation from distal non-invasive photoplethysmogram waveform.

sion model. In Section III, the results, discussion, and future perspectives are shown. Finally, Section V summarizes the obtained results.

II. Materials and Methods

A. In-silico Virtual Population

To validate the proposed method, we utilize a virtual, prevalidated database of simulated pulse waves (PW) [11], publicly available [1]. It is considered as a useful resource to evaluate the pre-clinical assessment of PW analysis algorithms. The database encompasses mainly these arterial PWs: 1) flow velocity, 2) luminal area, 3) pressure, and 4) photoplethysmogram pulse waves at different sites of the arterial network such as the ascending aorta, carotid artery, brachial artery, and radial arteries, etc. The database represents samples of 4,374 virtual healthy adults aged from 25 to 75 years old, in ten-year increments (six age groups). For each age group, 729 virtual subjects based on pulse waves were created by varying specific cardiac and arterial parameters like the arterial stiffness and heart rate within normal ranges. In this study, photoplethysmogram signals at the level of the radial, brachial and digital arteries have been investigated to evaluate the proposed methodology. Fig.1 illustrates the general framework.

B. Features Extraction for PPG signals

In this study, PPG features are extracted as follows:
Step 1: Detection of the fiducial points from the PPG and its derivatives signals (first derivative: PPG$'$, second derivative: PPG$''$, and third derivative: PPG$'''$). Fig. 2 shows an example of a PPG waveform simulated at the level of the radial artery, its derivatives, and the corresponding detected fiducial points. Referring to this plot the red circles show:

- Three fiducial points on the original pulse wave, PPG that are: (s) the systolic peak, (dic) the dicrotic notch and (dia) the diastolic peak.
- One fiducial point, (ms), on the first derivative pulse wave that corresponds to the maximum upslope [8].
- Five fiducial points (a, b, c, d, and e) on the second derivative wave [20].
- Two fiducial points (p_1 and p_2) from the third derivative that denotes the early and late systolic components [21].

[1]https://peterhcharlton.github.io/pwdb/index.html

TABLE I: Features calculated from PPG pulse waves. Definitions: t—time since pulse onset (beginning of systolic upslope); w, w', w", w"'—PPG signal and derivatives; T—duration of cardiac cycle (s).

Pulse	Feature	Formula
PPG, w	ΔT, [12]	$\mathrm{t(dia)} - \mathrm{t(s)}$
	CT, [13]	$\mathrm{t(s)}$
	$\mathrm{prop_s}$, [14]	$\mathrm{t(s)/T}$
	$\mathrm{t_{sys}}$, [15]	$\mathrm{t(dic)}$
	$\mathrm{t_{dia}}$, [15]	$\mathrm{T - t(dic)}$
	$\mathrm{t_{ratio}}$, [15]	$\mathrm{t(s)/t(dic)}$
	$\mathrm{prop_{\Delta T}}$, [15]	$\mathrm{(t(dia) - t(s))/T}$
	$\mathrm{t_{p_1-dia}}$, [15]	$\mathrm{t(dia) - t(p_1)}$
	$\mathrm{t_{p_2-dia}}$, [15]	$\mathrm{t(dia) - t(p_2)}$
	IPR, [15]	$\mathrm{60/T}$
	AI, [16]	$\mathrm{(w(p_2) - w(p_1))/w(s)}$
	RI, [12]	$\mathrm{w(dia)/w(s)}$
	$\mathrm{RI_{p_1}}$, [15]	$\mathrm{w(dia)/w(p_1)}$
	$\mathrm{RI_{p_2}}$, [15]	$\mathrm{w(dia)/w(p_2)}$
	$\mathrm{ratio_{p_2-p_1}}$, [15]	$\mathrm{w(p_2)/w(p_1)}$
	A1, [15]	Area from pulse foot to dicrotic notch
	A2, [15]	Area from dicrotic notch to pulse end
	IPA, [15]	A2/A1
PPG$'$, w$'$	ms, [13]	$\mathrm{w'(ms)/w(p_1)}$
PPG$''$, w$''$	b/a, [16]	$\mathrm{w''(b)/w''(a)}$
	c/a, [16]	$\mathrm{w''(c)/w''(a)}$
	d/a, [16]	$\mathrm{w''(d)/w''(a)}$
	e/a, [16]	$\mathrm{w''(e)/w''(a)}$
	AGI, [16]	$\mathrm{(w''(b)–w''(c)–w''(d)–w''(e))\ /w''(a)}$
	$\mathrm{AGI_{int}}$, [17]	$\mathrm{(w''(b)–w''(e))/w''(a)}$
	$\mathrm{AGI_{mod}}$, [18]	$\mathrm{(w''(b)–w''(c)–w''(d))/w''(a)}$
	$\mathrm{t_{b-c}}$, [15]	$\mathrm{t(c) - t(b)}$
	$\mathrm{t_{b-d}}$, [15]	$\mathrm{t(d) - t(b)}$
	$\mathrm{slope_{b-c}}$, [15]	d/dt of straight line between b and c, normalized by a
	$\mathrm{slope_{b-d}}$, [15]	d/dt of straight line between b and d, normalized by a
Combined (w$''$ & w)	IPAID, [15]	$\mathrm{(A2/A1) + d/a}$
	k, [19]	$\mathrm{w''(s)/(w(s) - w(ms))/w(s)}$

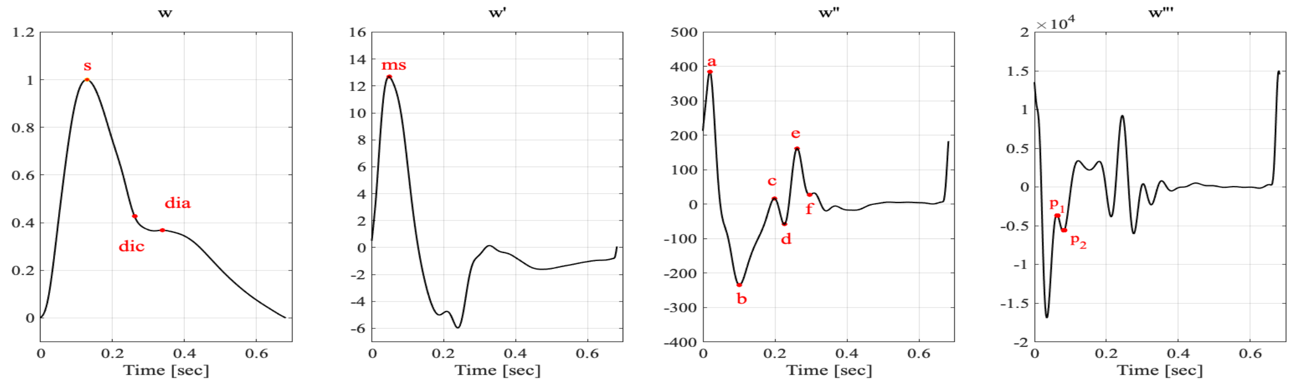

Fig. 2: Detection of fiducial points on the PPG signal (w) and its first derivative (w′), second derivative (w′′) and third derivative (w′′′).

Step 2: Computation of features based on the detected fiducial points. Table 1 lists the formulas used to calculate these features. As claimed in [8], these features were identified from publications describing techniques for assessing arterial stiffness from pulse waves. In addition, the criterion along with the MATLAB code[2] used to detect the fiducial points and extract the corresponding features are provided in this article, [8].

C. Regression models

The input PPG data are used to generate the features explained in section II-B and Table I, which are fed to different Multi-layer Perceptron or Neural Network (NN) models. The NN model has two hidden layers of 100 neurons with a '*ReLu*' activation function for each hidden layer. The used model uses the '*lbfgs*' solver, which is an optimizer in the family of quasi-Newton methods. The optimal L_2 penalty parameter '*alpha*' is set to 0.001.

For this regression experiment, half of the randomly shuffled data is used for training, and the remaining half is used for testing. The estimation performance is measured by the mean absolute percentage error (MAPE) of the testing set as follows:

$$\mathrm{MAPE}\ [\%] = \frac{1}{\mathrm{N}} \sum_{\mathrm{n}=1}^{\mathrm{N}} \frac{|\mathrm{cf{-}PWV}^{\mathrm{n}}_{\mathrm{real}} - \mathrm{cf{-}PWV}^{\mathrm{n}}_{\mathrm{predicted}}|}{\mathrm{cf{-}PWV}^{\mathrm{n}}_{\mathrm{predicted}}}, \tag{1}$$

where N is the size of the training set. $\mathrm{cf{-}PWV}^{\mathrm{n}}_{\mathrm{real}}$ and $\mathrm{cf{-}PWV}^{\mathrm{n}}_{\mathrm{real}}$ are the real and estimated cf–PWV, respectively. In addition, for ease of visualization of the goodness of the proposed model, we assessed the sum of the squared differences (SSE), R-square (R^2) which is the square of the correlation and, the root mean square error (RMSE) between the real values and the predicted response values, as follows

$$SSE = \sum_{n=1}^{N} (cf{-}PWV^n_{real} - cf{-}PWV^n_{predicted})^2 \tag{2}$$

[2]https://peterhcharlton.github.io/pulse-analyse/index.html

$$R^2 = 1 - \frac{SSE}{\sum_{n=1}^{N} \left(cf{-}PWV^n_{real} - \mu(cf{-}PWV_{real})\right)^2} \tag{3}$$

$$RMSE = \sqrt{\frac{SSE}{N}} \tag{4}$$

where μ is a function that evaluates the mean of $\mathrm{cf{-}PWV_{real}}$ over N subjects.

III. Results and Discussion

A. cf–PWV *model result*

TABLE II reports the estimation performance-based criterion, {MAPE, SSE, R^2 and RMSE}, of the proposed model, using PPG signals collected at different measurement sites of the arterial network: the digital, radial, and brachial arteries. Overall, for the three sites, the model is performing well and shows acceptable capabilities. The best goodness of prediction, on the whole, validation dataset, was obtained at the level of the radial artery with a MAPE value equal to 1.94 %. Besides, for the digital and brachial sites, this criterion was marginally larger, but it does not exceed 2.5 %. Besides, in Fig. 4, we show, in the first row, the ($\mathrm{cf{-}PWV_{predicted}}$) versus ($\mathrm{cf{-}PWV_{real}}$) of the validation dataset for the three arterial sites. The square of the correlation, R^2, between the tested data and the estimated response is around 0.96 for the radial and digital site and marginally smaller for the brachial site. The second row of Fig.4 shows Bland-Altman plots along with the mean difference value and the limits of agreements of the prediction results for each PPG-based measurement site. The mean difference is minimal in all cases. For instance, the mean difference value in the case of collecting PPG from the radial site is equal to 0.004, and the limits agreement is approximately equal to $(+0.8043)$ and (-0.7964). From these plots, it is clear that the proposed model is performing better for the prediction of cf–PWV less than 12 [m/sec] and above this value the error starts to increases.

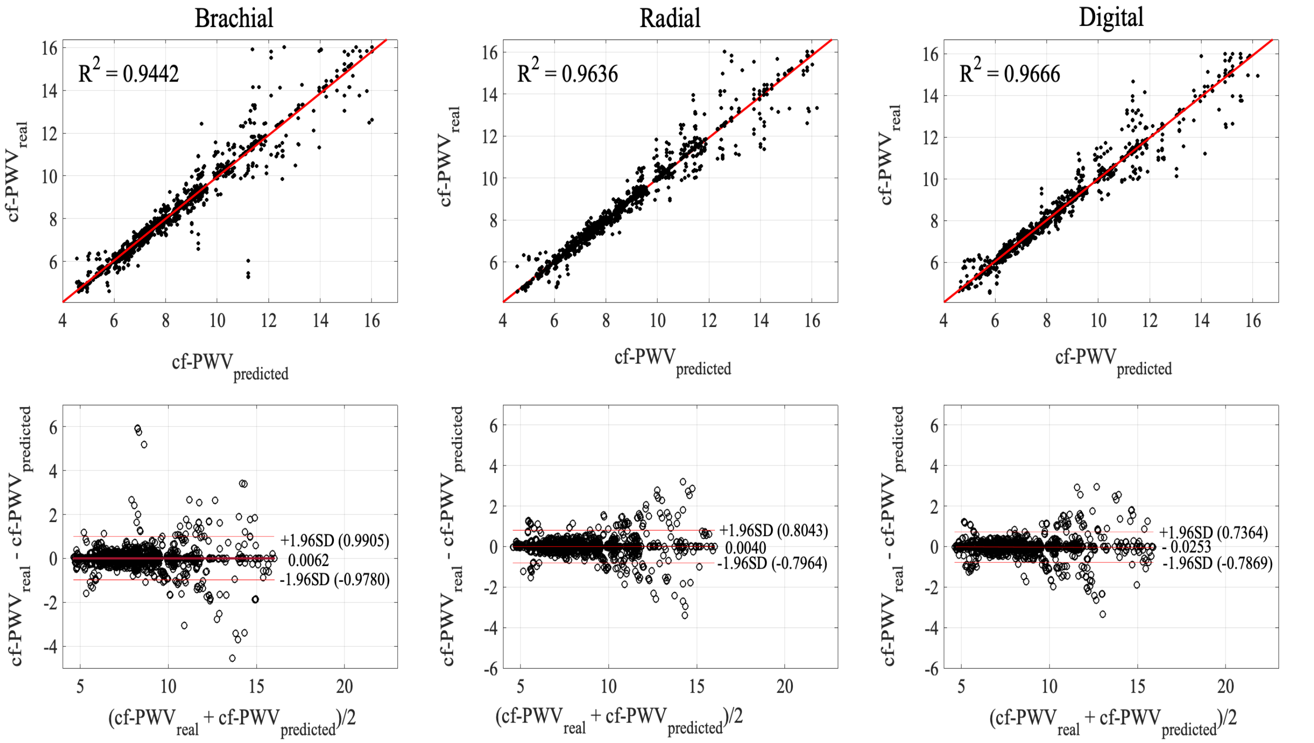

Fig. 3: cf–PWV estimated performance on testing set using features-based PPG waveforms and its derivatives collected at the level of brachial, radial and digital arteries. The first row represents the plots of the predicted cf–PWV versus the real tested cf–PWV. The second row shows the cf–PWV Bland-Altman plots along with the limits of agreement and the mean difference.The unit of all the axes is [m/sec]. We can observe from these plot that the more estimation error correspond to the larger cf–PWV (more than 12 m/sec).

B. Advantages

The above results demonstrate the potential of the proposed approach to estimate the central arterial stiffness index, cf–PWV, using PPG waveform, collected at the level of distal arteries. The main advantages of having an acceptable estimate of the cf–PWV from a feature based-PPG signal would be: PPG an ideal ambulatory device; it is inexpensive and cheap; it consumes very less power; it is used non-invasively and does not need specialized training or guidance. In addition, PPG technology is usually integrated into fitness devices as well as smartphones or tablets. In fact, more than ten companies are producing these sensors commercially.

TABLE II: Estimation performance evluated by the mean absolute percentage error (MAPE), the sum of the squared differences (SSE), R-square (R^2) which is the square of the correlation and, the root mean square error (RMSE) between the real values and the predicted response values.

Arterial site	MAPE [%]	SSE	R^2	RMSE
Brachial	2.41	545.3	0.94	0.50
Radial	1.94	357.6	0.96	0.40
Digital	1.95	328.5	0.96	0.39

C. Limitations

It is worthy to note the limitations to this study. Firstly, in this work, due to non-availability of real data, we used *in-silico* data. Although this database mimics the real physiological human states, *in-vivo* investigations are required to validate and verify the reliability of this approach. Secondly, the extraction of features was based on only one single PPG wave (one cardiac cycle). Future work should derive metrics from multiple PPG cycles. This will help to assess and take into account the inter-beat interval variability. Finally, this study does not consider the noise effect on the PPG features. In fact, several sources of noise can be allocated with the PPG signal, such as the movement artifacts, poor sensor contact, and optical interference, etc. Accordingly, considering the noise can impact the utility of the PPG-based features in predicting cf–PWV. In the future, the robustness of the derived features against the different sources of noise should be studied and analyzed. This is extremely important, especially for personal use, to assess arterial stiffness.

IV. Conclusion

CVDs are the number one cause of premature death worldwide. Beside, arterial stiffness is considered the major risk of developing CVDs. Therefore, attention needs to be given to the prognosis and diagnosis of arterial stiffness.

Functionally, the arterial stiffness is assessed by applanation tonometry by measuring the carotid to femoral pulse wave velocity that is considered a clinical gold standard measure. Although measuring $\mathrm{cf{-}PWV}$ is performed non-invasively; this clinical routine is deemed to be expensive and intrusive. Therefore, in this work, we investigated the use of an artificial technique to assess the central arterial stiffness index, $\mathrm{cf{-}PWV}$. Our approach uses PPG waveform collected at the level of the distal artery, such as brachial, radial, and digital arteries. We identified features that are suitable for the estimation of arterial stiffness. They are derived based on the timing fiducial points of the PPG signal along with its first, second, and third derivative. The results demonstrate a good estimation performances with a R^2 correlation coefficient around 0.94 and MAPE less 2.5 %. Although the *in-silico*-based results are auspicious, many limitations are presented within this study, such as the use of a virtual database; the extraction of the features is based only on a single PPG wave and the non-consideration of the noise impact. In the future, it might have a great utility to overcome the above limitations and integrate the proposed approach for personal healthcare application.

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