An easy-to-use hand-to-hand impedance-based sensor to obtain carotid pulse arrival time

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***Abstract*— Pulse arrival times (PAT) are time intervals between the electrocardiogram (ECG) and an arterial pulse wave (APW) widely used to obtain cuffless blood pressure. Although some distal APW's can be easily measured using, for example, a photoplethysmography (PPG) sensor on a finger, proximal APW's, such as the one of the carotid in the neck, are much more difficult to obtain for unskilled users. To overcome this, we propose an impedance-based sensor using only two electrodes in contact with each upper extremity (one to inject current and one to measure voltage at each hand or wrist), which can measure both ECG and an APW (an impedance plethysmogram, (IPG)) to obtain the PAT. Since the injected current flows from hand to hand across the upper torso, we hypothesize that the measured IPG should be sensitive to the arrival of the APW near the heart and, therefore, that the obtained PAT could be used as a surrogate of a proximal PAT even when measured on the hands. We have verified this by comparing the hand-to-hand impedance PAT obtained with the sensor with a gold-standard proximal PAT obtained in the carotid by tonometry in a cohort of 84 volunteers aged 20 to 61 years, showing a correlation of r = 0.90 between the two. These results support the feasibility of future inclusion of these proximal PAT measurements in easy-to-use devices to obtain cuffless BP or other cardiovascular information with improved performance by non-specialist users outside clinical settings.**

***Index Terms*— Arterial pulse wave, pulse arrival time, pulse transit time, impedance-based sensor, impedance plethysmography, tonometry.**

I. INTRODUCTION

Cardiovascular diseases (CVD) are, directly and indirectly, the leading cause of hospitalization (48%), readmission (20-50%) and mortality (32%) [1]. Moreover, the recent COVID-19 pandemic crisis has highlighted the limits of the healthcare system and the need for other screening/monitoring strategies to decongest hospitals [2], [3] with the aggravating factor of the progressive aging of the population [4]. For these reasons, interest in out-of-clinic devices is growing and, according to the World Health Organization (WHO), non-clinical devices for CVD screening are more sustainable, improve adherence, rehabilitation, and survival rate of CVD patients [1], [4], [5]. The essential requirements of non-clinical devices are non-invasiveness, simplicity, self-measurement, cost-effectiveness, and convenience. One of the most relevant cardiovascular risk markers measured with them is blood pressure (BP) and in recent years a great research effort has been made to obtain it with cuffless systems that meet the above requirements [6], also including machine learning techniques [7]. The main classical approach [8] to measure cuffless BP involves the use of pulse arrival time (PAT), the time interval between the R-peak of an electrocardiogram (ECG) and the foot of an arterial pulse wave (APW) (Fig.1) that is usually obtained using, for example, a photoplethysmography (PPG) sensor on a finger. However, the PAT has the drawback that it includes the pre-ejection period (PEP), which depends on cardiac contractility and may result in unreliable BP measurements [9], [10]. For this reason, other authors prefer to use pulse transit time (PTT), the delay time between a proximal APW (close to the heart) and a more distal one to avoid PEP interference. In addition, PTT can be used to assess pulse wave velocity (PWV), another interesting index reflecting the propagation velocity of a pulse wave and related to arterial stiffness, which is also a relevant cardiovascular (CV) risk marker [11] that can predict future CV events and all-cause mortality [12], [13].

However, PTT measurements cannot be easily included in non-clinical devices, as proximal APW measurements at the torso or neck, to measure carotid artery APW, are much more uncomfortable, cumbersome, and difficult to obtain for unskilled users. The tonometer is the sensor commonly used as the gold standard for these PAT and PTT measurements [11]. However, like neck or torso PPG measurements, it requires skilled operators, long scan times, and suffers from motion and respiratory

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artifacts (swallowing, coughing, etc.) [14]. In addition, the application of forces against the carotid artery may be contraindicated for some patients with CVD [15]-[18].

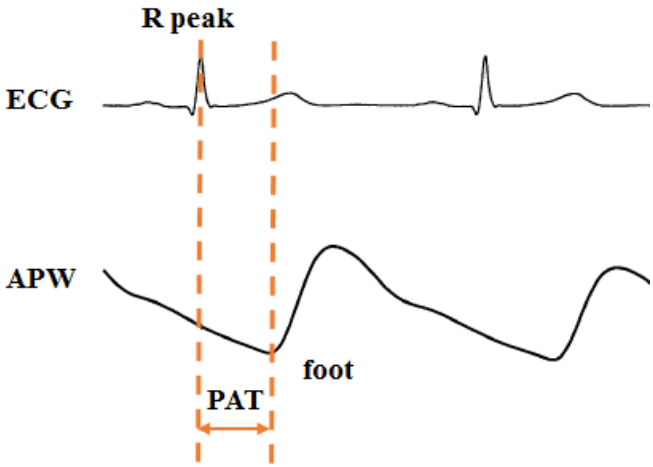

Figure 1. PAT measured from an ECG and an APW.

To overcome these drawbacks that prevent the use of proximal PAT measurements in non-clinical devices, we propose to use an impedance plethysmogram (IPG)-based sensor, similar to those used in bioelectrical impedance analysis (BIA) and other bioimpedance sensors [19]-[22]. Compared to other methods, IPG obtained using dry electrodes allows short, convenient, and non-invasive self-measurements, necessary in non-clinical settings. Moreover, the cost-effectiveness, robustness, easiness of assembly and use of dry electrodes is much better than that of sensors used in other devices (photodetectors or piezoelectric). In our case, we propose the use of a system [23] that only requires the subject to place two pairs of electrodes in contact with his upper extremities (one to inject current and the other to measure the voltage on each hand or wrist). As the injected current flows from hand to hand across the upper torso and this hand-to-hand IPG has a shorter PAT than that of a local IPG on the hand [24], we hypothesize that the measured IPG should be sensitive to the arrival of the APW near the heart and, therefore, that the obtained PAT could be used as a surrogate of a proximal PAT as measured in the carotid artery of the neck. To test this, in this work we compare the hand-to-hand impedance PAT obtained with the sensor with a reference proximal PAT obtained in the carotid by tonometry in a cohort of 84 volunteers. In doing so, we aim to validate the feasibility of using this hand-to-hand impedance-based sensor as an easy-to-use alternative to the carotid tonometer to obtain proximal PAT.

To the best of our knowledge, no previous device allows proximal PATs to be obtained by measuring at distal sites such as the hands or wrists. With these, when combined with distal PATs already easily obtained at the hands, it will be possible to calculate PTT to obtain more reliable cuffless BP or other CVD information outside of clinical settings in a much more compact and easier way.

II. MATERIAL AND METHODS

A. Sensor Concept

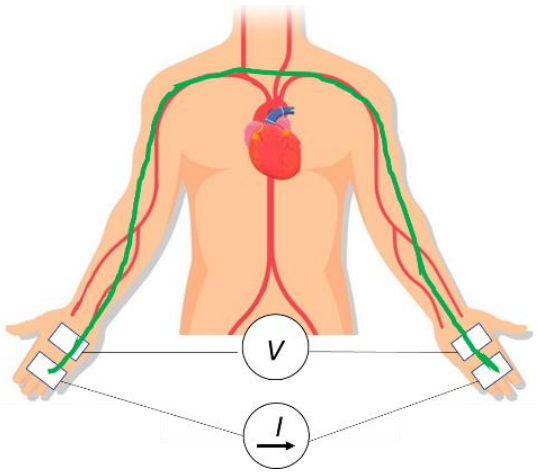

Figure 2. Current path (green line) flowing through the arteries proximal to the heart created by the impedance-based sensor that injects a current *I* through two electrodes on the hands and measures a voltage drop *V* with two other electrodes.

IPG is the measurement of impedance changes in a body segment caused by volume changes related to APW propagation through arteries (elastic or muscular). Our device uses only two pairs of electrodes, one pair for each extremity (hands or wrists). It injects a safe alternating current (< 0.25 mA) of frequency 20 kHz, included in the 10 kHz to 100 kHz band commonly used in bioimpedance measurements/devices. This band is selected because in this band the blood behaviour is almost resistive and lower frequencies increase the electrode impedance while higher frequencies lead to capacitive coupling between wires or circuit traces [19], [20]. Current is injected through the external electrode pair, defining a current path (green line in Fig.2) along the current lines, and the voltage drop is detected between the other electrode pair, which defines the measurement segment. The current lines follow the arteries because they are the path of least resistance compared to bone, muscle, tissue, and fat. The IPG is then sensitive to volume changes resulting from dilatation and contraction of the arteries along the measurement segment due to the propagation of the pressure wave through them. The pressure wave starts with the ejection of blood through the aortic valve in the heart and, as the current flows close to it, through the aortic arch, our hypothesis is that it will be possible to detect the arrival of the pressure wave proximal to the heart by detecting the initial time segments (the foot) of the measured IPG even when obtained in the hands. Therefore, we expect that it will be possible to use the PAT obtained between the ECG and this hand-to-hand IPG as a feasible surrogate of a proximal PAT such as the carotid PAT. The carotid PAT, obtained between an ECG and a carotid APW measured by a tonometer or by photoplethysmography, is also a proximal PAT obtained at a point close to the heart. Therefore, we expect that a direct relationship can be found between it and the hand-to-hand impedance PAT, so that it will be possible to

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obtain the proximal PAT information provided today by these cumbersome methods using instead a much more convenient alternative.

B. Experimental Setup

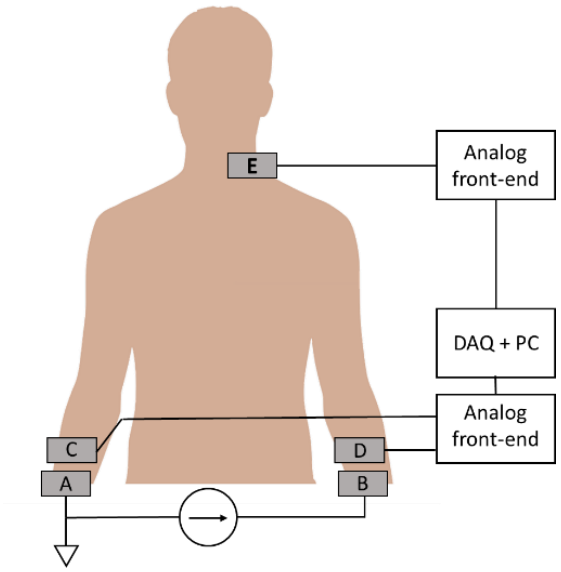

Figure 3. Setup schematic with electrodes (A, B, C, D) and tonometer (E) placed on the body.

Fig.3 shows a schematic view of the entire proposed experimental setup to simultaneously obtain both hand-to-hand impedance PAT using the impedance-based sensor and carotid PAT using a neck tonometer connected to the DAQ system for comparison purposes. Fig.6 shows a block diagram of the circuits used to obtain the ECG and IPG and, from them, the hand-to-hand impedance PAT.

For the IPG conditioning system, see Fig. 6, we used the four-wire technique to minimize the effect of electrode contact impedance. The whole system is powered at ± 5 V, with high gain, so that it was possible to obtain an impedance pulse signal with a high enough SNR to allow us to subsequently detect all desired parameters. As bioimpedance measurements require the injection of a known low-level current into the patient, we designed a single-ended current source based on a Wien bridge oscillator Fig.4 a), to generate a 20 kHz sine-wave voltage, and a Howland circuit Fig.4 b) to convert the voltage into current, with an output impedance of more than 1 MΩ and a transimpedance of 115 µA/V. The circuit generates a 20 kHz, 0.25 mA (rms) current, therefore harmless to subjects. When a single-ended current source is used in an impedance measurement system, the common mode voltage is the current multiplied by the impedance of the ground electrode, which causes an offset error. However, since the measured CMRR of the system is about 75 dB, this error is kept below 1% [25]. Furthermore, characterization of the device has shown that the pulsed impedance variations when measuring between both hands were about 400 mΩ, which means that, for an injected current of 0.25 mA, the expected voltage variations are about 0.05 mV. Therefore, to obtain approximately 1 V of amplitude at the output, it is necessary to amplify them with a gain of approximately 10000. However, in order to implement this, the signal conditioning stage needs a first amplifier stage with a fully differential AC coupled amplifier with a small gain (G = 5) to avoid saturation of its output voltage due to the DC impedance component (basal impedance) which is about 1000 times higher than the AC component. Since the ECG and IPG circuits share the same electrodes, to preserve the SNR and eliminate the contribution of the ECG signal from the IPG system, a fully differential first order passive bandpass filter (1kHz-100 kHz) is applied to the signal. A coherent demodulator, based on a +1/-1 gain amplifier circuit, is then used to obtain the modulus of the baseband signal (by multiplying the signal by itself and then rectifying). Once the bioimpedance signal has been demodulated and the basal impedance has been filtered (0.5 Hz passive high pass filter), the resulting AC signal is amplified. The gain of this stage has been selected large enough, around 2000, to meet the overall gain requirements, but at the same time not so high as to cause output voltage saturation due to amplifier voltage offsets. Finally, a second-order active low-pass filter with 20 Hz corner frequency at the output determines the noise bandwidth of the system.

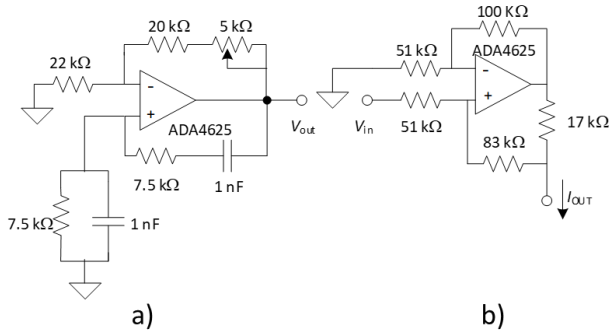

Figure 4. a) Wien bridge oscillator schematic, b) Howland current circuit schematic.

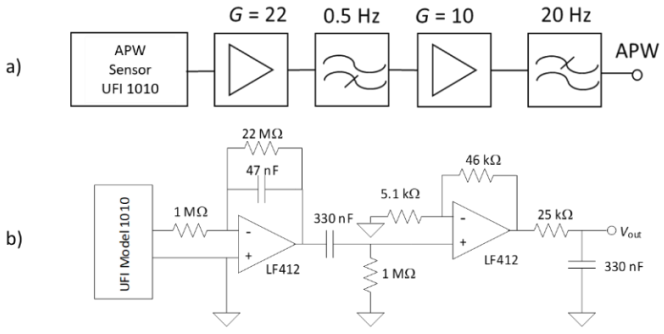

Figure 5. Tonometer a) block diagram, b) circuit schematic.

For the ECG conditioning system, see Fig. 7, the circuit uses 3 dry electrodes shared with the electrical impedance measurement circuit. The first stage is a fully differential first order passive bandpass filter with bandpass from 0.5 to 100 Hz, to avoid interference from intermodulation products of the modulated signal. The differential amplification stage has a gain of about

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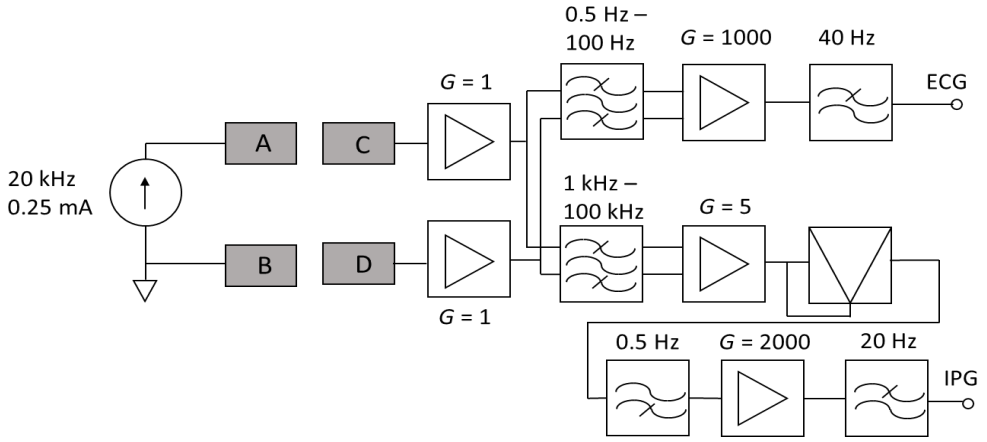

Figure 6. ECG + IPG device block diagram.

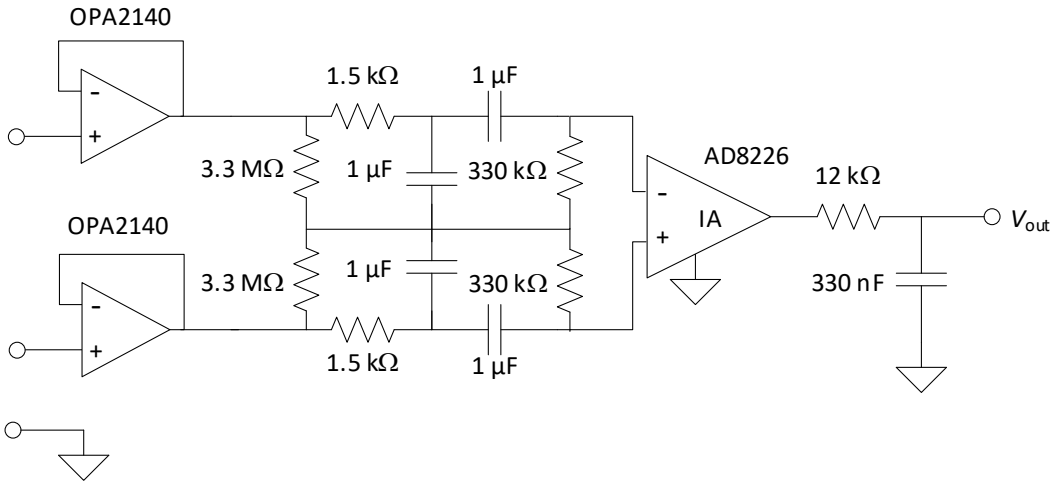

Figure 7. ECG circuit schematic.

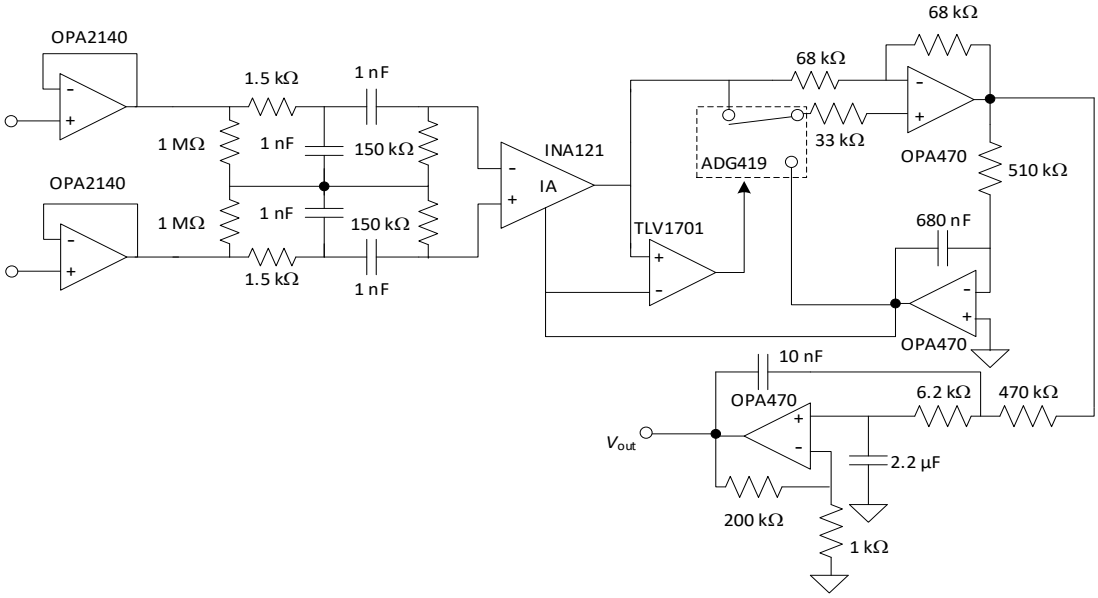

Figure 8. IPG circuit schematic.

1000 and is followed by a first order passive bandpass filter with 40 Hz bandwidth.

To obtain carotid APW, we used a UFI model 1010 piezoelectric pulse transducer (tonometer) and the manufacturer's recommended circuit, see Fig. 5 a) and b), which consists of a gain 22 charge amplifier together with a first-order passive high-pass filter with corner frequency of 0.5 Hz, followed by a gain 10 amplifier stage and a first-order passive low-pass filter with corner frequency of 20 Hz as the output stage.

Both the output of the tonometry system (Fig.7) and the IPG+ECG system (Fig.6 a)) were connected to a data acquisition system (Measurement computing USB-231-OEM), which has a resolution of 16 bits. In our application, the programmable sampling rate is set to 1 kHz.

C. Experimental Protocol

A general population cohort of 84 Caucasian volunteers (50 men and 34 women), age (mean ± standard deviation), 40.6 ± 12.4 years ranging from 20 to 61 years, were measured in the facilities of the Exercise Physiology Laboratory of the University of Barcelona (Spain). Subjects were asked to remain motionless on a modified weighting scale holding a handlebar, which contained the two pairs of dry electrodes (a total of 4 curved stainless-steel conducting rectangles on the handlebar, 50 mm x 45 mm (length x width) each, with an impedance of 20 kΩ at 20 kHz), leaving the arms downwards (without exerting force). The tonometer was placed by a skilled operator on the neck (pressing on the carotid artery) held by an elastic band. Using the proposed experimental setup explained above, we simultaneously measured and recorded an ECG (lead I), a carotid APW using a tonometer and a hand-to-hand IPG APW for 2 minutes for each subject. The Ethics Committee of the University of Barcelona (IRB00003099) approved the study, and all subjects gave written informed consent to participate.

D. Signal Processing

Pulse arrival times (PAT) between the ECG R-peak and tonometry and impedance signals were obtained for each beat in the 2 minutes of recording acquired for each subject. All recordings were post-processed offline using the tangent intersection method to find the foot of the two pulse waves due to its better performance against motion artifacts [26]. After this, the mean values of both impedance and PATs of the tonometer were calculated for each subject. Measurements from 7 subjects were discarded due to poor tonometry signal quality attributable to poor sensor placement, and 2 were discarded due to poor ECG or impedance recordings due to poor electrode contact when holding the handlebars. MATLAB 2020 was used for all signal processing procedures described.

III. RESULTS AND DISCUSION

Fig. 9 shows a single subject (Male, 20 years old, 172 cm tall, 82 kg weight) example of 5 s of the 120 s acquisition performed for each subject in which both impedance and tonometer signals are shown. It can be seen that the impedance waves arrived systematically after the tonometer waves.

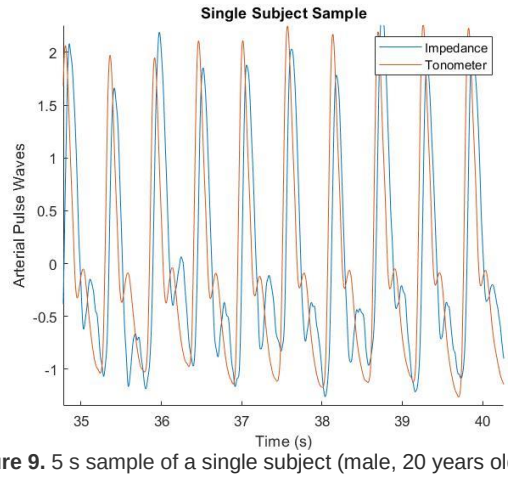

Figure 9. 5 s sample of a single subject (male, 20 years old, 172 cm height, 82 kg weight) acquisition of the impedance and tonometer pulse waves.

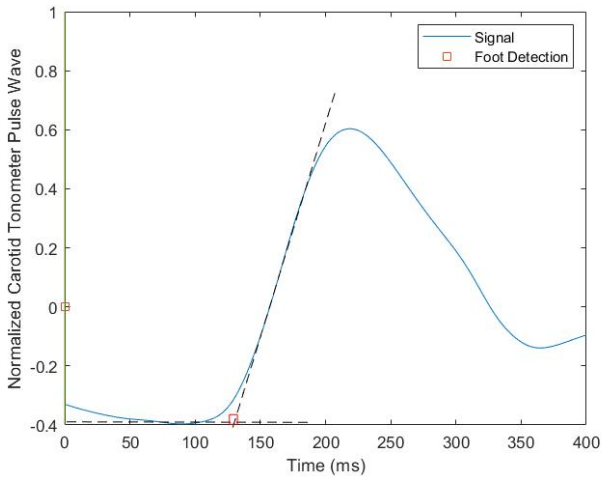

Figure 10. Foot detection for one single tonometer pulse wave using the intersect tangent method.

Fig.10 shows an example of foot detection for a single tonometer pulse wave using the tangent intersection method, where the foot point is determined as the intersection between the tangent to the upward slope of the wave and the horizontal tangent to the minimum of the wave. Fig. 11 shows the same detection procedure applied to a single impedance pulse wave. Despite the delay between the impedance and tonometer waves, Fig. 12 shows that there is a good correlation (r = 0.90) between the mean PAT values of each subject using both the carotid tonometry and hand-to-hand impedance methods for all subjects analyzed. In the adjustment performed, considering a unit slope, a y-intercept of -35.8 ms was obtained, which corresponds to the mean delay of the impedance waves with respect to the tonometer waves.

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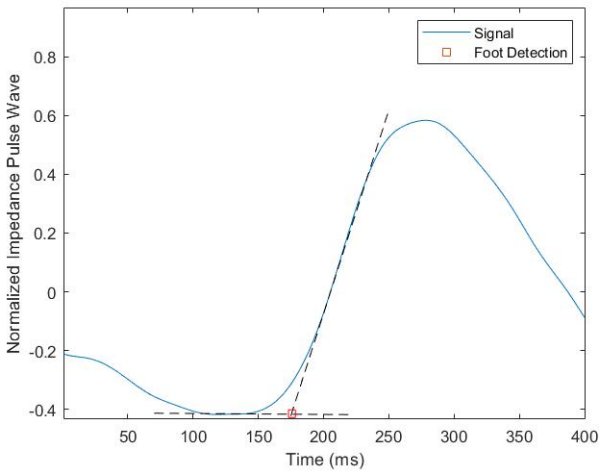

Figure 11. Foot detection for one single impedance pulse wave using the intersect tangent method.

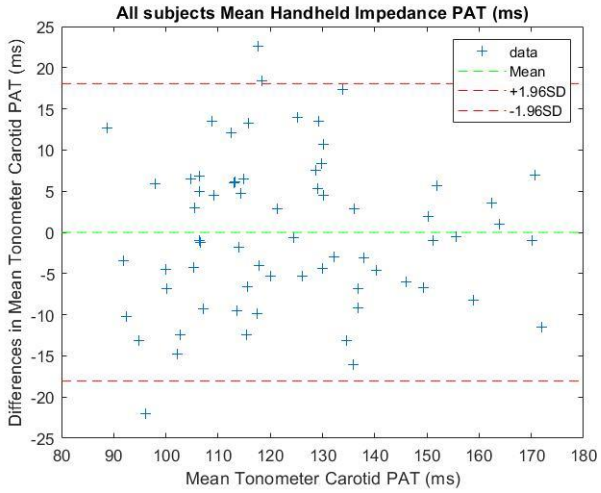

Figure 13. Bland – Altman plot of the correlation between mean PAT values obtained for each subject using both carotid tonometry and hand-to-hand IPG.

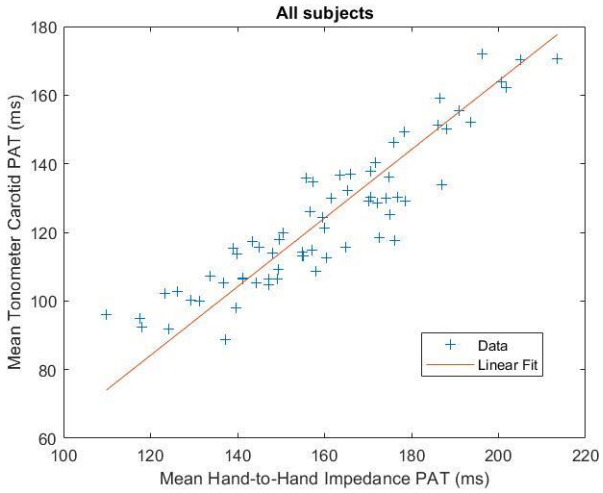

Figure 12. Correlation between mean PAT values obtained for each subject using both carotid tonometry and hand-to-hand IPG.

Fig. 13 shows the Bland-Altman plot of the correlation between the mean PAT values obtained for each subject using both carotid tonometry and hand-to-hand IPG. According to the definition of this type of plots, it can be seen that for all subjects included in a sample of ± 1.96 times the standard deviation, the carotid PAT from the tonometer can be obtained from the hand-to-hand impedance PAT with an error of no more than about ± 15 ms, which is in the range of other errors of this type of systems, such as that of the contact pressure in PPG [27]. Since these results involve a significant number of subjects over a wide age range, they suggest that hand-to-hand impedance measurement, with the subjects immobile in a resting state, could be used as a surrogate for carotid tonometry measurement. Since this type of measurement can be easily performed without external assistance compared to those involving a carotid tonometer, this impedance method is expected to greatly improve the ability to assess this cardiovascular parameter outside of a clinical setting.

IV. Conclusion

The results suggest that the presented hand-to-hand impedance-based sensing device, which uses only four electrodes, could be used as an alternative to the tonometer sensor to obtain carotid PAT. This simple electrode configuration can be easily embedded, for example, in a smartwatch, a wristband, a cell phone housing, or on the handlebars of a weighting scale or bicycle, allowing carotid PAT to be obtained directly without the involvement of well-trained personnel in a clinical setting. For example, in the case of a smartwatch that already measures ECG by touching a button with one finger of the other hand, a similar setup would be required but touching two buttons with two fingers instead of one. More recent smartwatches that implement body impedance analysis by contacting two buttons would already have directly the necessary four-electrode structure. In the case of cell phones, the four electrodes could be placed at the four corners of the casing, so that the electrodes can be contacted with two fingers of one hand and two fingers of the other hand when holding the device. Future developments devised for the presented device will include also obtaining local IPGs on the hands along with the hand-to-hand signal already obtained using only two electrodes on each hand. Therefore, using the local IPGs from this device or also if we combine the PAT from the proximal hand-to-hand IPG with a distal PAT obtained with any existing sensor for PPG or tonometry in the upper extremity, it will be possible to calculate a PTT or other useful features to obtain more reliable cuff-free BP measurements in a simpler and more compact way.

Another related ongoing research will be to try to obtain a surrogate of femoral tonometry (the artery of the upper leg) using foot-to-foot IPG measurement systems, which make the electric current flow along the legs and lower torso. Therefore, a system similar to the one presented here for the hands could easily be implemented in weighting scales or platforms that already measure IPG [28]. Finally, by combining both measurement systems, these impedance methods will hopefully help to promote CV disease prevention by making information related to

carotid-femoral pulse wave velocity (cf-PWV), the gold standard measurement of PWV [11], also more readily available in a wider range of population.

V. ACKNOWLEDGEMENTS

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