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Multi-Gaussian fitting for the assessment of left ventricular ejection time from the Photoplethysmogram

R. Couceiro, P. Carvalho, R. P. Paiva, J. Henriques, M. Antunes, I. Quintal and J. Muehlsteff

Abstract— **The Left ventricular ejection time (LVET) is one of the primary surrogates of the left ventricular contractility and stroke volume. Its continuous monitoring is considered to be a valuable hypovolumia prognostic parameter and an important risk predictor in cardiovascular diseases such as cardiac and light chain amyloidosis. In this paper, we present a novel methodology for the assessment of LVET based the Photoplethysmographic (PPG) waveform. We propose the use of Gaussian functions to model both systolic and diastolic phases of the PPG beat and consequently determine the onset and offset of the systolic ejection from the analysis of the systolic phase 3rd derivative. The results achieved by the proposed methodology were compared with the algorithm proposed by Chan et al. [1], revealing better estimation of LVET (15.84 ± 13.56 ms vs 23.01 ± 14.60 ms), and similar correlation with the echocardiographic reference (0.73 vs 0.75).**

I. Introduction

The use of systolic time intervals as indirect indices of myocardial performance dates back to 1960s when the period of isovolumetric contraction (IVCT) and pre-ejection period (PEP) were deeply investigated as measures of the cardiac systolic function, whereas the left ventricular ejection time (LVET) was used as a surrogate of LV stroke volume. An early application of these indices was proposed by Weissler et al. [2], who used an index of left ventricular function (PEP/LVET) in the identification of Heart Failure. More recently, Geeraerts et al. [3] indicated the LVET as a valuable prognostic parameter related to hypovolemia induced by a lower body negative pressure in conscious volunteers. Bellavia et al. [4] suggested LVET to be an essential parameter for the assessment of patients with cardiac amyloidosis and consequently the most important predictor of mortality for this disease. Migrino et al. [5] showed the potential of LVET as a robust and independent predictor of Light chain amyloidosis mortality for both short term and long term follow-up.

By definition, LVET refers to the time interval of the left ventricular ejection, i.e., from opening of the aortic valve to its subsequent closure and can be related to contractility [6] and cardiac output [7]. It is by itself a measure of cardiac function [8].

The current gold standard technique for the assessment of the cardiac function, non-invasivly, is echocardiography, using M-mode and Doppler. This technique enables the determination of indexes such as velocity of pressure rise, the velocity of ejection, the extent of ejection and the ejection fraction. However this kind of techniques is usually expensive, require specific skills, therefore trained personals and lack portability. Thus they are not suitable for primary and home care scenarios.

Driven by the demand for low cost, minimal intrusive and portable solutions in primary and home care settings techniques such as phonocardiography (PCG), impedance cardiography (ICG) and photoplethysmography (PPG) gained special importance in the last decade. In p-health, the ICG waveform analysis is the reference for the determination of systolic time intervals (STI). However, there is still some controversy on how to determine the ICG characteristic points that capture the opening (B-point) and closure of the aortic valve (X-point). More recently, Carvalho et al. [9] and Paiva et al. [10] proposed a method based on the analysis of the PCG waveform for the assessment of PEP and LVET.

The assessment of LVET based on the analysis of the PPG waveform was firstly introduced in a study involving the analysis of the ear densitogram [11]. Quarry-Pigott et al. suggested that the onset and offset of the systolic ejection could be recognized in the morphology of the first derivative. Based on this study, Chan et al. [1] proposed an algorithm for the assessment of LVET based on the analysis of the finger photoplethysmography. Here, LVET is determined by a rule-based combination of three LVET measures, resorting on the analysis and extraction of characteristic points from of the 1st to 3rd PPG derivatives.

In the present study a novel approach combining the segmentation and modeling of the PPG systolic and diastolic components is proposed to accurately estimate LVET. Our methodology resorts on the segmentation of the PPG beat waveform into systolic and diastolic phases and consequent modeling of the segmented phases into a sum of Gaussian functions. The assessment of the left ventricular ejection onset and offset is performed based on the 3rd derivative analysis of the systolic model rather than the whole PPG beat.

The remainder of the paper is organized as follows. In section II the data collection protocol is described. The proposed methodology for LVET assessment is presented in section III. The main results are presented and discussed in

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R. Couceiro, P. Carvalho, R. P. Paiva and J. Henriques are with the University of Coimbra, Department of Informatics Engineering, Science and Technology Faculty of the University of Coimbra, Pólo II, Coimbra, Portugal (e-mail: {rcouceir, carvalho, ruipedro, jh}@dei.uc.pt).

M. Antunes is with the Centro de Cirurgia Cardio-Torácica of the Hospital da Universidade de Coimbra, Coimbra, Portugal.

I. Quintal is with the Echocardiography Department of the Centro Hospitalar de Coimbra, Coimbra, Portugal (email: isabelquintal@chc.minsaude.pt).

J. Muehlsteff is with Philips Research Laboratories Europe, Eindhoven, Netherlands, (e-mail: {Jens.Muehlsteff}@philips.com).

section IV. Finally, in section V the main conclusions are presented.

II. Data Collection Protocol

To evaluate the performance of the developed algorithms, a data collection study was conducted at the "Centro Hospitalar de Coimbra" aiming at the simultaneous collection of PPG and echocardiography (ECHO). An ECG signal acquired simultaneously with the above mentioned signals was adopted as the reference for the co-registration procedure.

The data collected in the present study has been obtained from two distinct groups: one containing 33 healthy subjects and another with 35 subjects suffering from various cardiovascular diseases (CVDs), such as hypertension, acute infarction, heart failure and coronary artery disease. The population was not balanced for gender (51 male and 17 female). The biometric characteristics of the population are (mean ± std):

- Age: 29,72 ± 8,54 (Healthy subjects) and 58,97 ± 17,22 (CVD subjects) years
- BMI: 24,48 ± 2,41 (Healthy subjects) and 25,38 ± 3,10 (CVD subjects) Kg/m2

The measurement protocol was conducted by an authorized medical specialist and consisted of several acquisitions of echocardiography in Doppler mode and PPG collected at the right hand index finger. The echo-annotations of the opening and closing instants of the aortic valve were performed by an experienced clinical expert. In summary, the LVET was annotated in 2081 beats: 1109 beats were annotated from data corresponding to healthy subjects and 972 beats corresponding to CVD subjects.

III. Methods

The contour of the PPG is formed as a result of a complex interaction between the left ventricle and the systemic circulation and consists of an early peak created by the ventricular contraction and additional peaks due to pulse reflections with various delays. In healthy individuals, these wave reflections occur in early diastole and a well defined dicrotich notch is usually seen between the first and second peaks. Contrarily, in elder individuals or in individuals with multiple risk factors and/or established cardiovascular disease, in whom the large arteries present accentuated stiffening, the wave reflections may occur in the late systole preventing the distinction between direct and reflected waves.

Aiming at the extraction of pulse parameters from the volume pulse waveform, Rubins et al. [12] described the PPG beat as a combination of four waves: one direct wave and three reflected waves. It was assumed that the direct and the first reflected waves appear in the systolic portion of the PPG beat. However, part of the first reflected wave also contributes to the diastolic portion of the PPG beat. The end-diastolic part of the PPG beat includes an additional peak explained by secondary waves reflected from the periphery.

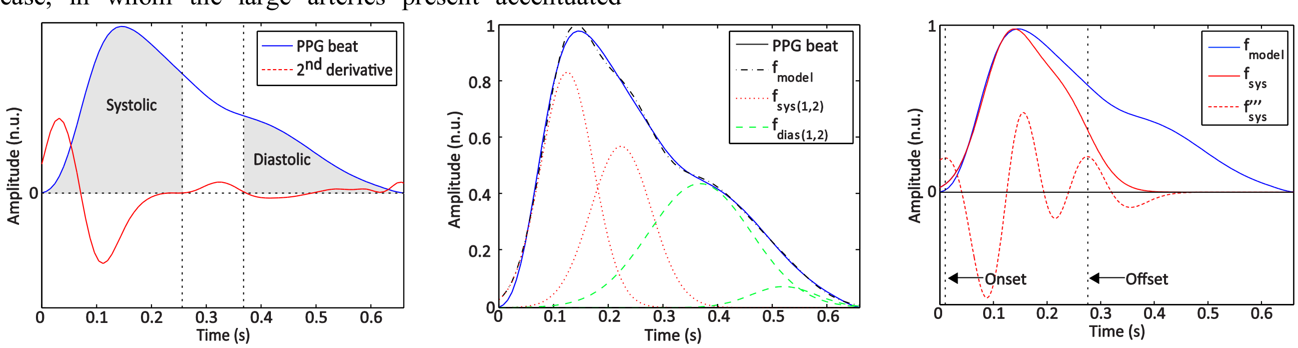
A. Estimation of Left Ventricular Ejection Time (LVET)

The proposed methodology for the LVET estimation consists of four main steps, that are: 1) pre-processing of the PPG signal; 2) segmentation of the PPG signal into PPG beats; 3) modeling of each PPG beat into its systolic and diastolic components 4) estimation of LVET based on a 3rd derivative analysis.

In the pre-processing stage, the high frequency noise (above 18 Hz) is removed from the PPG signal with a Butterworth low-pass filter. Additionally, the PPG baseline wander was removed by subtracting a low frequency approximation of the PPG signal based on a 2 second window moving average filtering of the original signal.

In the segmentation step, the PPG signal is firstly differentiated using a five-point digital differentiator, and the derivatives from order 1 to 3 are obtained. To detect the PPG pulses, a histogram based threshold detection algorithm was applied to detect the most significant local maxima of the 1st derivative and the corresponding local minima of the 3rd derivative. The PPG beat onset/offset was defined to be the most relevant peak prior to the detected most relevant valley.

Finally, each PPG beat was separated into two parts: the systolic part from the onset of the PPG beat to the onset of the dicrotich notch (or inflection) and the diastolic part, from the offset of the dicrotich notch to the end of the PPG beat (see Figure 1 a)). The onset and offset of the dicrotich notch was defined as the negative-to-positive and positive-to-negative zero crossings in the interval [0.2;0.4]s. In special cases where the zero-crossings lie outside the aforementioned interval, a combined analysis of the 2nd and 3rd derivative was conducted aiming the selection of the



a) b) c)

Figure 1. a) Separation of the PPG beat based on the detection of the onset and offset of the dicrotich notch (inflection). b) Model of the PPG beat composed by the systolic component f_{sys} and the diastolic component f_{dias}. c) Detection of the onset and offset of the left ventricular ejection time using the third derivative of the systolic model.

most suitable onset/offset characteristic points.

In the modeling stage, the PPG beat was modeled by four Gaussian functions, i.e. two functions representing the systolic phase and another two representing the diastolic phase. The various components of the 4-Gaussian model can be identified in Figure 1 b). The 4-Gaussian model is defined as follows:

$$f_m(t,\beta_j) = \sum_{j=1}^{4} a_j\, e^{\frac{-(t-c_j)^2}{2b_j^{\,2}}}, \qquad for\ \beta_j = \{a,b,c\}_j \tag{1}$$

where the parameters a_j, b_j and c_j correspond to the amplitude, location and length of the Gaussian function j. The adjustment of the model parameters was achieved using the nonlinear least squares algorithm combined with the 'Trust-Region' fitting algorithm [13].

The onset and offset of the systolic ejection were determined using a data driven approach, consisting on the extraction time intervals between several characteristic points (local maxima) from the 1st, 2nd and 3rd derivatives of the systolic model and posterior comparison with the reference LVET extracted from echocardiography. We concluded that the characteristic points that best defined LVET are the first and last most relevant local maxima of the 3rd derivative (see Figure 1 c)). Since the shape volume pulse wave suffers from smoothing when travelling to the peripheral sites, it is not surprising that the chosen offset characteristic point does not correspond to the exact ending of the systolic phase model. This low-pass filtered pulse is a result of cushion action of the proximal aorta and the arterial compliance [14].

IV. RESULTS AND DISCUSSION

This section compares the results achieved by our methodology with the approach proposed by Chan et al. [1]. The estimation performance of both algorithmic approaches is analyzed for the overall dataset, and the two corresponding subsets of "healthy volunteers" and "CVD volunteers".

The estimation errors were calculated by subtracting the measured parameters (x:{x_{COU},x_{CHAN}}) to the reference parameter in ECHO (x_{ECHO}), i.e. $x - x_{ECHO}$. In the presented table, the abbreviation "Error" stands for the error between measured and reference values ($x - x_{ECHO}$.), while "Abs. Error" concerns to the absolute estimation error ($|x - x_{ECHO}|$). The abbreviation "Abs. Error Perc." stands for the

TABLE I. SUMMARY RESULTS FOR LVET ESTIMATION

	Context	Error (msec.) Avg ± std	Abs. Error (msec.) Avg ± std	Abs. Error (%) Avg ± std	P
a)	Global	-3.93±20.48	15.84±13.56	5.64±4.83	0.73*
	Healthy	1.50±16.52	12.90±10.41	4.86±3.92	0.65*
	CVD	-10.44±22.79	19.28±16.02	6.46±5.37	0.78*
b)	Global	18.75 ± 19.78	23.01 ± 14.60	8.19 ± 5.20	0.75*
	Healthy	31.19 ± 12.26	31.03 ± 12.66	11.7 ± 4.61	0.71*
	CVD	6.49 ± 15.93	13.48 ± 10.68	4.52 ± 3.58	0.88*

a) Proposed methodology.
b) Chan et al. [1] methodology.
*Estimated values using Spearman's correlation.

percentage of absolute estimation error, i.e. $|x - x_{ECHO}|/\overline{x_{ECHO}}$. Furthermore, the agreement between x and x_{ECHO} is analysed using the Pearson and Spearman's correlation coefficients (ρ), the Bland-Altman plots (Figure 2), and the Regression plots (Figure 3). Error distributions were tested for gaussianity using the Kolmogorov–Smirnov test. Accordingly, statistical analysis was performed using the paired Student test and the two-sided Wilcoxon signed rank test.

The results achieved by our methodology and the algorithm proposed by [1] are shown in TABLE I a) and b), respectively. The close relationship between $LVET_{ECHO}$ and both $LVET_{COU}$ and $LVET_{CHAN}$ can be verified in the Blant-Altman plots present in Figure 2 and Figure 3.

Comparing both algorithms, one observes that the best estimation performance, in terms of absolute estimation error, was achieved by our algorithm (15.84 ± 13.56 msec. vs 23.01 ± 14.60 msec.). However, results have to be discussed depending on the specific study group. We achieved a significant improvement in LVET estimation with our method for healthy subjects (12.90 ± 10.41 msec.), compared to the algorithm proposed by Chan et al. [1] (31.03 ± 12.66 msec.). In contrast, Chan's method performs better for CVD patients compared to our implementation (13.48 ± 10.68 msec. vs 19.28 ± 16.02). Finally, study group specific correlation coefficients are better in the algorithm of [1] with correlation coefficients above 0.71.

The reason for the underestimation of the $LVET_{COU}$ can be attributed to both physiological and technical reasons. One possible reason is the dependence of the pulse

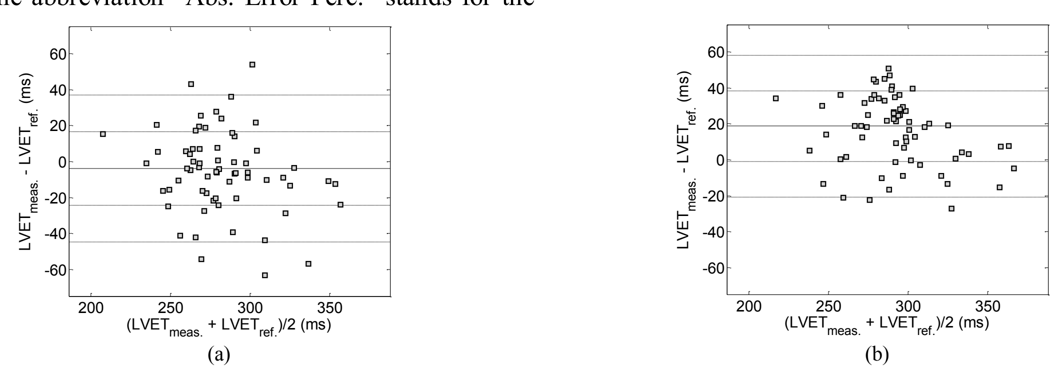


FIGURE 2. The Blant-Altman plot of the measured and reference LVET using (a) the proposed algorithm and (b) the algorithm proposed by Chan et al. [1] (All volunteers). Each point corresponds to an averaged LVET estimate of each volunteer.

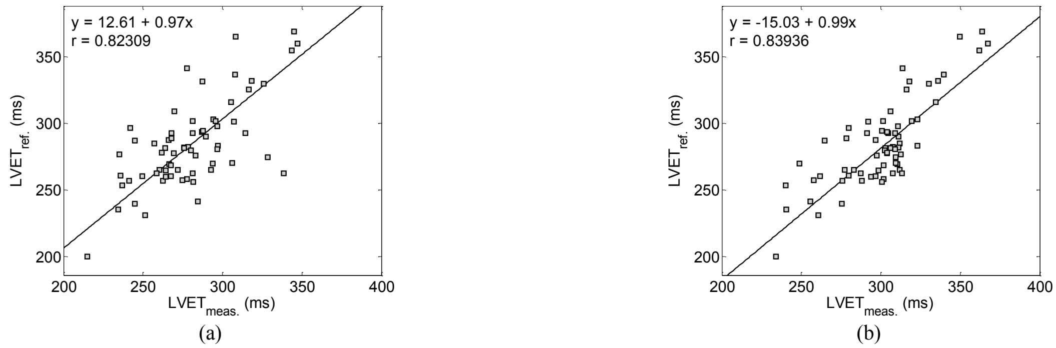


FIGURE 3. The regression plots of the reference LVET against the LVET measured using (a) the current algorithm and (b) the algorithm proposed by Chan et al. [1]. Each point corresponds to an averaged LVET estimate of each volunteer.

transmission time on the intravascular pressure. An increase in the intravascular pressure, which is usually seen in elderly subjects due to arterial stiffening, will lead to a faster transmission of the diastolic waveform, resulting in a reduction of the LVET measured at the finger [1].

Additionally, with the increasing proximity of the diastolic to the systolic waveform, the dicrotich notch becomes attenuated. In individuals with multiple risk factors and/or established cardiovascular disease, the reflected wave arrives so early during systole that it becomes difficult to distinguish the two waveforms [15]. This difficulty gains a special emphasis in the Gaussian modeling problem, where the function parameters, such as amplitude, location and length, are crucial for the construction of a good model that not only fits best to the shape of the PPG waveform, but also truly reflects the physiological and mechanical properties underlying the PPG waveform.

Furthermore, the central volume pulse, i.e. the pulse that arises from the left ventricle, is not symmetric around its peak position like the Gaussian pulse. Thus, it is likely that the peripheral volume pulse consists of a smoothed and asymmetric version of the central volume pulse. Contrarily, in the proposed methodology, we used Gaussian functions to model each PPG beat, which can be a potential source of error in the LVET assessment.

V. Conclusion

In the present study a novel approach for the beat-to-beat assessment of left ventricular ejection time (LVET) from the finger photoplethysmographic (PPG) waveform is presented. The proposed methodology is based on a combination of multi-derivative analysis and Gaussian function modeling. The performance of the proposed algorithm was evaluated and compared with algorithm proposed by Chan et al. [1] on 33 healthy subjects and 35 subjects with various cardiovascular diseases. The overall accuracy and precision of the proposed algorithm was significantly high and globally outperformed the algorithm proposed in [1]. However, a decrease in the performance of the current algorithm was seen for CVD specific context.

Future work will focus on the inclusion of priors in the selection of the model parameters. By conditioning the possible values of the model parameters it should be expected an increase in the accuracy and correlation coefficients of the proposed methodology.

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