

A Novel and Low Cost Acoustic based Probe for Local Pulse Wave Velocity Estimation

Experimental Characterization and in-Vivo Feasibility

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Abstract: The use of local pulse wave velocity (PWV) as an independent risk factor for cardiovascular events and as a marker of atherosclerosis has been gained clinical relevance over the years. A novel acoustic double headed probe for non-invasive measurement of the local PWV is presented in this paper. The PWV is assessed in one single location and involves the determination of time delay between the signals acquired simultaneously by two acoustic sensors, placed ≈ 11 mm apart. Several tests were performed in special purposes test bench systems in order to characterize the acoustic probe (AP) regarding the existence of crosstalk between the transducers, repeatability, waveform analysis and also its time resolution. Results demonstrate the effectiveness of the AP in acquiring repeatedly the same waveform, with the possibility to measure higher PWV (14 m/s), with a relative error less than 5%, when using two uncoupled APs. In-vivo acquisitions were also carried out with the AP in the carotid artery of 17 healthy volunteers with the intention of local PWV and other hemodynamic parameters estimation, such as left ventricular ejection time (LVET). For the total of subjects' sample, the obtained mean carotid PWV was 2.96 ± 1.08 m/s and the LVET mean value was 288.59 ± 21.42 ms.

1 INTRODUCTION

Over the last years, great emphasis has been placed on the role of arterial wall stiffening in the development of cardiovascular diseases and events. Aortic stiffness which results from the progressive degeneration of the wall's elastic fibres is generally associated with ageing and some pathophysiological conditions, such as hypertension, end-stage renal disease and diabetes (Laurent et al., 2001, Shoji et al., 2001). Currently, arterial stiffness is included in the guidelines of the European Society of Cardiology and European Society of Hypertension as an independent predictor of cardiovascular mortality and morbidity and as a new parameter of target organ damage that must be considered in cardiovascular risk stratification (Mancia et al.,

2007). The most simple, non-invasive and robust method to assess arterial stiffness is pulse wave velocity (PWV), i.e., the velocity at which the pressure wave, generated by ventricular contraction propagates along an artery (Pannier, 2002). Carotid-Femoral PWV is considered the gold standard measurement of arterial stiffness, being supported by several clinical studies that highlight the relevant contribution of PWV to the diagnosis, prognosis and follow-up of the general population/patient (Maldonado et al., 2011, Meaume et al., 2001). The most prominent commercial devices require low/moderate technical expertise; however they present several drawbacks in PWV assessment. The practical solution used by these systems relies on the acquisition of pulse waves at the carotid and femoral arteries, to determine the time delay measured between pressure upstroke at each site. The distance

between the two acquisition locations is usually measured using a tape and then PWV is determined using the linear ratio between distance and time delay (Boutouyrie et al., 2009). Nevertheless, this method not only neglects opposite wave propagation but also presents errors in estimating the distance between the recording locations (for example, the curvature of the arteries cannot be taken into account) (Segers et al., 2009). On the other hand, it introduces a rough estimate of local properties of the artery, since it integrates the different segments of arterial stiffness (carotid, aorta, iliac, femoral), being unable to differentiate between muscular and elastic segments. The possibility to assess to the local hemodynamics is in fact very useful, particularly in the carotid artery due to its predisposition to atherosclerotic plaques formation and its significance in the development of cerebrovascular diseases (Laurent et al., 2006).

Variables such as the local PWV, arterial distensibility, cross-sectional compliance or Young's modulus assess the local intrinsic properties of the arterial wall itself, being more related to the biomechanical properties of the artery (Gamble et al., 1994). Although local PWV has already been used as an independent risk factor for cardiovascular events such as coronary disease and stroke and as a marker for cardiovascular disease including atherosclerosis (Gasznier et al., 2012, Laurent et al., 2003), at the present moment there is no gold standard to the assessment of local PWV. In the past few years, several methods have been investigated with the intention of local PWV assessment. The generalized methods require simultaneous measurements of pressure, velocity or diameter at the same site (Rabben et al. 2004, Borlotti et al., 2012), while the most recent studies show that this hemodynamic parameter can also be obtained using the time delay calculated between the piezoelectric elements of an ultrasound probe, placed at a fixed distance (Hermeling et al., 2007). In all the methods, the assessment to the local variables require burdensome or specialized imaging technologies (ultrasound and echo tracking techniques), limiting the use to clinical practice.

The present work intends to present, characterize and validate an efficient and low-cost tool based on a non-invasive device that is placed over the carotid artery and can be easily handled in diagnostic trials by an operator. Based on a previous work, where a double headed piezoelectric probe was developed and characterized in laboratory (Pereira et al., 2010 and 2011), it was developed a simpler and novel system for local PWV estimation and other

parameters extraction, such as left ventricular ejection time (LVET). The device is based on a double configuration of two acoustic sensors that are placed at a fixed distance, d , allowing simultaneous acquisition of two (sound) pulse waves. The measurement of time delay between the waves, Δt , allows local PWV to be determined, simply, as:

$$PWV(m/s) = \frac{d}{\Delta t} \quad (1)$$

2 MATERIALS

2.1 The Double Headed Acoustic Probe

The developed probe, presented in figure 1, consists of two acoustic transducers (Pro-Signal, ABM-712-RC, microphone-solder pad) that are placed approximately 11mm apart and fixed at the top of a plastic box (Multicomp, 77 mm x 49 mm x 26.6 mm). The transducers, based on 9.7 mm diameter electret condenser microphones with an operating frequency of 100Hz to 10 kHz and noise cancelling directivity, are placed at the minimum separating distance, while avoiding mechanical contact. These elements form an ergonomic configuration that allows a safe and effective way of collecting the pulse wave on the carotid artery for both the patient and the operator.



Figure 1: Representation of the double headed probe. a- Microphone 1; b- Microphone 2; d1-distance between transducers centres: 11mm; d2- sensors height: 2mm.

The probe does not include any type of signal conditioning circuit, so the acoustic signals are acquired directly by a Personal Computer (PC) Sound Card. The AP uses parallel audio cable to convey the information obtained directly from the transducers, to the microphone input of the PC

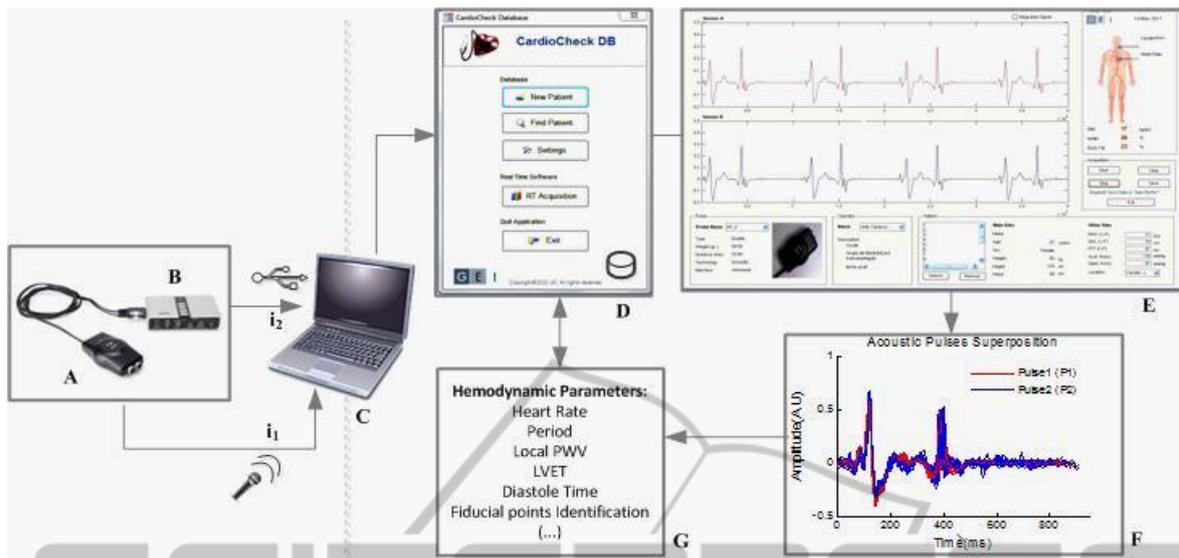


Figure 2: Schematic representation of the overall system used in in-vivo measurements. A- Acoustic Probe; B- External USB Sound Card; C-PC; D- Cardiocheck DB; E- Cardiocheck GUI; F-Data Pre-processing; G- Hemodynamic Parameters Extraction.

Sound Card. In circumstances in which the PC Sound Card does not have stereo input, the probe connects first to an external Sound Card (7.1 Sweex® USB Sound Card, 16-bit, 48 kHz Maximum Sampling Rate, 90 dB Signal to Noise Ratio) that then delivers the collected signals to the PC, via USB. The data acquisitions are displayed in real time, through a dedicated Matlab® Based Graphical User Interface (Cardiocheck GUI) and automatically stored in a non-commercial Microsoft Access® based database (Cardiocheck DB). The data is subsequently processed using different algorithms (detailed in section 3.3) that aim the extraction of several hemodynamic parameters, namely the PWV and the LVET (figure 2).

2.2 Test Setups

For characterizing the AP, as well as the various parameters extraction algorithms, it was developed two special purpose sets of test bench systems. The test setup I was designed to evaluate the ability of the probe in reproducing repeatedly different types of waveforms but also to evaluate the existence of crosstalk between both transducers. The setup uses a 700 μm stroke actuator, ACT, driven by a high voltage linear amplifier, HVA (Physik Intrumente GmbH P-287 and E-508, respectively) to generate a pressure wave that is fed to the acoustic probe by means of a “mushroom” shaped PVC interface (figure 3). This PVC interface (10 mm diameter),

coupled to the ACT, is in mechanical contact with the transducer, without affecting the output voltage since the sensors does not respond to DC excitation. With this mechanical adapter it is possible to transmit the ACT’s motion associated to the pressure wave, in such a way that the longitudinal forces are responsible for the transducer electric response. The waveforms are programmed and downloaded into an arbitrary waveform generator, AWG, Agilent 33220A that delivers the signal that is generated by the ACT and also the synchronism that triggers the data acquisition system, DAS (National Instruments®, USB6210). Although the AP is a prototype suitable for clinical tests, designed to be combined with a PC Sound Card, it was necessary to use a different DAS in test bench experiments, in order to acquire additional reference signals.



Figure 3: Representation of the mechanical structure of the test setup I. 1- ACT. 2- PVC interface. 3- AP.

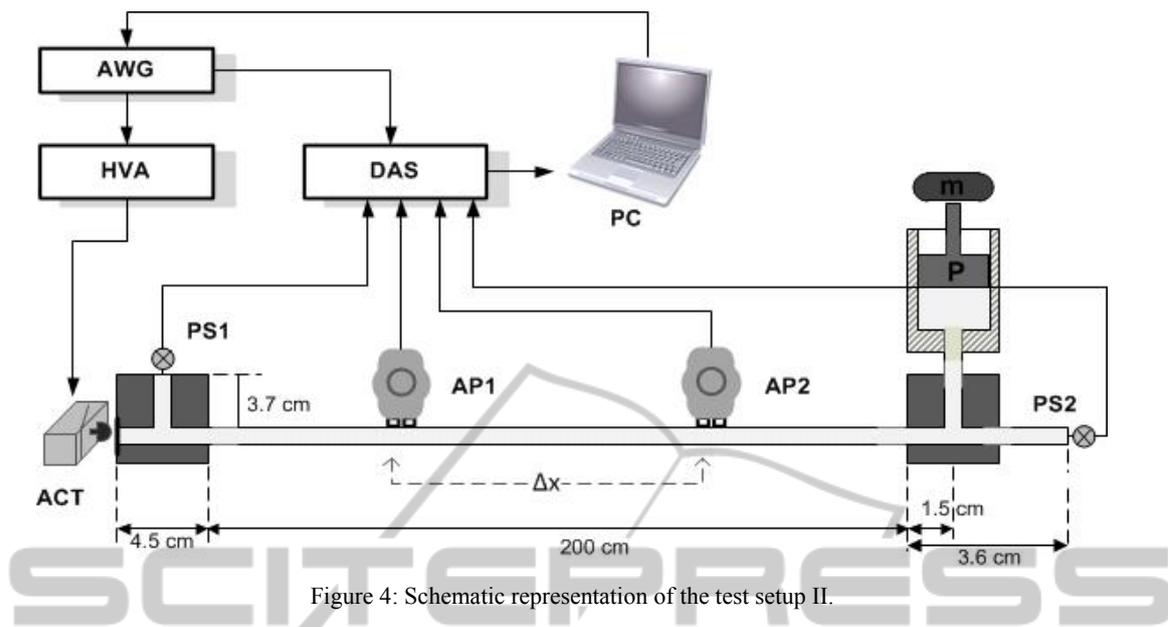


Figure 4: Schematic representation of the test setup II.

The test bench system II, schematically presented in figure 4, was developed aiming the assessment of the temporal resolution of the AP.

This test bench emulates the main arterial pressure wave propagation features of the cardiovascular system, presenting an upgrade in relation to the experimental setup developed previously by Pereira et al. (Pereira et al., 2009). The main difference is based on the use of a natural rubber latex tube, considered to be a reliable material to simulate the compliance of a human artery and providing a higher distensibility than the silicon tube originally used. As in the test bench I, the pressure waveform is firstly generated using the AWG and then delivered to the ACT/HVA, that through a piston (“mushroom” shaped PVC, 15 mm diameter) - rubber membrane mechanism launches the wave into a 200 cm long latex tube (Primeline Industries, 7.9 mm inner diameter, 0.8 mm wall thickness), filled with water. The tube’s sealing is made using a T-shaped scheme, guaranteeing geometric homogeneity. The wave is captured by the AP placed along the tube and by two pressure sensors PS1 and PS2 (Honeywell, 40PC015G1A), placed transversely and longitudinally to the tube. These sensors are used as the main reference for time delay/pulse wave velocity assessment but also monitor the DC pressure level of the tube, imposed by a piston P and a mass m at one of the tube’s extremities. The range of DC pressure levels in the tube varies, approximately, from 30 mmHg to 400 mmHg, including (and exceeding) the pressure variations registered in a healthy and non-healthy human system. Although the variation in the DC

pressure level interferes with the wave propagation velocity, the AP was tested at a constant DC pressure (≈ 66 mmHg), since it was not crucial for the present work having several wave propagation velocities.

To record simultaneously the different sensors response it was used the aforementioned DAS, triggered by the AWG.

3 METHODS

3.1 Experimental Characterization

The experimental characterization of the AP consisted in the evaluation of its performance regarding three main aspects: repeatability in assessing pressure waveform, occurrence of crosstalk phenomenon and estimation of time resolution. Several pressure waveforms were programmed and used as inputs in these studies, including Gaussian-like and Cardiac-like pulses. The last ones, synthesized using a weighted combination of exponentially shaped sub-pulses (Almeida et al., 2009), reproduce different states of arterial wall elasticity: type A and type B, correspond respectively to cases of pronounced and slight arterial stiffness (non-healthy subjects) and type C, commonly seen in healthy individuals, characterize elastic arteries (Murgo et al., 1980).

In all the experiments, the data acquisition was performed through a dedicated acquisition module of National Instruments (NI© USB6210) and data

logging was accomplished by NI LabView™ 2010 SignalExpress. All the signals were sampled at 5 kHz and stored for offline analysis using Matlab®. Data processing was undertaken in Matlab® 2009a and statistical analysis was performed using Microsoft Excel 2010.

3.1.1 Waveform Analysis/Repeatability

The first part of this study aimed to examine the probe's response for different types of waveforms generated by the Agilent 33220A and exerted by the ACT. To obtain the best response of the transducer it was selected for each input signal, the best amplitude (3.5V) and frequency (1Hz). All the sensors signals were submitted to a 300 Hz low pass filter and to a band cut filter of 49Hz-51Hz, in order to avoid, respectively, the presence of the resonant frequency of the actuator ($\sim 380\text{Hz} \pm 20\%$) and the 50Hz power line interference. It was also performed an integration of the transducer signals using the Matlab® function `cumsum` to compare them with the original input signals.

In the second part, it was intended to measure the same waveform repeatedly and under the same conditions by the AP. For this study, each sensor was excited with fifty independent impulses (with the same amplitude and width (Gaussian, 1 s width, 1Hz frequency). With those signals, it was determined the average signal which was used as reference to determine the root mean square error (RMSE), for each one. The RMSE was then computed to each signal.

3.1.2 Crosstalk Analysis

Since the two transducers composing the AP were incorporated in the same case with a very small separating distance, it was important to analyse whether some kind of interaction between them existed. The first part of this study was done simultaneously with the repeatability test, where one of the acoustic transducers was being actuated (microphone 1) and the other one was left free (microphone 2), that is to say without any contact with the PVC adapter/ACT (figure 3). The responses of both transducers for fifty independent impulses (Gaussian, 1 s width, 1 Hz frequency) were recorded and the average signals were estimated. This procedure was then applied to the other sensing element, such that the actuated transducer was microphone 2 and the free transducer was microphone 1.

The actuated transducers generated a typical differential signal with a good signal-to-noise ratio,

while the free transducers generated a much lower amplitude signal, with a profile substantially opposite to that obtained for the actuated transducers (see results section 4.1). Due to the characteristics of the signal obtained for the free transducers, it was necessary to perform an additional experiment to determine whether this transmission might interfere with one of the most important aspects of the probe: its time delay assessment. Thus, the second test consisted in the direct and simultaneous actuation of both transducers, with the purpose of time delay assessment. Both sensors were excited with three independent impulses (Gaussian, 1 s width, 1Hz frequency) and for each acquisition it was determined the time delay between both transducers, using different algorithms yet to be described on subsection 3.3. In this particular experiment, the signals were sampled at 12.5 kHz, the same sampling frequency used in in-vivo tests.

3.1.3 Time Resolution Evaluation

One of the main goals of the AP characterization was the evaluation of its ability of precisely assessing the time delay between two distinct points, separated from a very small distance.

In order to evaluate its time resolution, it was used two different APs (AP1 and AP2) that were placed on the tube of the test bench II, with the help of two external clamps (figure 4). One of the probes was kept fixed at the 50 cm position, while the other one was moving from 100 cm position to 54 cm position by 2 cm intervals. For each position, a Gaussian waveform (100 ms width, 10 Hz frequency) was delivered to the system, and then time delay and PWV were estimated between the first microphones of both probes and also between the pressure sensors (PS1 and PS2), attached at the extremities of the tube.

The relative errors between the reference PWV and the PWV obtained with the uncoupled transducers for each separating distance (Δx) were calculated, using the algorithms of section 3.3. The test was repeated for more two times, for a constant DC pressure of ≈ 66 mmHg.

3.2 In Vivo Measurements

3.2.1 Participants and Study Protocol

Seventeen young volunteers aged 22.12 ± 1.96 years were recruited and gave written informed consent prior to recording. Each participant was properly weighed and measured and after 5m of rest of supine

position, a blood pressure measurement was obtained from his right brachial artery, using an automatic clinically validated sphygmomanometer (MAM Colson BP 3AA1-2 ®; Colson, Paris). Next, a straight arterial segment of the right common carotid artery was identified by a skilled operator and a record of approximately 20s-30s was obtained with the probe longitudinally aligned to the artery. Data acquisition was performed with the dedicated real-time software Cardiocheck GUI and automatically stored in the Cardiocheck DB. Age, sex, weight, height, waist, systolic blood pressure (SBP) and diastolic blood pressure (DBP) were also stored in the same database.

All the signals were acquired at a sample rate of 12.5 kHz and were processed offline in Matlab 2009a®, aiming the extraction of carotid pulse wave velocity and other hemodynamic parameters.

3.3 Signal Processing

In the first part of this work (experimental characterization), a set of dedicated algorithms have been developed aiming the estimation of time delay in two main situations: between the signals of the AP transducers and between the signals of pressure sensors (test setup II). After a common pre-processing, based on a low-pass filter with a cut-off frequency of 100 Hz to reduce high frequency noise, four different methods were used for time delay estimation: a) maximum of cross-correlation function, b) maximum and c) minimum amplitude identification and d) zero-crossing detection. The cross correlation method uses the *xcorr* function of Matlab's Signal Processing Toolbox to determine the peak of cross-correlogram that allows delay estimation by subtracting the peak time position from the pulse length. The other methods ensure an accurate detection of some fiducial points of the signal, such as the maximum, the minimum and the zero. As so, the methods of maximum and minimum amplitude identification use a 6th polynomial fit in the maximum and the minimum region of the signals, while the zero-crossing method applies a linear fit to the region where the signal crosses the zero. For all the methods, time delay is estimated between the maxima, minima and zero points detected in each set of signals.

In the last part of this work, the AP was used to assess PWV and other hemodynamic parameters in human carotid arteries. Since the acquisitions were constituted by several cardiac cycles, it was necessary to apply a dedicated segmentation routine, based on a minima detection approach to divide the

data stream into single periods. Before applying the segmentation algorithm, the signals were filtered with the aforementioned 100 Hz low pass-filter and then heart rate was determined. For each cardiac cycle, the maximum of cross-correlation was used for carotid PWV estimation and an average value was obtained. Besides PWV, it was also possible to determine hemodynamic parameters, such as: LVET, defined as the period of time from the start of the pulse (aortic valve open) to the dicrotic notch (closure of the aortic valve) and diastole phase (DP), defined as the period of time from the dicrotic notch to the end of the pulse. These parameters were extracted based on the conviction that the onsets of the first and second carotid sounds (S1 and S2) coincide respectively with the onset and with the dicrotic notch of the carotid pulse waveform (Hasegawa et al., 1991). The onsets of carotid sounds S1 and S2 were identified as the maxima of the second time derivative of the acoustic signal. LVET and DP were calculated for each cardiac cycle. Data were expressed as mean \pm SD.

4 RESULTS AND DISCUSSION

4.1 Experimental Characterization

The first part of probe's experimental characterization consisted in the evaluation of the AP output to different waveforms and its repeatability. The response obtained by the AP for each one of the waveforms is presented in figure 5. The AP profiles are similar to those expected by a differentiator circuit; however it is not possible to precisely recover the original pressure waveform. When the acoustic signals are integrated there are noticeable similarities with the input signals, however the RMSE between both signals is quite high (approximately 13% for each case). This performance was predictable, since the sensitivity of the acoustic sensors must be reduced for low frequencies that are below the microphone's 3dB bandwidth (100 Hz-10 kHz). Since low frequencies are determinant for the precise reconstruction of arterial pressure waveform, the use of these acoustic sensors limits the possibility of the AP for waveform estimation purposes. Nevertheless, this fact does not disqualify the use of this probe for its main purpose: PWV estimation, once the method does not depend on the waveform accuracy.

The results regarding the repeatability test are shown in table 1 and figure 6.

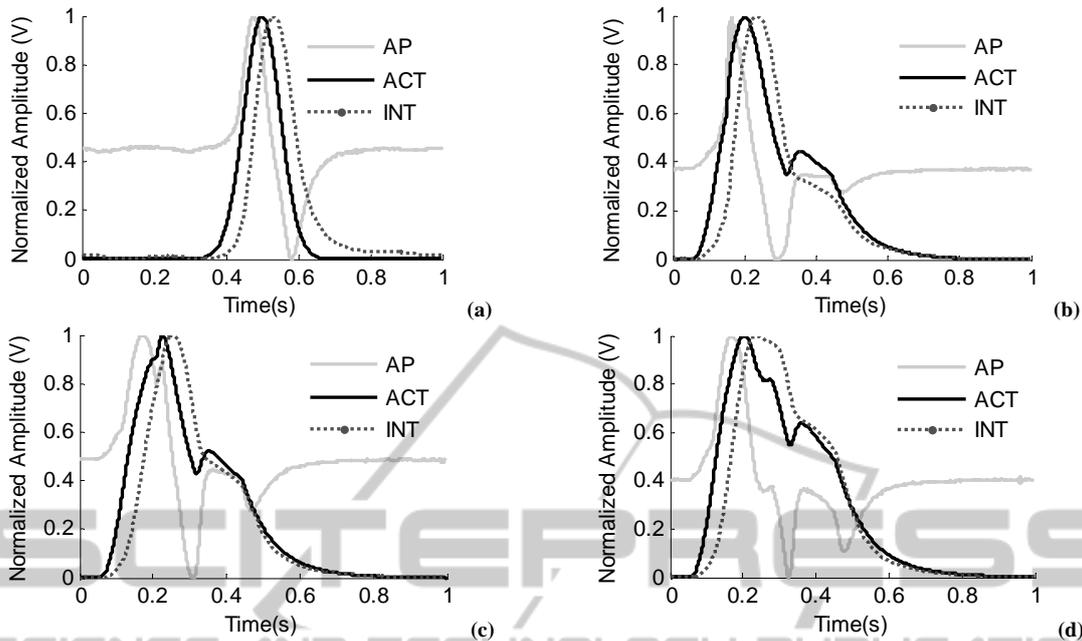


Figure 5: Acoustic sensor responses to different excitation pressure waveforms. (a) Gaussian-like Pulse. (b) Type A Cardiac-like Pulse. (c) Type B Cardiac-like Pulse. (d) Type C Cardiac-like Pulse. AP- Acoustic Sensor Signal. ACT- Input Signal. INT- Integrated Sensor Signal.

Table 1: Statistics of the measurements obtained in the repeatability test.

Transducer	Mic 1	Mic 2
N° Acquisitions	50	50
Mean (%)	1.1781	0.6198
Std. Deviation (%)	0.0345	0.0298
Maximum (%)	1.2849	0.7379
Minimum (%)	1.1174	0.5890

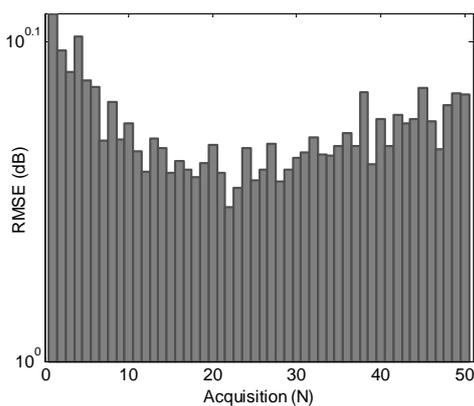


Figure 6: Graphic representation of the RMSE distribution between the reference signal and the microphone 2 output, obtained in the repeatability test.

Although the microphone 2 (0.6198 ± 0.0298) exhibits a better performance than the microphone 1 (1.1781 ± 0.0345), the RMSE variance values obtained for both probes are identically low, evidencing the reliability of the system.

The second part of the AP's characterization intended to study the presence or absence of crosstalk effect in both transducers. The first results achieved in this study are illustrated in figure 7. The actuated sensors present a good signal-to-noise ratio and a typical profile when compared with the one obtained previously in the waveform analysis test (figure 5 (a)).

The free transducers also present a slight profile but of much lower amplitude. Although the results suggest the existence of crosstalk effect, this phenomenon was seen as a mass inertial effect (transducer resistance to conserve its idle state), since the profile of the free transducer had an inversed shape relatively to the actuated one. This assumption could not be proven in the present work but it will be aim of futures studies. Nevertheless, and since the main purpose of this probe is the assessment of local PWV, it was employed a different approach, in order to determine if this "transmission" might interfere with the AP's time delay. For this purpose, both transducers were simultaneously actuated with three independent

Gaussian waves and time delay was calculated using different algorithms. The results regarding this experiment are presented in table 2 and figure 8.

Table 2: Time delay values obtained for each algorithm when both transducers are simultaneously actuated with three independent Gaussian impulses.

N	Time Delay Estimation Method			
	xcorr	max	min	zc
1	8e-5	0.0134	0.0136	0.0037
2	8e-5	0.0109	0.0142	0.0038
3	8e-5	0.0103	0.0140	0.0035

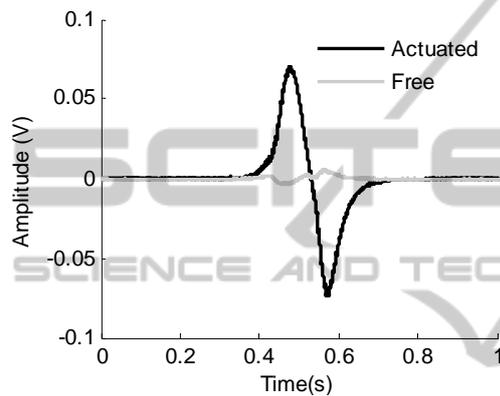


Figure 7: Crosstalk phenomenon study: average response of both AP's transducers to fifty independent pulses. The actuated transducer is microphone 2 and the free transducer is microphone 1.

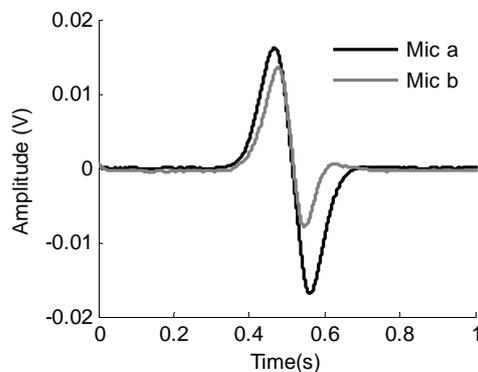


Figure 8: Crosstalk phenomenon study: typical response of both AP'S transducers to a Gaussian pulse, simultaneously delivered to them.

The time delay obtained for each one of the algorithms is very different and actually surprising. It was not expected to obtain such a variable and elevated time delay values for maximum, minimum and zero crossing algorithms. In contrast, the cross-correlation algorithm presented a great performance, where time delay always matched the minimum

detectable time, limited by the system, i.e., the sampling time (1/12500Hz). In order to understand the achieved results, the AP's response was also analysed (figure 8). It is visible that the profiles obtained for each one of the transducers are identical; however, they present important differences in terms of amplitude and peaks correspondence. It was expected that the maxima and the minima of both signals were in agreement, but actually that didn't happen. These slight profiles difference can be justified with the experiment level of difficulty. It is extremely important that the simultaneous actuation of both transducers is made rigorously under the same conditions; otherwise the waveforms of each transducer can be affected. This also suggests that time delay algorithms that depend only on a fiducial point are more susceptible to error, especially if the waveforms don't have exactly the same profile. Finally and in what concerns to crosstalk effect, it can be concluded that the existence of a possible transmission between sensors does not affect the time delay, when the cross-correlation algorithm is used. In order to prove the effectiveness of the other algorithms, it will be necessary to proceed to additional experiments.

The last test concerning AP's experimental characterization intended to evaluate its time resolution. In this test, it was determined the PWV for two uncoupled AP's in successively smaller separation distances and the PWV reference obtained using the pressure sensors PS1 and PS2. The PWV results obtained for each algorithm and the relative errors between the reference PWV and the PWV obtained with the uncoupled transducers, for each separating distance and method are presented, respectively, in figures 9 and 10.

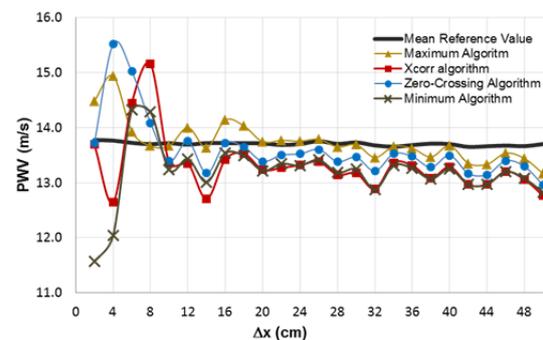


Figure 9: Time Resolution study: PWV values of uncoupled acoustic sensors and pressure sensors, yielded by the four algorithms. Each point is an average of three trials.

The statistics of the measurements are synthesized in table 3.

Table 3: Statistics of the measurements obtained in the time resolution test.

Algorithm	PWV(m/s)		Relative Error Mean (%)
	Pressure Sensors (reference)	Acoustic Sensors	
Maximum	13.856±0.037	13.742±0.372	2.083
Xcorr	13.716±0.037	13.308 ±0.524	4.246
ZC	13.702±0.034	13.592 ±0.560	2.863
Min	13.540±0.039	13.176±0.547	3.550

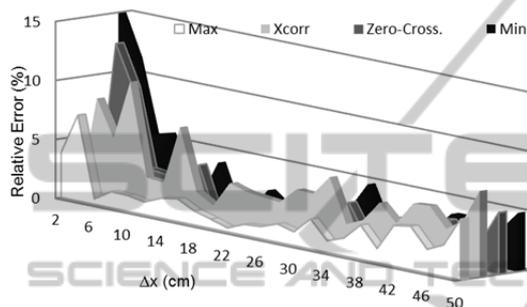


Figure 10: Time Resolution study: relative errors for each distance and method.

The algorithms with the best and worst general performance are the maximum and the cross-correlation with an average error less than 3% and 5%, respectively. However, and for the minimum distance achieved (2 cm) the magnitude of the errors is less than 1%, when considering cross-correlation and zero-crossing algorithms.

The results obtained for AP time resolution for each algorithm, exhibit a very good performance suggesting that the AP have enough accuracy to be considered an interesting stand-alone instrument for local PWV assessment.

4.2 In-vivo Measurements

Following the preliminary tests of the probe in the test benches, it was performed a set of measurements in human carotid arteries, in order to test the AP in in-vivo conditions (figure 11). The characteristics of the patients, as also the results of the parameters assessed by the AP, (heart rate, local PWV, LVET and DP) are given in table 4.

In order to assess pulse wave velocity, it was only used the cross-correlation algorithm, since it has presented the best performance both on crosstalk and on time resolution studies. The range of obtained values for carotid PWV are slightly lower than the values obtained by other reference studies

that also assess the carotid PWV (≈ 4 m/s) (Borlotti et al., 2012 and Hermeling et. al., 2006). However, the number of analysed subjects not only is small as also include very young people (22.12 ± 1.96 years), which can justify a lower PWV mean (≈ 3 m/s), due to the high elasticity of young and healthier arteries. Although the obtained PWV variance is high ($N=17, \approx 1$ m/s), it is concordant with the PWV variance obtained in a recent study for a significant number of healthier subjects ($N=1774, \approx 1.64$ m/s) (Borlotti et al., 2012).

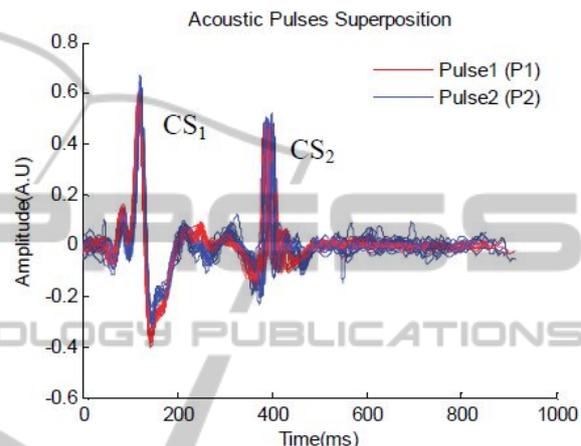


Figure 11: Preliminary results of the AP acquiring data in a healthy young subject. CS₁- First Carotid Sound. CS₂- Second Carotid Sound.

Table 4: Main characteristics of the volunteers and AP parameters assessment.

Variable	Mean ± SD
Age, years	22.12 ±1.96
N(Male/Female)	17(6/11)
Height, cm	166.82±11.73
Weight, Kg	66.18±18.87
BMI, Kg/m ²	23.50±4.94
Waist, cm	75.35±14.85
Brachial SBP, mmHg	114.35±12.62
Brachial DBP, mmHg	70.94±7.11
Heart Rate, bpm	67±12.09
Local PWV(m/s)	2.96±1.08
LVET (ms)	288.59±21.42
DP (ms)	611.07±148.84

Nevertheless and in order to address more accurate results, it will be necessary to assess to a higher number of subjects, not only with a broader range of ages but also with pathologies, such as hypertension or atherosclerosis, where is expected to observe an increase of local PWV. The use of a reference method is also indispensable to validate the developed algorithms for AP hemodynamic

parameters extraction. Currently, the probe presented a good performance in acquiring signals with a good bandwidth and signal-to-noise ratio in human carotid arteries, allowing the application of various algorithms that extract clinically relevant information.

Regarding the LVET values, we believe that is actually possible to determine this parameter as the time delay between the main onsets of each carotid sounds, since the estimated values are generally close to the expected for healthy subjects (Willems et. al., 1970). This parameter will be the subject of a further study, to evaluate the robustness of the algorithm.

5 CONCLUSIONS

A novel and low-cost doubled headed probe specifically designed to assess local PWV has been developed and characterized in dedicated test setups.

The probe demonstrated good performance on the dedicated test setups and results showed that its signals are repeatable and crosstalk effect do not interfere with its time resolution when the cross-correlation algorithm for time delay estimation is used.

It is also possible to conclude favourably towards the effectiveness of the AP in the measurement of local PWV. The maximum amplitude and the cross correlation algorithms exhibited the capability of measuring higher PWV ($\approx 14\text{m/s}$) with an error less than 10%, for the several separating distances (50 cm to 2 cm).

The natural follow-up of this work will be the continuation of the assessment of local PWV and other hemodynamic parameters in a significant numbers of patients (normal and with different pathologies), under medical control. The obtained AP values must also be compared with the values obtained with standard commercial systems.

Although studies to validate the clinical use of AP are still required, this device seems to be a valid alternative system, to local PWV stand-alone devices.

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REFERENCES

- Almeida, V., Pereira, T., Borges, E., Figueiras, E., Cardoso, J., Correia, C., Pereira, H. C., Malaquias, J. L. and Simões, J. B. 2009. Synthesized cardiac waveform in the evaluation of augmentation index algorithms. In *Proceedings of BIOSIGNALS 2010, Valencia, Spain*.
- Borlotti, A., Khir, A. W., Rietzschel, E. R., De Buyzere, M. L., Vermeersch, S. & Segers, P. 2012. Noninvasive determination of local pulse wave velocity and wave intensity: changes with age and gender in the carotid and femoral arteries of healthy human. *J Appl Physiol*, 113, 727-35.
- Boutouyrie, P., Brie, M., Collin, C., Vermeesch, S. and Pannier, B. 2009. Assessment of pulse wave velocity. *Artery Research*, 3, 3-8.
- Gamble, G., Zorn, J., Sanders, G., Macmahon, S. & Sharpe, N. 1994. Estimation of arterial stiffness, compliance, and distensibility from M-mode ultrasound measurements of the common carotid artery. *Stroke*, 25, 11-6.
- Gaszner, B., Lenkey, Z., Illyes, M., Sarszegi, Z., Horvath, I. G., Magyari, B., Molnar, F., Konyi, A. & Cziraki, A. 2012. Comparison of aortic and carotid arterial stiffness parameters in patients with verified coronary artery disease. *Clin Cardiol*, 35, 26-31.
- Hasegawa, M., Rodbard, D. & Kinoshita, Y. 1991. Timing of the carotid arterial sounds in normal adult men: measurement of left ventricular ejection, pre-ejection period and pulse transmission time. *Cardiology*, 78, 138-49.
- Hermeling, E., Reesink, K. D., Reneman, R. S. & Hoeks, A. P. 2007. Measurement of local pulse wave velocity: effects of signal processing on precision. *Ultrasound Med Biol*, 33, 774-81.
- Laurent, S., Boutouyrie, P., Asmar, R., Gautier, I., Laloux, B., Guize, L., Ducimetiere, P. & Benetos, A. 2001. Aortic stiffness is an independent predictor of all-cause and cardiovascular mortality in hypertensive patients. *Hypertension*, 37, 1236-41.
- Laurent, S., Cockcroft, J., Van Bortel, L., Boutouyrie, P., Giannattasio, C., Hayoz, D., Pannier, B., Vlachopoulos, C., Wilkinson, I., Struijker-Boudier, H. & European Network for Non-Invasive Investigation of Large, A. 2006. Expert consensus document on arterial stiffness: methodological issues and clinical

- applications. *Eur Heart J*, 27, 2588-605.
- Laurent, S., Katsahian, S., Fassot, C., Tropeano, A., Gautier, I., Laloux, B. and Boutouyrie, P. 2003. Aortic stiffness is an independent predictor of fatal stroke in essential hypertension. *Stroke*, 34, 1203-1206.
- Maldonado, J., Pereira, T., Polonia, J., Silva, J. A., Morais, J., Marques, M. & Participants in The, E. P. 2011. Arterial stiffness predicts cardiovascular outcome in a low-to-moderate cardiovascular risk population: the EDIVA (Estudo de Distensibilidade Vascular) project. *J Hypertens*, 29, 669-75.
- Mancia, G., De Backer, G., Dominiczak, et al., Management of Arterial Hypertension of the European Society Of, H. & European Society Of, C. 2007. 2007 Guidelines for the Management of Arterial Hypertension: The Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *J Hypertens*, 25, 1105-87.
- Meaume, S., Rudnichi, A., Lynch, A., Bussy, C., Sebban, C., Benetos, A. & Safar, M. E. 2001. Aortic pulse wave velocity as a marker of cardiovascular disease in subjects over 70 years old. *J Hypertens*, 19, 871-7.
- Murgo, J. P., Westerhof, N., Giolma, J. P. & Altobelli, S. A. 1980. Aortic input impedance in normal man: relationship to pressure wave forms. *Circulation*, 62, 105-16.
- Pannier, B. M., Avolio, A. P., Hoeks, A., Mancia, G. & Takazawa, K. 2002. Methods and devices for measuring arterial compliance in humans. *Am J Hypertens*, 15, 743-53.
- Pereira, H. C., Cardoso, J. M., Almeida, V. G., Pereira, T., Borges, E., Figueiras, E., Ferreira, L. R., Simões, J., Correia, C. 2009. Programmable testbench for hemodynamic studies. *IFMBE Proceedings 25/IV* 1460ff.
- Pereira, H. C., Pereira, T., Almeida, V., Borges, E., Figueiras, E., Simoes, J. B., Malaquias, J. L., Cardoso, J. M. & Correia, C. M. 2010. Characterization of a double probe for local pulse wave velocity assessment. *Physiol Meas*, 31, 1449-65.
- Pereira, H. C., Basílio, J. B., Malaquias, J., Pereira, T., Almeida, V., Borges, E., Figueiras, E., Cardoso, J. and Correia C. 2011. Double Headed Probe for Local Pulse Wave Velocity Estimation – A new device for hemodynamic parameters assessment. *In Proceedings of BIOSIGNALS 2011, Rome, Italy*.
- Rabben, S. I., Stergiopoulos, N., Hellevik, L. R., Smiseth, O. A., Slordahl, S., Urheim, S. & Angelsen, B. 2004. An ultrasound-based method for determining pulse wave velocity in superficial arteries. *J Biomech*, 37, 1615-22.
- Segers, P., Kips, J., Trachet, B., Swillens, A., Vermeersch, S., Mahieu, D., Rietzchel, E., Buyzere, M. and Bortel, L. 2009. Limitations and pitfalls of non-invasive measurement of arterial pressure wave reflections and pulse wave velocity. *Artery Research*, 3, 79-88.
- Shoji, T., Emoto, M., Shinohara, K., Kakiya, R., Tsujimoto, Y., Kishimoto, H., Ishimura, E., Tabata, T. & Nishizawa, Y. 2001. Diabetes mellitus, aortic stiffness, and cardiovascular mortality in end-stage renal disease. *J Am Soc Nephrol*, 12, 2117-24.
- Willems, J. L., Roelandt, J., De Geest, H., Kesteloot, H. & Joossens, J. V. 1970. The left ventricular ejection time in elderly subjects. *Circulation*, 42, 37-42.