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Characterization of Optical System for Hemodynamic Multi-Parameter Assessment

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Abstract—Cardiovascular diseases are a growing epidemiological burden in today's society. A great deal of effort has been made to find solutions able to perform non-invasive monitoring and early diagnosis of such pathologies. The pulse wave velocity and certain waveform characteristics constitute some of the most important cardiovascular risk indicators. Optical sensors are an attractive instrumental solution in this kind of time assessment applications due to their truly non-contact operation capability and better resolution than commercial devices. This study consisted on the experimental validation and a clinical feasibility for a non-invasive and multi-parametric optical system for evaluation of the cardiovascular condition. Two prototypes, based on two different types of photodetectors (planar and avalanche photodiode) were tested in a small group of volunteers, and the main hemodynamic parameters were measured, such as pulse wave velocity and indexes of pulse waveform analysis: the Augmentation Index, Subendocardial Viability Ratio and Ejection Time Index. The probes under study proved to be able to measure the pulse pressure wave in a reliable manner at the carotid site, and demonstrated the consistency of the parameters determined using dedicated algorithms. This study represents a preliminary evaluation of an optical system devoted to the clinical evaluation environment. Further development to take this system to a higher level of clinical significance, by incorporating it in a multicenter study, is currently underway.

Keywords—Optical probes, Pulse wave velocity, Pulse waveform analysis, Hemodynamics parameters, Cardiovascular risk factors.

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INTRODUCTION

The monitoring of the cardiovascular system and cardiac activity has been growing in importance on the diagnosis and management of many disease states, including hypertension, coronary artery disease, diabetes, obstructive sleep apnea, *etc*.[2,17]

Blood pressure and the arterial pulse have long been known as fundamental medical signs.[1] Throughout the ages numerous conventional non-invasive techniques have been developed to detect cardiovascular pulsation and blood pressure. The first methods were the oscillometric methods, stethoscopes, phonocardiograms, and manual palpation of superficial arteries, which were non-suitable for continuous monitoring. Emerging trends in cardiovascular monitoring are moving away from more invasive technologies to portable and non-invasive solutions. An optical method for non-contact measurement of skin surface vibrations with the distension of the carotid artery is promising nowadays.[21] Measurement of the structural and functional properties of the carotid arterial segment yields a host of indexes for the assessment of cardiovascular risk, vascular adaptation, and therapeutic efficacy.[4]

The pressure wave generated by the contraction of the left ventricle, that ejects blood and propagates along the arterial vessels, originates distensions in its walls. During the cardiac cycle, pressure and distension waves can be used interchangeably for many analyses due to their similar wave profile.[3]

In peripheral arteries like the carotid, this distension can be optically assessed by the measurement of the reflection characteristics of the skin and other superficial tissues.

The developed optical probes are based on photodiodes as sensing elements and on an illumination scheme provided by light emitting diodes (LEDs), which showed to be capable of reproducing the arterial waveform with a higher resolution than the gold standard for carotid distension waveform assessments, the ultrasound system, in a previous validation.[3]

The assessment of the cardiovascular system condition based on multi-parameters allows a more precise and accurate diagnosis of the heart and the arterial tree condition. Risk indicators, that can be assessed from the developed system that measures and analyses the distension waveforms which can be determined from the main parameters extracted from the waveform, its time characteristics and the pulse wave velocity (PWV). The pulse wave analysis (PWA) allows the non-invasive determination of the main indices of cardiovascular function: Augmentation Index (AIx), Subendocardial Viability Ratio (SEVR %), maximum rate of pressure change ($dP/dt_{\max}$), Ejection Time Index (ETI) and area under the pulse pressure.

Several studies have focused on the determination of normal and reference PWV values in groups with healthy subjects and patients with cardiovascular diseases (CVDs), hypertension, diabetes or heart disease. In the Reference Values for Arterial Stiffness Collaboration,[28] an European cross-sectional study, performed in 11,902 subjects, where PWV was assessed regionally (carotid-femoral) using several devices (Sphygmocor® and Complior® among others), shown that the obtained PWV values were lower in the group classified as normotensive (without cardiovascular risk factors subjects), from which the authors had established normal values of PWV. This same group showed a less pronounced increase of PWV with increasing age. The results also demonstrated that PWV increases with age and hypertension severity.[28] The normotensive group had a PWV mean distribution between 6.6 ± 0.8 (ms^{-1}) for subjects under 30 years old, and 11.7 ± 2.9 (ms^{-1}) for the age category above 70 years old.

Although all these studies were performed for regional PWV, the local measurement of the PWV is preferred because of the arteriosclerosis local nature. In the early stage, fibrous spots with small diameter are scattered on the arterial wall and, in the final stage, the arterial wall becomes homogeneously hard. For this reason, it is important to have an early diagnosis tool able to measure the local stiffness of the arterial wall.[16]

Some studies explored an ultrasound method for local PWV assessment in the carotid artery and obtained estimated PWV in the range of 4–9 ms^{-1}.[22] In 2008, an experimental method for the local determination of PWV in the carotid artery obtained values for PWV of 3–4 ms^{-1}.[26]

The proposed optical system represents a significant advance in PWV estimation since it allows the evaluation of this parameter on a single large artery near the aorta, such as the common carotid artery. In clinical terms, this local information assumes utmost importance, since it enables a more reliable assessment of the real physiological state of the carotid artery where complications, such as atherosclerosis, may occur. Furthermore, it also allows the determination of PWV with greater precision and accuracy, since it is done in a single artery and not at two distant locations, like the femoral and carotid arteries.[14] This is accomplished with two sensors separated by a fixed and well known distance, thus ensuring greater accuracy in the determination of pulse transit time, and avoiding rough approximations and measurements between two distant arteries.

In the pulse wave analysis, the AIx is the most widely researched index with several studies indicating that it is independently predictive of adverse cardiac events.[31] AIx describes the increase of systolic blood pressure due to an early backward wave, produced by the reflection of the forward systolic wave on the peripheral arterial tree structure. This index is defined as the ratio of blood pressure amplitudes at the timings of the reflection point (RP) and systolic peak (SP), thus resulting in RP/SP expressed as a percentage.[6] A positive AIx means that the reflected wave arrival occurs earlier than the systolic peak while a negative value of AIx indicates that the reflected wave arrives after the systolic peak.

Several studies have focused on the relation between AIx and heart rate (HR) and a strong negative correlation between these two parameters is known. This is explained due to the early return of the reflected wave in systole when the HR is lower. In this case, because the heart is contracted during a longer period of time, the reflected wave returns during the systole. As the HR increases, the return of the reflected wave is shifted to diastole, thus, decreasing AIx.[24,31]

The Subendocardial Viability Ratio, or Buckberg Index, is a parameter that estimates the myocardial oxygen supply–demand relative to the cardiac workload and is an indicator of subendocardial ischaemia.[5,24,27] The coronary perfusion, and consequently the oxygen supply of the heart, occurs mainly during diastole. In opposition during the systole, due to the contraction of the heart, there is great energy consumption.[5,24] Normal and healthy heart operation requires an energy balanced systole–diastole cycle without which myocardial overload is expected and CVD risk increases. This heart cycle energy trade-off can be directly estimated by pulse wave analysis through the ratio of the diastole and systole areas (pressure–time integrals) on the pulse waveform.[6] Results from some studies in healthy subjects show that SEVR varies between 119 and 254%.[6,25]

Another important cardiovascular parameter available through PWA is the Ejection Time Index. The ejection time, also referred as Left Ventricular Ejection

Time, or LVET, corresponds to the ventricular systolic ejection time between the aortic valve opening and closing. Its ratio to the total duration of the cardiac cycle represents the ETI (%) and is an important component in evaluating left ventricular performance. In healthy subjects the ejection time is inversely related to the heart rate and varies directly with the stroke volume. It is reported that in patients with cardiac failure the pre-ejection time increases while the LVET decreases.[29,30] Several studies provided evidence that the ETI varies between 30 and 42% in healthy individuals.[9,31]

The ventricular contractility can also be evaluated by a parameter that reports the maximum rate of pressure change, $dP/dt_{\max}$, in the systolic upstroke. It is known that this index gives information about the initial velocity of the myocardial contraction, which is also an index of myocardial performance.[9] In situations where fluid edema enters the myocardial interstitium, affecting the stiffness of the heart and the myocardial function, the $dP/dt_{\max}$ index decreases.[12] A study performed on a 10 healthy people group reported a carotid $dP/dt_{\max}$ of 772 $\pm$ 229 (mmHg/s).[18]

The area under the curve (AUC) of arterial pulse waveform (APW) is calculated by means of an integral function. Using blood-pressure measurements recorded in 1,655 women, the results show an area under the curve of 0.56 (95% CI, 0.54–0.58).[15]

Two preliminary tests were made to evaluate the optical system capability in determining the hemodynamic parameters. The main objective of the first study was to estimate the repeatability of the parameters determined by the developed system as a preliminary evaluation test with a small group of volunteers and infer about its clinical feasibility. Signals were acquired with non-commercial prototype optical probes during 4 weeks in 10 volunteers and the results for the different parameters were evaluated. In the second test, a comparison was made between the optical system and the gold-standard in the regional PWV assessment, a Complior Analyse® device, to explore the correlations and differences in the results obtained using the two techniques of measuring the pulse pressure wave velocity.

METHODS

Technology

The current study makes use of two non-commercial optical probes, developed to measure the arterial pulse wave profile at the carotid site, along with the arterial distension waveforms generated by ventricular contraction, in order to assess clinically relevant information.

The proposed probes were developed to measure the arterial pulse wave profile at the carotid site and are based on the reflectance fluctuations of the skin surface during the underlying pulse wave propagation. The propagation of the pulse pressure waveform causes distension in the artery wall. This distension, known as distension wave, changes the optical reflectance angle of the wall which produces a change in the reflection characteristics of the skin, causing an amplitude modulation of the light. This effect can be used to generate an optical signal that correlates with the passing pressure wave. All the probes have a common functional structure: an illumination source provided by a combination of several high brightness, 635 nm monochromatic light emitting diodes (LEDs), and two photodetectors (placed at a precise and well-known distance of 20 mm), that detect the pulse wave propagation, along the arterial segment, through the skin reflectance variations (Fig. 1a). In this study two probes that differ in the photodetectors type are tested. One probe uses two planar photodiodes (PPD) and the other two avalanche photodiodes (APD). The probes architecture guarantees the local pulse wave profile assessment at two distinct spots thus providing the determination of local PWV. Figure 1a shows only half of the components of the probe, that further comprises a second photodetector and two more LEDs, which are not represented in the figure for simplicity.

All the probes are enclosed in a plastic box with two holes for the LEDs and the photodetectors on the same face. This probe structure results in an ergonomic configuration, allowing the transmission of the emitted light and the modulation of the light reflection. The box ensures a non-contact signal acquisition, by keeping a small distance between the probe and skin, 3 mm. The signals from the photodetectors were digitized with a 16-bit resolution data acquisition system (National Instruments, USB6210) with a sampling rate of 20 kHz and stored for offline analysis using Matlab®. The sampling rate value chosen allows the discrimination of two points with a time resolution of 1 ms, for velocities up to 20 ms^{-1}.[20] This ensures a correct measurement of the pulse wave velocity far beyond the expected physiologically velocities, even in pathology cases like arterial stiffness, which is mainly responsible for the increased value of the propagation velocity of the pulse pressure wave in the arteries.[28] All the developed algorithms for PWV and PWA were developed using Matlab®.

Study Protocol

In vivo tests were performed in a set of healthy individuals. The study protocol was approved by the ethical committee of the Centro Hospitalar de Coimbra, Portugal. All the subjects were volunteers and gave a written informed consent. The main purpose of these tests was to assess the capability of the system in

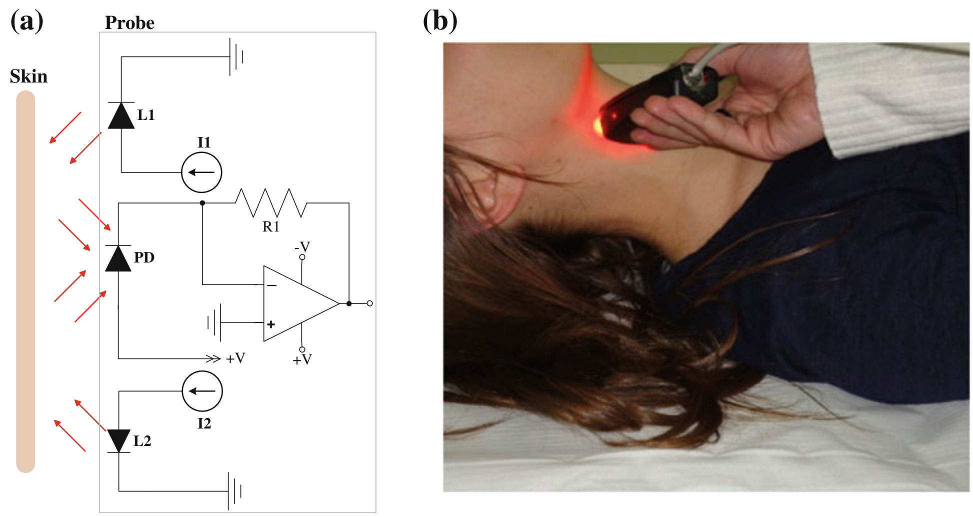

FIGURE 1. Optical probe. (a) Schematic of one photodetector (PD) and light sources (L1 and L2) of the probe and light interaction with skin; (b) optical probe method for non-contact measurement of skin surface in carotid local.

determining the pressure waveform features and pulse wave velocity. The assessment trials were made during four consecutive weeks for each of the 10 subjects for the different parameters evaluate. The PWV study validation was an independent test that was presented before, and a different group of volunteers was requested to assess a regional PWV.

Each exam procedure consisted in the acquisition of a set of cardiac cycles at the carotid artery during a few minutes, with the patient in the supine position (Fig. 1b), although few seconds of acquisition are enough to the signal processing. The carotid artery is the natural probing site for pulse waveform measurement due to the heart proximity and because it is easily accessible (i.e., it is close to the skin surface).

The acquisitions for each volunteer is weekly based, with the two developed probes (PPD and APD), during four consecutive weeks. The procedure was continued for each of the acquisitions, and the different hemodynamic parameters were determined.

Collected signal data were stored directly into a portable computer. These signals were then processed offline in order to parameterize the APW and calculate the corresponding cardiovascular performance indexes. A schematic overview of the methods for signal processing is represented in Fig 2. The acquired signals evidence great consistency in the waveform of the pressure wave. For the pulse waveform analysis and for PWV determination there are two different sequences of signal processing, described in Fig. 2.

Assessment of arterial blood pressure by conventional measurement with a sphygmomanometer was performed prior and after the exam for reference purposes. The diastolic and systolic pressure values of arm blood pressure were used to calibrate the system.

Pulse Wave Analysis

The several steps for the pulse wave analysis (PWA) are described in Fig. 2. A set of cyclic waveforms coming from one of the channels, with some seconds of duration, undergo segmentation and normalization to the diastolic–systolic pressure interval. The signal segmentation is performed using the wave foot, detected by the minimum.

The average pulse are digitally low-pass filtered (with a cut-off frequency of 30 Hz), which removes the noise, thus allowing the signal differentiation.

The feature extraction algorithm, capable to detect remarkable points of the PWA represented in Fig. 3, was implemented to detect the systolic peak, reflection point, dicrotic notch (DN) and dicrotic peak (DP) in the average pulse determined. For the optical system, the developed algorithm for waveform features determination is based on differential calculus and was applied to the remarkable points as a tool to quantify arterial pressure waveform features.[9,11,18] This method uses the consecutive zero-crossing of the first, second and third derivatives to detect inflection points that correspond to the clinically interesting features of the waveform.

The last step for PWA is the linear normalization of the carotid pressure wave that was accomplished with the values collected at the brachial artery, brachial diastolic pressure (DBP) and mean arterial pressure (MAP). It was assumed that MAP is relatively constant along the arterial tree and that DBP do not vary considerably between the carotid and brachial arteries, whereas systolic blood pressure (SBP) increases along the arterial tree.[13,15,20] These values were used to calibrate the carotid pressure waveform as recommended

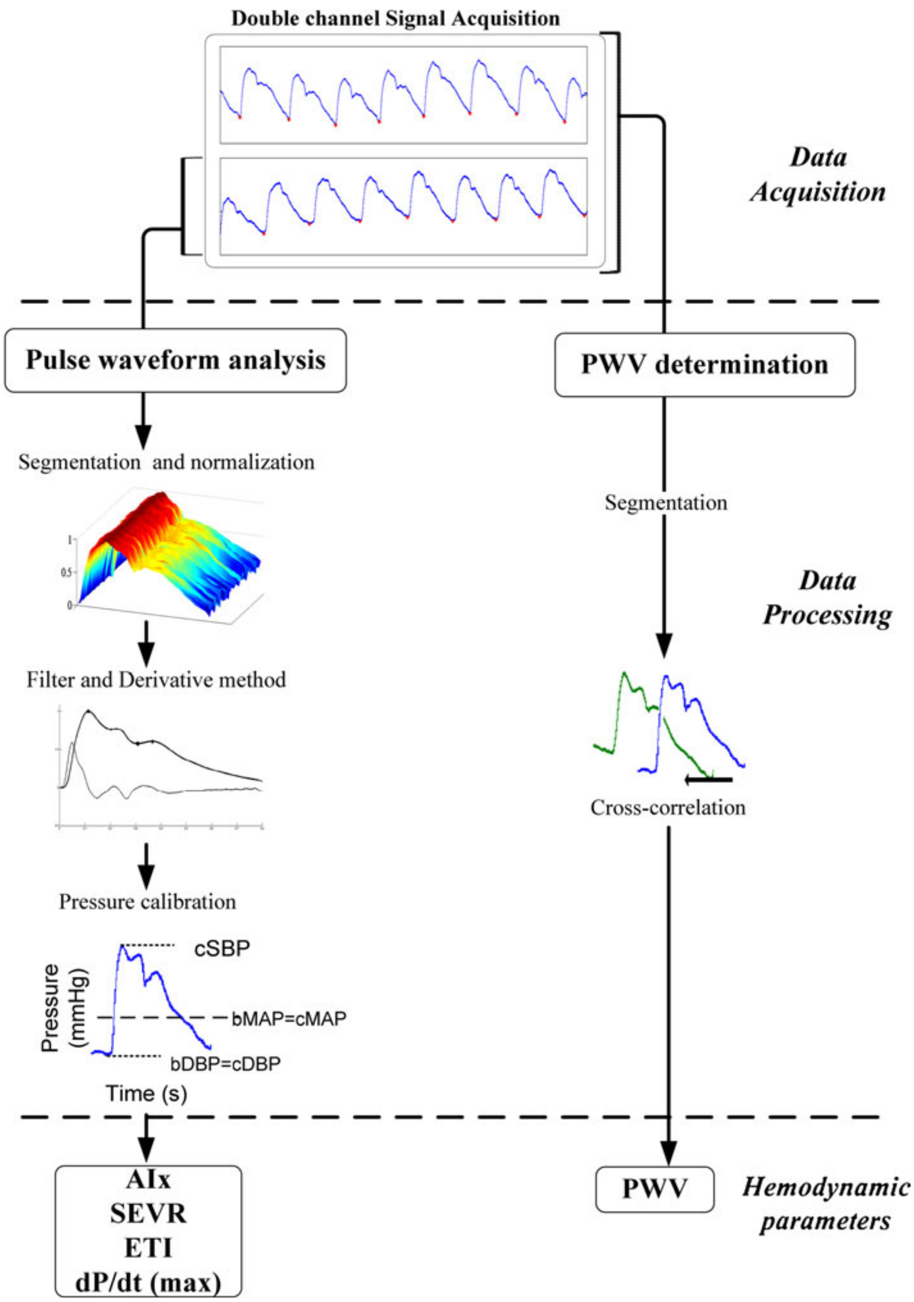

FIGURE 2. Schematic overview of the data processing workflow to determine the hemodynamic parameters.

and according to the calibration method proposed by Kelly and Fitchett.[10,23]

After this sequence for pulse waveform analysis the AIx, SEVR, ETI, HR and $dP/dt_{\max}$ were determined.

Pulse Wave Velocity

For the set of cyclic waveforms detected, segmented and normalized for PWV, three different algorithms for extraction of the time delay from the two detector's signals were applied. They are referred to as Maximum, Threshold and Cross-Correlation algorithms. The other levels of signal processing for PWV determination are the same for the three different algorithms, but Cross-Correlation is the only represented in the Fig. 2, just to simplify the structure of the schematic.

The Maximum algorithm consists on the determination of the time delay by calculating the time delay between the maxima of the two waves acquired by the two optical sensors. The Threshold method consists on the determination of the time delay between two points in the threshold of the waves. The threshold was

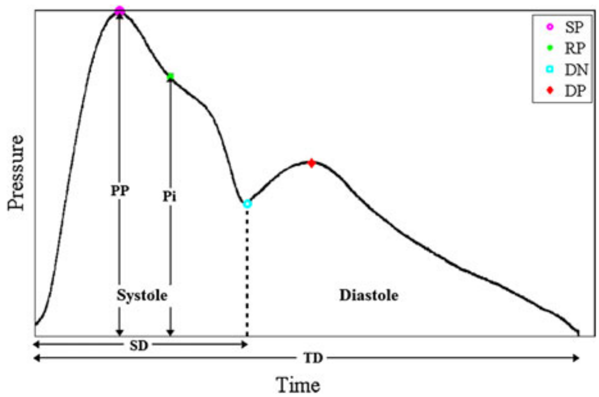

FIGURE 3. Typical pressure waveform of a healthy subject and its main features used to compute the indices of cardiovascular function: pulse pressure (PP), systolic peak (SP), reflection point (RP), dicrotic notch (DN), dicrotic peak (DP), systolic duration (SD), total duration (TD) and pressure in the reflection point (Pi).

assumed to be the point that corresponds to 10% of the pulse pressure amplitude.[4] The Cross-Correlation algorithm is based on the well-known property of the peak of the crosscorrelogram, which allows the computing of the time delay by subtracting the peak time position from the pulse length.[19]

For each acquisition, the three algorithms above mentioned were used for the PWV determination. Further tests were made to compare the results and study the variability between different measures and subjects.

RESULTS

The characteristics of the volunteers are presented in Table 1. The group consisted of 10 subjects (5 male and 5 female), normotensive and with no documented history of cardiovascular disorders or diabetes, with average (±SD) age of 24.4 ± 2.5 years old.

A reliable estimation of PWV, AIx, ETI, HR and $dP/dt_{\max}$, and area under the curve were obtained in all the subjects with the two probes of the optical system. The values of systolic and diastolic pressure were obtained from brachial pressure measurement with sphygmomanometer (blood pressure cuff) using a commercial system.

All the data were analyzed as mean ± SD (standard deviation) with Predictive Analytics Software Statistics 18 (SPSS, Inc, Chicago, IL).

Reproducibility of PWV

The results from the three algorithms for PWV determination were compared to select the one that exhibits the best results. The average PWV, obtained by the Maximum algorithm, is 4.37 ms^{-1} with SD of 1.79 ms^{-1}, for the Cross-Correlation method the result is 4.58 ± 1.29 ms^{-1} and for Threshold method 4.78 ± 1.89 ms^{-1}. All algorithms exhibit a good performance, and the correlations between all of them were evaluated. The best correlation was found for the Cross-Correlation and Threshold methods, as shown in Fig. 4a.

The average difference between the two methods, Threshold and Cross-Correlation, was 0.78 ms^{-1} with a SD of 2.52 ms^{-1} as shown in a Bland–Altman plot in Fig. 4b. The Cross-Correlation method analyzes the pulse pressure waveform as a whole, incorporating all moments of the arterial pulse, while the Threshold is based on a pulse by pulse single point identification (at the diastole) followed by for time delay assessment. For this reason the Threshold method should be more sensitive to noise and artifacts on the baseline.[7] Due to lower SD for the values obtained with the Cross-Correlation, this method was preferred for the PWV determination. The values of pulse wave velocity determined by the optical system are slightly lower than those reported in the literature.[14,28] However, the values mentioned above are for a regional PWV while the values determined here are for local PWV and there is no consistent reference for this type of measurement.

TABLE 1. Main characteristics of the volunteers.

Characteristics	
n, Males/Females	10 (5/5)
Age (years)	24.4 ± 2.5
Height (cm)	168.1 ± 10
Weight (kg)	63 ± 11.2
BMI (kg/m^2)	22.2 ± 2.6
Brachial SBP* (mmHg)	104.6 ± 11.1
Brachial DBP* (mmHg)	68.0 ± 8.6
Heart Rate* (bpm)	64.6 ± 8.4

Values are numbers or mean ± SD.
BMI body mass index, *SBP* systolic blood pressure, *DBP* diastolic blood pressure.
* Measure in brachial, with commercial system based in sphygmomanometer (blood pressure cuff).

Reproducibility of AIx

The distribution of AIx values was also assessed for each subject (Fig. 5). The results show that the AIx values are consistently negative, except for one of the subjects. This is consistent with the waveform observed for each subject, since the subject 8 always shows an early reflected peak that corresponds to a positive Augmentation Index and could indicate a case of arterial stiffness.

The correlation between AIx and heart rate was evaluated. The results of Pearson-Correlation test were

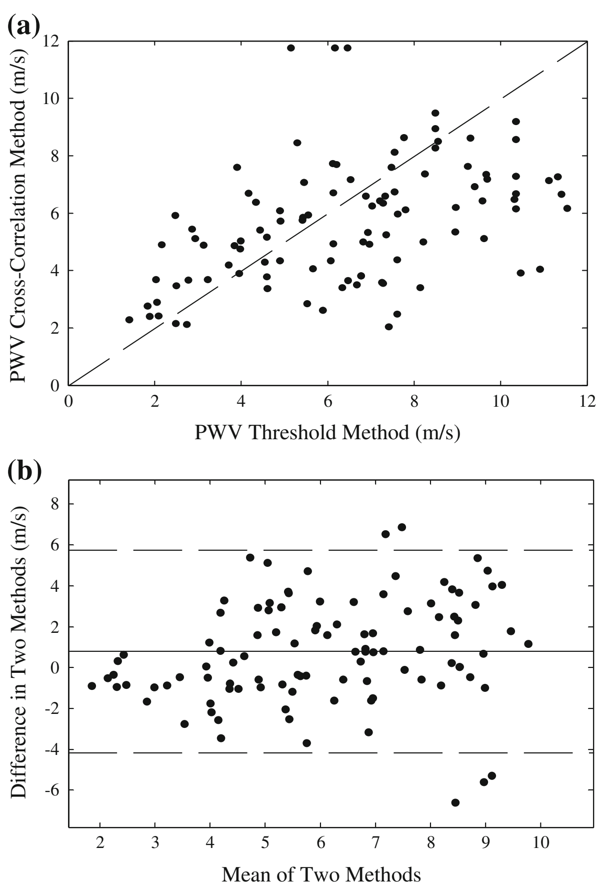

FIGURE 4. Comparison between Threshold and Cross-Correlation methods. (a) Correlation between the two methods for PWV; (b) Bland–Altman plot displaying the difference between two methods.

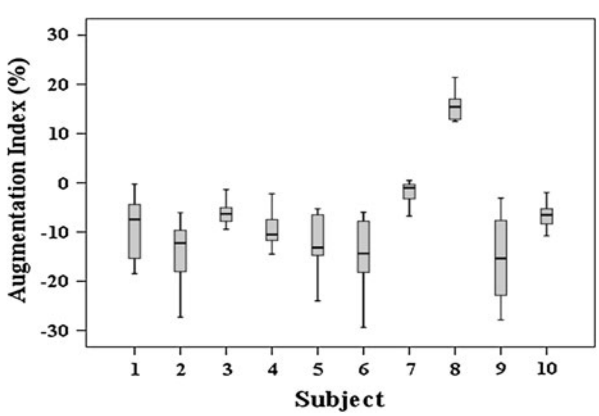

FIGURE 5. Box plot of data from the AIx determined for the all the subjects.

compatible with a significant negative correlation, between HR and AIx at a 0.01 level (2-tailed), as it was found in other studies.[24,31] Even though the strength of the relationship found between these two variables is medium, since the Pearson Correlation is −0.315.

It should be noticed that the obtained values by the proposed system are predominantly negative, and therefore lower than those found in previous studies.[31] However, it is significant that in these studies, the mean age of the sample population (63 years) is much higher comparing to this sample, which have an mean age of 24.4 years (range 20–29 years), which may explain this trend to lower values. Once again, the subject who had higher values of AIx (subject 8) is the oldest in this sample.

Reproducibility of other PWA Parameters

The other parameters described before, such as HR, area under the curve, dP/dt_{max}, SEVR and ETI were determined by the optical system with a PWA algorithm; all data was analyzed as mean ± SD and is shown in Table 2. The SD presented in Table 2 for the PWA parameters represents the standard deviation for each volunteer during the different measures of the four consecutive weeks. The results obtained for the subjects submitted to this study are consistent over time for all parameters. For the area under the normalized curve, the values obtained are closer than described in literature, 0.54–0.58,[15] in spite of the differences in volunteers of the study. This fact suggests that there is no variation over gender for the area under the pressure curve.

For the dP/dt_{max} and SEVR parameters the values obtained were within the range expected for a sample of healthy individuals. For the SEVR parameter were expected values for healthy individuals greater than 100%, in which the perfusion of the heart is made during a time period longer than the period of contraction, which is energy consumption. In some volunteers, the perfusion period is twice the time of contraction (systole) and the SEVR is about 200%.

There is a consistency between the trials for Ejection Time index and that there are no large variations in its value to the same subjects. The expected values are included between 30 and 42% in other studies.[6,8] The results obtained by the optical system are within the expected range.

Comparison Results between Two Probes

The developed multi-parametric system is composed of two types of probes, PPD and APD, used in this study for all subjects. The parameters previously obtained were determined from acquired data with the two probes. To allow certain values in their differentiation the comparison was made in the PWV values determined for the three algorithms under study.

The results showed a carotid PWV mean value (±SD) of $4.72 \pm 1.22\ ms^{-1}$ for planar probe while

TABLE 2. Hemodynamic Parameters obtained with the optical system.

Subject	HR (bpm)	Area	dP/dt_{max} (mmHg/s)	SEVR (%)	ETI (%)
1	63.2 ± 19.3	0.5 ± 0.1	566 ± 187.6	201.1 ± 41.4	30.93 ± 1.75
2	84.5 ± 8.2	0.3 ± 0.04	731.6 ± 83.2	117.5 ± 15.6	44,59 ± 3,70
3	67.5 ± 5.0	0.5 ± 0.04	509.3 ± 93.6	167.7 ± 21.4	35,90 ± 3.05
4	66.9 ± 3.1	0.5 ± 0.1	682.7 ± 105	143.3 ± 26.9	32.87 ± 9.70
5	56.8 ± 6.0	0.5 ± 0.1	541.2 ± 83.1	221.2 ± 30.3	28.97 ± 3.23
6	76.3 ± 12	0.4 ± 0.1	570 ± 113.7	171.2 ± 29.6	35.16 ± 5.33
7	73.5 ± 6.4	0.5 ± 0.1	466.3 ± 110	173.7 ± 30.9	35.83 ± 4.34
8	64.2 ± 3.4	0.5 ± 0.05	504.1 ± 93.1	197.3 ± 18.8	32.98 ± 1.62
9	64.6 ± 3.8	0.5 ± 0.1	746.6 ± 150	176.3 ± 29.5	33.86 ± 0.65
10	76.8 ± 8.0	0.4 ± 0.1	790.8 ± 269	189.8 ± 7.4	29.49 ± 3.69
Total	69.7 ± 10.8	0.5 ± 0.1	620.0 ± 166	171.7 ± 36.2	34.06 ± 3.71

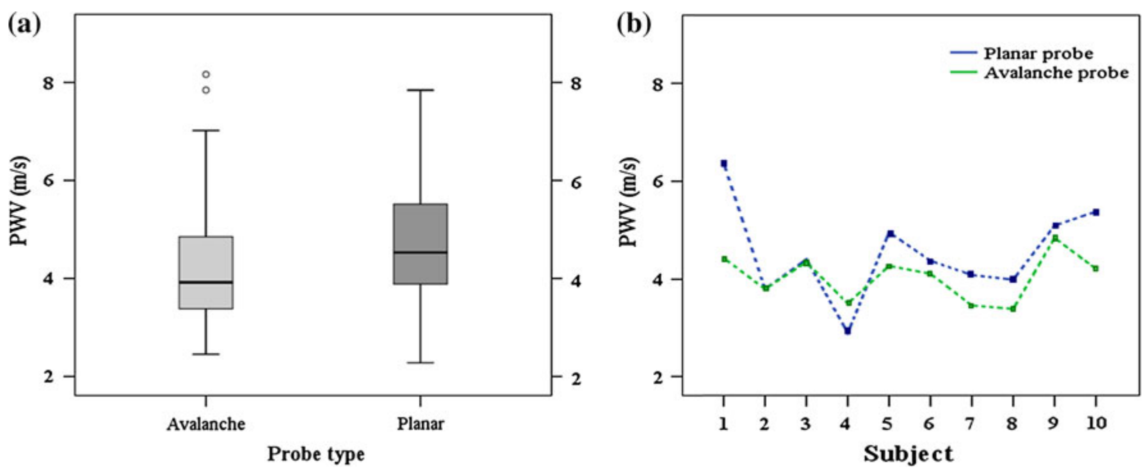

FIGURE 6. PWV determined by two probes. (a) Box plot for comparison of PWV determined by Cross-Correlation for the two optical probes, Avalanche and Planar; (b) mean of PWV values for each subject.

avalanche probe showed a mean PWV value of 4.32 ± 1.38 ms^{-1}, represented in Fig. 6a. In Fig. 6b it is visible that there are no major variations between the PWV values obtained by the two probes for each subject.

The results obtained for PWV suggest an underestimation of values in the case of the APD probe. The avalanche photodiodes are almost punctual and the signal-to-noise ratio is worse, therefore increasing the difficulty in the determination of the delay between the two acquired signals.

The good results obtained with the PPD combining with the much lower cost of the PPD detector than the APD and the fact that in the acquisition of signals *in vivo* with APD probe was more difficult than with the PPD probe, the solution based in the planar photodiodes becomes the best option.

Preliminary Validation Study for PWV

Based on what has been discussed previously, the probe composed of the planar photodiode along with the Cross-Correlation method represents the best combination for PWV determination. In order to validate the data obtained by the developed optical system, a number of volunteers had been previously submitted to a signal acquisition procedure, using simultaneously the proposed optical device and a gold-standard in the PWV assessment, a Complior Analyse® device. This study was undertaken in 14 healthy subjects (9 females/5 males, average age 23.2 ± 5.5 years).

The results evidence a striking consistency between the PWV obtained with these two devices. In spite of this comparison, it is worth to point out that the nature of the PWV determination is different in the optical system, that is based on local assessment (carotid artery measure) and the Complior® system, which is based on a regional assessment (carotid-fem oral measures).

Using a non-parametric correlation analysis between the values obtained from the two systems, the Pearson correlation value is 0.819, which is a strong correlation and significant at the 0.01 level (2-tailed).

The agreement between the PWV values obtained by the Complior® and the optical probe is shown in Fig. 7a. The values of PWV obtained by the two systems are correlated ($r^2 = 0.67$) being the average difference between the two systems, Complior and Optical probe, was $-1.8557\ \mathrm{ms}^{-1}$ with a SD of $0.5744\ \mathrm{ms}^{-1}$ as shown in a Bland–Altman plot in Fig. 7b. As shown in Fig. 7a, there is a shift towards a have systematic lower values from the optical probe device in comparison to those of Complior®. This may be due to the fact that the parameters correspond to slightly different PWV determination processes (local vs. regional) and lower values are expected for PWV in the carotid than the PWV in a carotid-femoral measure. This issue could explain the obtained associated error.[22,26,28]

Altogether, these results allow the use of the proposed optical system as a reliable method to determine local carotid PWV.

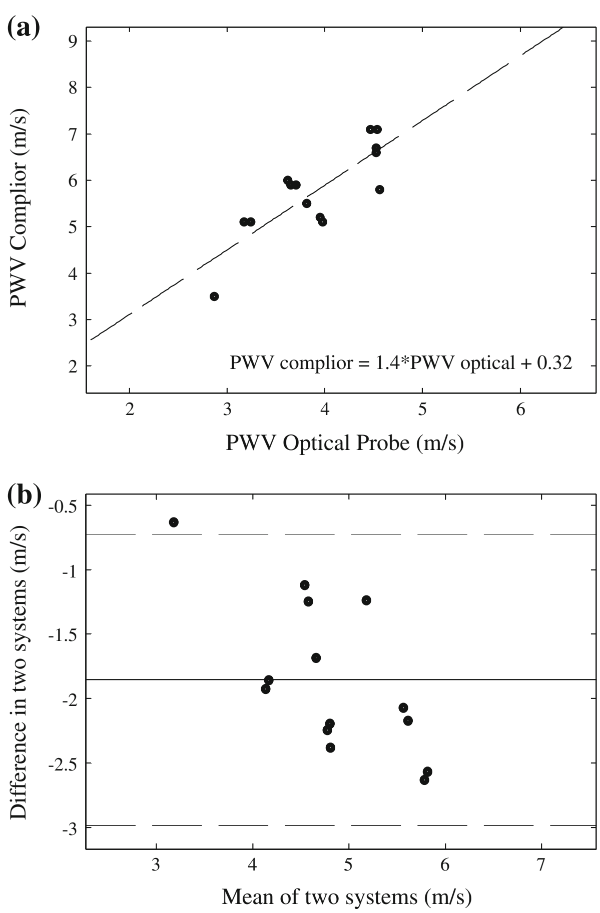

FIGURE 7. Comparison between the Complior® and Optical probe. (a) Correlation between the two systems for PWV determination; (b) Bland–Altman plot displaying the difference between the two systems (Complior® and Optical probe) as a function of the average of the determined PWV.

CONCLUSIONS

These tests were carried out over 4 weeks, in a small group of volunteers and led to an experimental validation of the optical system under study composed by two types of optical probes, APD and PPD. This study allowed the selection of the best algorithms for PWA and PWV computing.

It should be noted that the parameters assessment in this study is local, i.e., only at the carotid artery and, unlike some commercial system (e.g., Complior ®), does not require measurements at two distant points to determine PWV. This represents an important advance because it allows the analysis of this type of parameter without the coarse approximations of the distance between test points in arteries. In the local PWV approach the detectors are spaced by a fixed well known distance and the outcome gives a glimpse over the physiological status of a particular arterial segment.

In fact, the values found in the literature are referred exclusively to regional PWV, which does not allow to do a direct comparison between the values obtained with the optical probes and other regional assessment devices.

The shown algorithms, developed for the determination of PWV have a good overall performance. The best algorithm for PWV determination is based in Cross-correlation method while the algorithm based on differential calculus for PWA allows the determination of the main hemodynamic parameters used in clinical practice.

The two types of probes in study proved to be able to reliably measure the pulse pressure waveform at the carotid site. However, the determination of the PWV with the APD probe evidences an underestimation of this parameter. Furthermore, the acquisition of signals *in vivo*, with the APD probe, was more difficult than with the PPD probe, because the SNR is significantly lower. This is due to the fact that the sensitive area of the avalanche photodiodes is almost punctual, which makes positioning of both photodiodes over the carotid artery tougher. The good results obtained with the PPD, combining with the much lower cost of the PPD, does the solution based in the planar photodiodes the best option.

For the determination of parameters like AIx, SEVR, ETI and $dP/dt_{\max}$, it was necessary to calibrate the system with the systolic and diastolic pressure. With this purpose each evaluation was preceded of brachial blood pressure measurement with a clinical sphygmomanometer.

Preliminary tests allowed a study of repeatability of the parameters inferred by the system validation, showing great consistency over time for different subjects.

The PWV obtained by the developed optical system was validated by comparing results with Complior® that showed a great consistency between the PWV obtained with the two devices, even though their direct comparison should be carefully taken due to the fact that they refer to different PWV parameters (Complior® is regional PWV, while the designed probes measure local PWV at the carotid).

The validation test on a small sample showed the clinical feasibility of the optical probes, preceding a large study of patients with different pathologies and cardiovascular diseases and healthy subjects. Large-scale clinical trials, with Central hospital partners, are mandatory for the future validation of these optical probe systems. Further probe trials include an extensive study in a larger healthy group and complementary, a comparative analysis of the pulse waveform obtained with an invasive method would validate the optical system's performance with undeniable diagnostics advantages.

REFERENCES

[1] Avolio, A. P., M. Butlin, and A. Walsh. Arterial blood pressure measurement and pulse wave analysis—their role in enhancing cardiovascular assessment. *Physiol. Meas.* 31(1):R1–R47, 2010.

[2] Blacher, J., R. Asmar, S. Djane, G. M. London, and M. E. Safar. Aortic pulse wave velocity as a marker of cardiovascular risk in hypertensive patients. *Hypertension* 33(5):1111–1117, 1999.

[3] Boutouyrie, P., M. Briet, S. Vermeersch, and B. Pannier. Assessment of pulse wave velocity. *Artery Res.* 3(3–8):2009, 2009.

[4] Boutouyrie, P., *et al*. Common carotid artery stiffness and patterns of left ventricular hypertrophy in hypertensive patients. *Hypertension* 25(4):651–659, 1995.

[5] Chemla, D., *et al*. Subendocardial viability ratio estimated by arterial tonometry: a critical evaluation in elderly hypertensive patients with increased aortic stiffness. *Clin. Exp. Pharmacol. Physiol.* 35(8):909–915, 2008.

[6] Crilly, M., C. Coch, M. Bruce, H. Clark, and D. Williams. Indices of cardiovascular function derived from peripheral pulse wave analysis using radial applanation tonometry: a measurement repeatability study. *Vasc. Med. (London, England)* 12(3):189–197, 2007.

[7] Hermeling, E., *et al*. Noninvasive assessment of arterial stiffness should discriminate between systolic and diastolic pressure ranges. *Hypertension* 55(1):124–130, 2010.

[8] Istratoaie, O., R. Mustafa, and I. Donoiu. Central aortic pressure estimated by radial applanation tonometry in hypertensive pulmonary oedema. *J. Hypertens.* 28, 2010.

[9] Kara, S., M. Okandan, G. Usta, and T. Tezcaner. Investigation of a new heart contractility power parameter. *Comput. Methods Programs Biomed.* 76(2):177–180, 2004.

[10] Kelly, R., and D. Fitchett. Noninvasive determination of aortic input impedance and external left ventricular power output: a validation and repeatability study of a new technique. *J. Am. Coll. Cardiol.* 20(4):952–963, 1992.

[11] Korpas, D., J. Hálek, and L. Dolezal. Parameters describing the pulse wave. *Physiol. Res.* 58(4):473–479, 2009.

[12] Laine, G. A. Change in (dP/dt)max as an index of myocardial micravascular permeability. *Circ. Res.* 61:203–208, 1987.

[13] Lamia, B., D. Chemla, C. Richard, and J.-L. Teboul. Clinical review: interpretation of arterial pressure wave in shock states. *Crit. Care (London, England)* 9(6):601–606, 2005.

[14] Millasseau, S. C., A. D. Stewart, S. J. Patel, S. R. Redwood, and P. J. Chowienczyk. Evaluation of carotid-femoral pulse wave velocity: influence of timing algorithm and heart rate. *Hypertension* 45(2):222–226, 2005.

[15] Miller, R. S., C. B. Rudra, and M. A Williams. First-trimester mean arterial pressure and risk of preeclampsia. *Am. J. Hypertens.* 20(5):573–578, 2007.

[16] Nagasaki, T., *et al*. Clinical utility of heart-carotid pulse wave velocity in healthy Japanese subjects. *Biomed. Aging Pathol.* 1(2):107–111, 2011.

[17] Nelson, M. R., J. Stepanek, M. Cevette, M. Covalciuc, R. T. Hurst, and J. Tajik. Noninvasive measurement of central vascular pressures with arterial tonometry: clinical revival of the pulse pressure waveform? *Mayo Clin. Proc.* 85(5):460–472, 2010.

[18] Payne, R. A., R. C. Hilling-Smith, D. J. Webb, S. R. Maxwell, and M. A. Denvir. Augmentation index assessed by applanation tonometry is elevated in Marfan Syndrome. *J. Cardiothorac. Surg.* 2:43, 2007.

[19] Pereira, T., et al. Non-contact Pulse Wave Velocity Assessment. Berlin: Springer, 2012 (BIOSTEC 2011, CCIS 273, no. 2, pp. 246–257, 2012).

[20] Pereira, T., M. Cabeleira, P. Matos, E. Borges, J. Cardoso, and C. Correia. Optical methods for local pulse wave velocity assessment. In: 4th International Joint Conference on Biomedical Engineering Systems and Technologies, Rome, Italy, pp. 74–81, 2011.

[21] Pereira, T., et al. Signal analysis in a new optical pulse waveform profiler for cardiovascular applications. Signal and Image Processing and Applications/716: Artificial Intelligence and Soft Computing, no. Sipa, pp. 19–25, 2011.

[22] Rabben, S. I., *et al*. An ultrasound-based method for determining pulse wave velocity in superficial arteries. *J. Biomech.* 37(10):1615–1622, 2004.

[23] Safar, M. E. Arterial stiffness: a simplified overview in vascular medicine. *Atheroscler. Large Arter. Cardiovasc. Risk* 44:1–18, 2007.

[24] Sharman, J. E., J. E. Davies, C. Jenkins, and T. H. Marwick. Augmentation index, left ventricular contractility, and wave reflection. *Hypertension* 54(5):1099–1105, 2009.

[25] Siebenhofer, A., C. Kemp, A. Sutton, and B. Williams. The reproducibility of central aortic blood pressure measurements in healthy subjects using applanation tonometry and sphygmocardiography. *J. Hum. Hypertens.* 13(9):625–629, 1999.

[26] Sørensen G. L., J. B. Jensen, J. Udesen, and I. K. Holfort. Pulse Wave velocity in the carotid artery. 1(1):1386–1389, 2008.

[27] Tsiachris, D., *et al*. Subendocardial viability ratio as an index of impaired coronary flow reserve in hypertensives without significant coronary artery stenoses. *J. Hum. Hypertens.* 26(1):64–70, 2012.

[28]Vermeersch, S. J., B. Dynamics, and L. Society. Determinants of pulse wave velocity in healthy people and in the presence of cardiovascular risk factors: 'establishing normal and reference values'. *Eur. Heart J*. 31(19):2338–2350, 2010.
[29]Weissler, A. M., W. S. Harris, and D. Clyde. Systolic time intervals in heart failure in man. *Circulation* 37:149–159, 1968.
[30]Weissler, A. M., R. G. Peeler, and W. H. Roehll, Jr. Relationships between left ventricular ejection time, stroke volume, and heart rate in normal individuals and patients with cardiovascular disease. *Am. Heart J*. 62(3):367–378, 1961.
[31]Wilkinson, I. B., H. MacCallum, L. Flint, J. R. Cockcroft, D. E. Newby, and D. J. Webb. The influence of heart rate on augmentation index and central arterial pressure in humans. *J. Physiol*. 525(Pt 1):263–270, 2000.