Assessment of the Pulse Wave Variability for a New Non-invasive Device

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Abstract— **The main motivation of this work was to provide a valid contribution for the assessment of the cardiovascular condition by the analysis of several Arterial Pressure Waveform (APW) parameters collected by a new non-invasive device. Three sets of recordings for the carotid pressure waveform at left and right carotid arteries were performed, under standardized conditions, in 20 volunteers by three trained operators. The mean of the inter-operator differences were higher for the right artery, comparatively to the left artery. In this case, an Augmentation Index (AIx) value of -2.31 ± 7.29 % and a Systolic Wave Transit Time (SWTT) value of -12.94 ± 31.46 ms were observed, which are higher than the left measurements, 0.94 ± 7.52 % and -2.96 ± 22.67 ms, respectively. Intra-operator differences were calculated for each of the three sets of measurements and showed good reproducibility. The pulse-by-pulse variability analysis gives very good markers for the Left Ventricular Ejection Time (LVET), Dicrotic Wave Amplitude (DWA), Reflection Wave Amplitude (RWA), Coefficient of Variation (CV) < 10 %, and satisfactory values for the AIx (CV<30 %). The SWTT and Reflected Wave Transit Time (RWTT) also presented satisfactory results (10 %<CV<30 %). Results demonstrated the reproducibility of the parameter, being a simple and non-invasive device, that can be used to assess central hemodynamics.**

Keywords— **Cardiovascular diseases, arterial pressure waveform, reproducibility.**

I. INTRODUCTION

The increasing awareness of arterial stiffness in cardiovascular studies [1] started a new era of search for parameters capable of, directly or indirectly, quantifying its development. There are several advantages of using non-invasive methods, over invasive ones. For instance, these methods can be used in follow-up trials of populations free from symptomatic Cardiovascular Diseases (CVD), such as children or young adults, and be a tool for risk assessment in addition to the established risk factors [1].

The non-invasive measurement of arterial stiffness implies the measure of surrogate parameters that are intrinsically associated with its development [2, 3]. In the field of pulse wave analysis, the wave reflections are probably the most studied, often addressed in several studies [4]. The Augmentation Index (AIx) is one of the most relevant parameters, which expresses the ratio of the augmented pressure, assigned to the reflected wave into the overall pulse. Furthermore, other parameters can be identified based on the most relevant feature points. Parameters, such as the Reflected Wave Transit Time (RWTT), which is calculated as the elapsed time from the wave foot to the systolic inflection point can be referred as an indirect measurement of the arterial compliance. The Systolic Wave Transit Time (SWTT) can also be computed. Additionally, Left Ventricular Ejection Time (LVET) related with the elapsed time between the beginning of the pulse and the closure of the aortic valve can also be computed. The most relevant amplitude parameters are the Systolic Wave Amplitude (SWA), Reflection Wave Amplitude (RWA) and Dicrotic Wave Amplitude (DWA).

This work finds its motivation in the foreseeable impact that an accurate, non-invasive and easy-to-use instrument for hemodynamic condition assessment could impart on the diagnosis and follow-up of the CVD. A multi-modular platform was developed allowing to add up several technologies and methodologies used in the traditional clinical path of cardiovascular patients, in order to provide a refined assessment of their physiological status [5]. An optical device was also developed for local pulse wave velocity (PWV) assessment and other hemodynamic parameters analysis [6]. Along this work the Arterial Pressure Waveform (APW) module dedicated to pulse wave analysis is detailed. This platform also integrates the development of data-mining tools, incorporating personalized machine learning algorithms capable to deal with a wide set of APW features [7]. Moreover, it is presented the validation tests performed to evaluate the precision of the instrument. In this sense, intra and inter-operator reproducibility values are evaluated. The paper is organized as follows: the APW module,

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the subjects and parameters selected, as well as the validation tests description are presented in Section II, the results and the discussion are presented in Section III and the conclusions are drawn in the last section.

II. Methods

A. APW Module

A previously prototype version system was developed to assess the performance of piezoelectric (PZ) sensors [8]. The module presented in Figure 1 is the final version of the laboratory prototype in which a dsPIC controller was integrated. The board assembly was performed in a 100x60 mm^2 standard Eurocard board, with 64 pins DIN plug, and an appropriate front panel plate. A detailed description of the main blocks is in [5, 8].

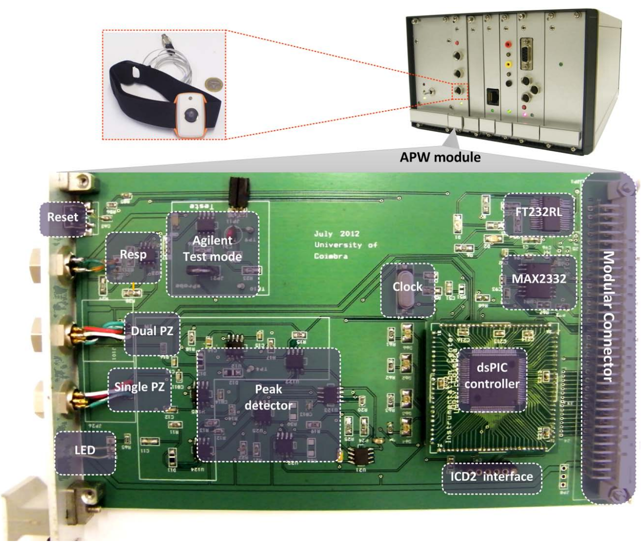

Fig. 1: (a) Multichannel platform; (b) PZ probe; (c) APW module.

B. Subjects

The dataset was obtained from 20 healthy subjects (12 female, 8 male), under 30 years old, and with no documented history of cardiovascular disorders. The acquisitions were done by three operators with different levels of experience and training. Two operators (operator 1 and operator 2) have received one week of intensive instruction and training before the measurements recording. The other (operator 3) had, at the time, more than 2 years of experience. Each operator performed several measurements, which consisted of three sessions for each one of the carotid arteries (left and right), comprising a set of 18 acquisitions of about $60 - 90\ s$ for a single subject.

C. APW Parameters

Pulse wave analysis relies on a clean waveform, in which the morphological features are reliably identified. The APW is the result of the the interaction of the amount of blood that is pumped out of the heart along the wall vessels of arterial tree. The APW contains important physiological information concealed on its morphology: the Systolic Peak (SP), the Point of Inflection (Pi) and the Dicrotic Wave (DW) [4]. SP results from the action of the left ventricle blood pumping, while Pi results from both action: the forward wave travelling along the arterial tree and the backward wave returning towards the heart, from the reflection sites [1]. These waves superimpose originating a visible inflection change in APW profile. DW occurs when the aortic valve closes moving a small portion of the ejected blood back to the left ventricle. The evaluated parameters were computed based on algorithm based on the first-order derivative of the APW [5, 7], such as schematically represented in Figure 2, for a Type A waveform (detailed in [5]).

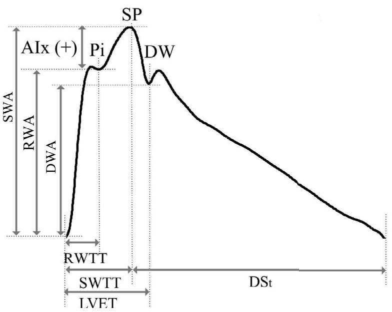

Fig. 2: Schematic representation of the pulse wave analysis, for a Type A waveform, where DS_t is the downstroke time.

D. Inter and Intra-operator Variability

The measurements by the same operator in different, but close, occasions (intra-operator variability) by two independent operators (inter-operator variability) was evaluated calculating the limits of agreement, using Bland-Altman's plots. In these plots the differences between the studied parameters are plotted against the mean values. The coefficient of variation (CV) was used for the pulse-by-pulse variability assessment.

E. Accuracy Standards

Three levels of acceptance of the measurements have been used in literature. Good variability is defined if below 10 %; variability values between 10 % and 30 % are considered satisfactory (but dependent of the use in practice the cost, and the availability of alternative methods); and, finally, variabilities over 30 % are considered unsatisfactory [9, 10].

III. RESULTS

A. Intra-operator variability

For the calculation of the intra-operator reproducibility, each of the three sets of data recordings, performed by each operator, were analysed. So, for each operator 3 pairs of values ($n = 51$) were considered (session1 *versus* session2, session1 *versus* session3 and session2 *versus* session3), for both arteries (left and right). Bland-Altman plots were analysed for all data. The observed differences are presented in Tables 1 and 2, for the left and right carotid arteries, respectively.

Table 1: Intra-operator mean differences ± 2 SD derived from the Bland-Altman plots ($n = 51$), obtained for the left carotid artery.

Parameter	Operator1	Operator2	Operator3
SWTT(ms)	5.74±17.32	5.41±15.12	1.71±29.08
RWTT(ms)	−2.4±18.54	−5.09±10.85	2.74±15.50
LVET(ms)	3.44±13.05	6.59±22.36	1.53±21.84
RWA(%)	1.02±4.87	−0.90±3.13	−0.01±3.59
DWA(%)	0.96±4.41	0.24±4.51	0.37±4.85
AIx(%)	−0.36±5.16	0.96±3.26	0.52±3.58

Table 2: Intra-operator mean differences ± 2 SD derived from the Bland-Altman plots ($n = 51$), obtained for the right carotid artery.

Parameter	Operator1	Operator2	Operator3
SWTT(ms)	4.18±19.74	−4.18±30.41	0.61±25.46
RWTT(ms)	−2.27±17.67	−8.97±23.80	2.70±17.24
LVET(ms)	0.19±15.73	−4.32±22.67	3.63±25.36
RWA(%)	−0.16±3.29	−1.18±8.06	−0.92±7.63
DWA(%)	0.59±4.38	0.90±5.34	−0.31±4.31
AIx(%)	0.02±6.01	2.18±6.70	0.90±7.21

Generally, the verified differences were lower for the operator 3, comparatively to the others, which is probably due to its larger experience in performing pulse wave measurements. The results are similar (or better) to the other data reported in literature. In the AIx analysis, it was observed a difference in the intra-variability < 1 %, for the majority of cases (excluding the 2.18 % variability value, observed by the operator 2, at right carotid artery). The significance of the differences was also assessed using the Kruskal-Wallis test and it was confirmed that the operator 3 presented a better performance, since the measurements have lower significant differences among sessions [5].

Frimodt-Moller *et al.* [11] reported an RWTT variance of -6.9 ± 52.7 ms, -2.7 ± 32.8 ms, -3.2 ± 33.9 ms. Similar values were verified in this study: -2.27 ± 17.67 ms, -8.97 ± 23.80 ms, 2.70 ± 17.24 ms, for the operators 1, 2 and 3, respectively. The other timing variables (SWTT, RWTT) also show low differences, for the same order of values. RWA and DWA mean differences were about 1 % (in reference to the normalized amplitude) for all measurements.

B. Inter-operator Variability

The calculation of the inter-operator variations was based on the averaging of 153 double recordings performed by all the operators (each pair of values comprises two measurements from different operators. Results are presented in Table 3. Higher differences were observed for the right carotid artery, comparatively to the left carotid artery. In this case, an AIx value of -2.31 ± 7.29 % and a SWTT value of -12.94 ± 31.46 ms are observed, higher than the left measurements, 0.94 ± 7.52 % and -2.96 ± 22.67 ms, respectively. Probably, the values occur due to the implemented acquisition protocol and operators positioning.

Siebenhofer *et al.* [12] reported an AIx mean difference of 0.4 ± 6.4 %, while Crilly *et al.* [13] reported 1.0 ± 3.9 % mean value. Frimodt-Moller *et al.* [11] state up 0.9 ± 15.8 %, similar to the values verified in this study (0.94 ± 7.52 %). It can be also observed that the lowest inter-operator variability value was recorded for the RWTT value, -0.83 ± 27.10 ms, which represents an excellent value, comparing to the Frimodt-Moller *et al.* [11] observed value of -1.9 ± 30.8 ms. The RWA and the DWA mean differences presented good variability range (< 3 %) for all measurements.

Table 3: Inter-operator mean differences ± 2 SD derived from the Bland-Altman plots ($n = 153$).

Parameter	Left	Right
SWTT(ms)	−2.96±22.67	−12.94±31.46
RWTT (ms)	−0.83±27.10	−1.08±23.49
LVET (ms)	−5.83±26.06	−9.57±23.03
RWA (%)	−0.25±7.58	2.46±7.21
DWA (%)	0.67±7.39	−1.07±6.86
AIx (%)	0.94±7.52	−2.31±7.29

C. Pulse-by-Pulse Variability

There are no previous studies concerning the pulse-by-pulse variability for the APW features. In this study, the CV was assessed for all pulses in the dataset (comprising session1, session2 and session3) measured by each operator. Results are presented in Figure 3. Variability values were very good for the LVET, the DWA and the RWA (CV< 10 %), and satisfactory for the AIx (28.07 %, 21.51 % and 24.85 % for the operators 1, 2 and 3, respectively). The SWTT and RWTT also presented satisfactory results (10 %<CV<30 %). AIx presented the higher variability values. Thus, this parameter should be reserved mainly to highly trained operators. All of the parameters give good indicators, concerning their potential use for cardiovascular risk assessment.

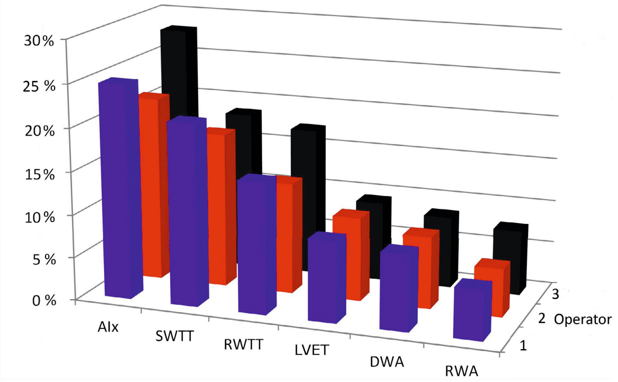

Fig. 3: CV values (right carotid artery) obtained for each operator.

IV. Conclusion

Concerning the data acquisition, it was demonstrated that operators can be easily trained in the use of this prototype, being the variability analysis dependent of a good acquisition. Different operators, with only one week of training, produced quite reasonable results. The intra-operator "limits of agreement" are good markers comparatively to the values available in the literature. These results have important implications concerning the use of this prototype for the patients clinical assessment and suggest that APW indices are reproducible and repeatable, when measured by different operators at different occasions.

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