Assessing Systolic Time-Intervals from Heart Sound: a Feasibility Study

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Abstract— **Systolic time intervals are highly correlated to fundamental cardiac functions. In this paper we investigate the feasibility of using heart sound (HS) to accurately measure the opening and closing moments of the aortic valve, since these are crucial moments to define the main systolic timings of the heart cycle, i.e. the pre-ejection period (PEP) and the left ventricular ejection time (LVET). We introduce a HS model, which is applied to define several features that can be applied to identify clear markers that define these moments in the HS. Using these features and a comparative analysis with registered echocardiographies from 17 subjects, the results achieved in this study suggest that HS can be used to accurately estimate LVET and PEP.**

I. INTRODUCTION

SINCE Robert Hooke's discovery of the diagnostic potential of heart sound (HS), cardiac auscultation has been a key instrument for non-invasive and low-cost diagnosis. In the last few decades, due to the introduction of new and powerful diagnostic tools such as ultrasound and Doppler imaging, as well as due to the high proficiency required for accurate heart auscultation, heart sound auscultation has been relegated to a minor role in daily acute medical practice. Conversely, developments in digital signal processing and analysis are leading to renewed interest in heart sound. It has emerged as a powerful (easy to use, low intrusive, repeatable and accurate) and inexpensive bio-signal to develop monitoring systems, mainly in the context of chronic disease management, where low-cost and reliable solutions for cardiovascular function assessment are required for long-term patient follow-up.

There are several theories regarding the origin of heart sounds. One of the most accepted theories is the valve theory. In opposition to the cardiohemic theory where HS is attributed to vibration of the entire cardiohemic system (heart cavities, blood and valves), in the valvular theory the first heart sound (S1) is produced by the closure of the mitral and the tricuspid valves, which may not coincide, whereas the second heart sound (S2) is linked to the closure of the aortic and pulmonary valves. In the later, the first component is always the aortic component, which may coincide with the pulmonary valve closure. The first heart sound (S1) is mainly characterized by two well-defined high frequency components. As was pointed out by Lakier *et al.* [1], there is good evidence that the first component of S1 is induced by the (eventually non-simultaneous) closure of the mitral and the tricuspid valves, while regarding the second component, it is suspected to be mainly related to the vibration induced by the aortic valve opening.

The timings between HS's main components, its morphology as well as its spectral content can be applied to directly estimate relevant cardiac parameters [2][12]. Currently it is observed that most computer-aided diagnostic systems based on heart sound focus on the morphology and spectral content analysis of its components. For instance, Teitz *et al.* [3] have introduced algorithms for heart valve dysfunction diagnosis for prosthetic heart valves. Other successful applications of computer-aided heart sound analysis are for the detection of heart failure using the third HS component [4] and the assessment of the Pulmonary-Aortic Pressure [6]. Xiao *et al.* [7] proposed two indicators of cardiac reserve using the analysis of the amplitude of the first heart sound.

Using heart sounds as a reference for systolic and diastolic time intervals measurement is not a new idea. It was a common practice prior to the introduction of ultrasound. The procedure was based on the combination of the carotid pulse (variants exist where other markers for the systolic ejection are applied), the HS and the ECG. By neglecting the time distortion caused by pulse propagation, the carotid pulse wave was analyzed to identify the aortic valve timings and enabled the estimation of the left ventricular ejection time (LVET). The pre-ejection period (PEP) was measured indirectly by subtracting LVET from RS2 [5][12], where RS2 is the time interval from the ECG R-peak to S2.

One aspect that has not been fully explored using HS is the possibility to accurately measure the main cardiac time intervals using this signal without resorting to the carotid pulse. Several studies [9][10] have shown that cardiac systolic and diastolic time intervals are highly correlated to major and fundamental cardiac functions. Of major relevance in assessing cardiac reserve and the left ventricular function are PEP and LVET. By definition, PEP is the time interval between the start of ventricular depolarization and the moment of aortic valve opening (for detection accuracy

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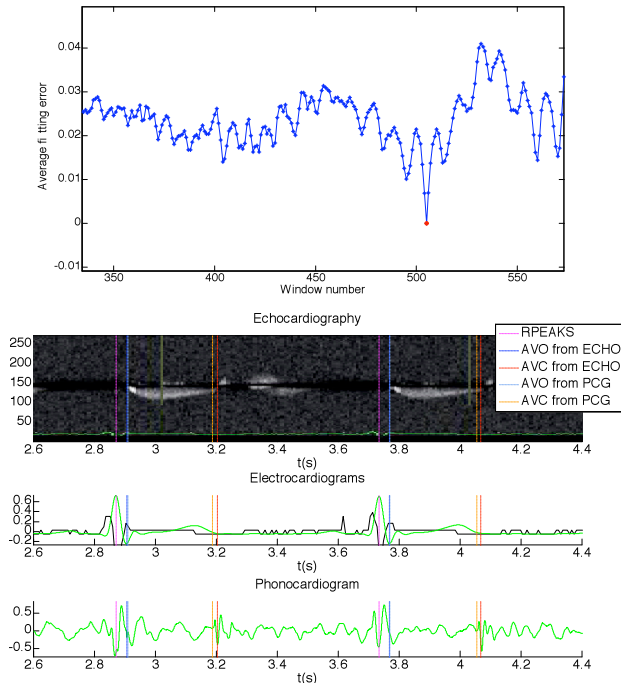
Fig. 1. Data registration. (top) Typical registration error profile using the R-R ECG interval. (bottom) Registration results showing echocardiography (second from top), superimposed ECGs (third from top) and HS.

in this paper PEP is defined as the interval between the R-peak of the ECG and the opening of the aortic valve), whereas the LVET is defined as the time interval of left ventricular ejection, which occurs between the opening of the aortic valve and its subsequent closure. PEP is an index of the left ventricular function and reflects changes in myocardial contractility, left ventricular end-diastolic volume and aortic diastolic pressure. Another important application of PEP is in non-invasive beat-by-beat estimation of blood pressure. A review on the prominent role of PEP in the assessment of BP surrogates can be found in Muehlsteff et al. [11]. The left ventricular ejection period (LVET) can also be related to contractility and to cardiac output [10]. It is by itself a measure of cardiac function [12].

In this paper the goal is to assess the feasibility to accurately extract the systolic time intervals (PEP and LVET) using HS and ECG. The underlying hypothesis is that the first and the second heart sounds encode the movements of the aortic valve and that these components exhibit noticeable and specific signatures that enable their identification using this signal. The interested reader is referred to [15] where we introduce an algorithm to identify PEP and LVET from HS.

In section II the experimental design of the study and the data analysis procedure are described. In section III the main results are presented and discussed. Finally, in section IV the main conclusions are presented.

II. FEASIBILITY STUDY

As already mentioned, the primary goal of the study is to evaluate the feasibility in using heart sounds to determine the opening and the closing of the aortic valve, in order to define the main systolic time intervals, i.e. PEP and LVET. Heart valve movements are not instantaneous, but rather transitory processes that have their intrinsic dynamic. Due to this reason, PEP as well as LVET definitions do not have precise measurement points. This may induce considerable variations / imprecisions between different measurement techniques in assessing many PEP and LVET related parameters. Therefore, a secondary goal of this study is the assessment of the accuracy in using heart sounds to measure the start time of both processes of aortic valve movement, i.e. opening and closing. This is particularly important, since the uncertainty underlying PEP and LVET measurements is also common to other measurement principles such as impedance cardiography (ICG), one of the reference methods for portable devices in measuring these parameters. As was stated by Ermishkin et al. [13], compared to the PEP and LVET values extracted using the Gold Standard method – the echocardiography, PEP values extracted from the ICG using a visual inspection method for B-point determination based upon the dZ/dt is delayed by 3-20ms relative to the onset of blood flow in the left ventricular trace.

A. Experimental Setup

17 volunteer students at the Centro Hospitalar de Coimbra have been asked to participate in the data collection study aimed at the simultaneous collection of heart sounds (HS) and echocardiography (echo). A synchronous ECG with each of the above signals was also acquired and served as a reference signal for co-registration. The population was not balanced for gender (14 male and 3 female). All persons involved in this study did not have any known congenital or other heart disease. The biometric characteristics of the population were:

- Age: 22.53 ±3.81 years
- BMI: 23.27 ± 2.15 Kg/m^2

The measurement protocol was conducted by an authorized medical specialist and consisted of several acquisitions of echocardiography in different modes (Doppler and M-mode) and heart sound collection sites (LSB – left sternum border, and apex). More precisely the following steps were observed:

- The patient was in supine position, turned left (approximately 45º) – the usual echo observation position for the aortic valve.
- The echo device was configured for M-mode and the stethoscope was positioned in the Apex region.
- Runs of 8 sec. data acquisitions of HS, Echo and ECG were performed repeatedly.
- The echo was configured for Doppler-mode and the stethoscope was positioned in the LSB region.
- Runs of 8 sec. data acquisitions of HS, Echo and ECG were performed repeatedly.

The following signals have been acquired:
- Echocardiography and ECG using a Siemens Acuson CV70 device. This device produces a DICOM output
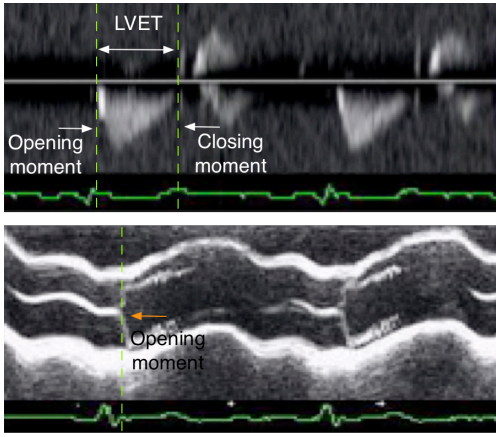
Fig. 2. Annotation of aortic valve timings using two different modes of echocardiography. (top) Doppler mode echocardiography. (bottom) M-mode echocardiography.

with images of time resolution equivalent to 272 Hz. The echo DICOM SOP (Service Object Pair) does not allow for simultaneous recording of time-series and images. Therefore, the echo ECG was recorded as part of the image at 272 Hz. (see fig. 2)

- Heart Sounds and ECG: a Meditron Stethoscope and Analyzer were applied to record HS and ECG at 44.1 kHz. The bandwidth of the HS sensor is 20 kHz.

B. Data Analysis

As already mentioned, the data streams originating from the HS and the Echocardiography were synchronized using the simultaneously acquired ECG signals. The algorithm applied for data registration using the ECG signals is based on the analysis of the ECG's R-R interval matching least square error minimization. Let $R_1(k)$, $k=1,…,n$, and $R_2(w)$, $w=1,…,m$ ($n<m$) be the R-R intervals of the ECGs to be registered. The registration instant t is obtained from:

$$t = \underset{w=1,…,m-n}{\arg\min}\left\{\frac{1}{n}\sum_{k=1}^{n}\left(R_1(k)-R_2(w+k)\right)^2\right\} \quad (1)$$

A typical fitting error profile and HS-echo registration result is shown on top of fig. 1.

The data provided by the Echo device required some post-processing in order to extract the ECG from the DICOM image and to compose a linear image from the circular 3sec. image buffer shown on-screen and saved by the device to DICOM using M-JPEG type video coding.

The annotations of the opening and closing instants of the aortic valve using the echocardiographies were performed under the supervision of an experienced clinical expert in echocardiography. In the M-mode echocardiographies it is observed that the closing of the aortic valve is not always identifiable. In these situations only the opening of the aortic valve was annotated. For this mode, the opening of the aortic valve was annotated at the start of the dynamic opening process, i.e. when the aortic valve leaflets start the opening movement (see fig. 2). Regarding the Doppler mode echocardiographies, the opening instant of the aortic valve was annotated as the onset of the ejection lobe of the left
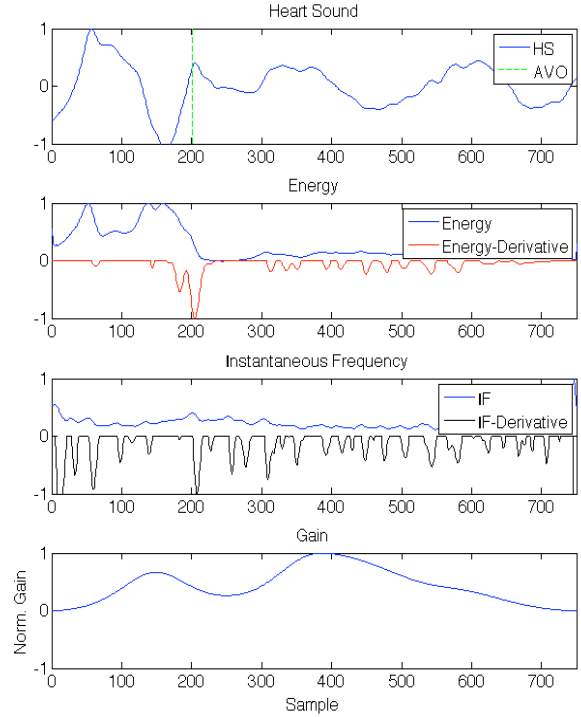

Fig. 3. Features extracted and applied to visually annotate the onset of the opening of the aortic valve (all values are normalized; derivatives are clipped to negative values).

ventricle, while the closing point was defined immediately before the onset of the closing click produced by the residual reflux after the aortic valve cusps have closed, as can be observed in fig. 2. It should be noted that this click corresponds to the end of the dynamic process related to the closing of the valve cusps.

The annotations of the heart sounds were carried out by one of the team members. This has been performed without echo reference, i.e. only the HS and ECG signals as well as features extracted from the HS were shown during annotation. Regarding S1 annotation, it is assumed that it is mainly characterized by two well-defined high frequency components: the working hypothesis in this study is that the first of these components corresponds to the closing of the mitral and (eventually non-simultaneous) the tricuspid valves; the second one is induced by the opening of the aortic valve. Both components are assumed to follow a signal model described by amplitude modulated chirp signals. It is also assumed that both components only marginally overlap in time. From the above, we assume that the first heart sound is modeled by eq. (2), where $A_i(t)$ is the non-linear time dependant gain and $\varphi_i(t)$ represents the time dependent instantaneous frequency of the signal component.

$$s(t) = \sum_{i=1}^{2} A_i(t)\sin\left(\varphi_i(t)\right), \ A_i(t) \geq 0 \quad (2)$$

Signal	Average±SD	Range
Echo	54.04±18.22	[22.06, 109.97]
HS	52.82±17.13	[27.77, 106.58]
Error*	5.81±4.91	-

* $|PEP_{HS}-PEP_{Echo}|$.

TABLE II
LVET IDENTIFICATION RESULTS

Signal	Average±SD	Range
Echo	266.01±27.67	[180.54, 328.95]
HS	255.13±25.41	[176.85, 326.05]
Error**	14.76±10.94	-

** $|LVET_{HS}-LVET_{Echo}|$.

TABLE III
AVC IDENTIFICATION RESULTS

Signal	Average±SD	Range
Echo	320.05±26.46	[222.63, 386.76]
HS	307.95±22.84	[250.49, 362.98]
Error§	-15.48±11.06	-

§ $AVC_{HS}-AVC_{Echo}$, where AVC stands for Aortic Valve Closure

Furthermore, it is assumed that $A_i(t)$ is a smooth function, i.e. with much lower frequency content compared to $\varphi_i(t)$. Since on the one hand the instantaneous frequency of the vibration induced during valve membrane movement is a function of the pressure across the valves [14] and, on the other hand, the pressure differences that govern the movements of the mitral and the aortic valves tend to be significantly different, given the marginal overlap of both signal components, a noticeable variation in (*i*) instantaneous frequency and (*ii*) energy is expected in the signal. These are the main features applied for the detection of the opening of the aortic valve in S1. The instantaneous energy and frequency are computed using the Wigner-Ville transform and the non-linear gain is obtained using a combined homomorphic and low-pass filtering approach. In fig. 3 these features are shown for one S1 sound. As can be observed there are significant changes in the instantaneous frequency and power of the signal that enable the detection of the onset of the aortic valve opening. An algorithm based on some of these features is introduced in [15]. To detect the closing of the aortic valve, the high frequency signature developed in [8] is applied as a reference.

III. RESULTS

The main results obtained in this study are summarized in tables I, II and III. The achieved results suggest that it is possible to accurately identify the systolic time intervals using HS. As can be observed in fig. 4, both PEP as well as LVET obtained from HS closely follow with high correlation the beat-by-beat values identified for these intervals using the echocardiography. Namely, it is observed that the correlation between the PEPs measured using
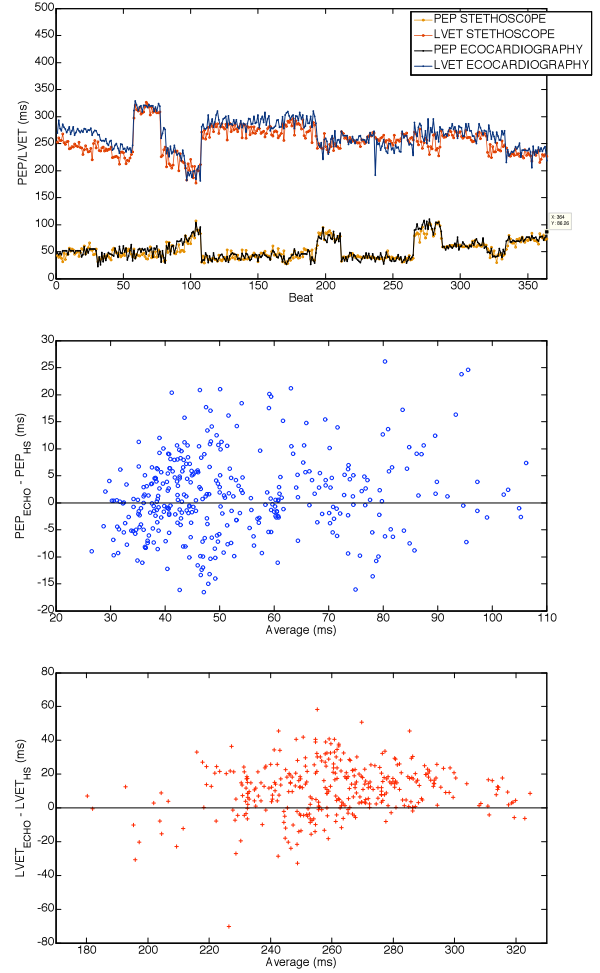

Fig. 4. Observed PEP and LVET values using heart sound and echocardiography for 17 subjects. (top) beat-by-beat values. (middle) PEP estimation difference dispersion as a function of the beat-by-beat $(PEP_{HS}+PEP_{Echo})/2$. (bottom) LVET error dispersion as a function of the beat-by-beat $(LVET_{HS}+LVET_{Echo})/2$.

echocardiography and HS is 0.91 ($p<0.0001$). On average, it is seen that using HS the opening of the aortic valve is detected before (see fig. 4 middle) it is observed in the echocardiography. The average bias is of the same order as the time resolution of the echo ($\approx 3.7ms$). It should be noticed that in both measurement scenarios the observed PEPs are lower than those that are usually reported in literature for similar populations. This is linked to the fact that PEP is usually defined as the time interval between the Q-peak of the ECG to the onset of the opening of the aortic valve, while in this paper we have used the R-peak as the reference ECG point.

Regarding the measured LVET beat-by-beat series extracted from the echocardiographies and HS, it is observed that the correlation coefficient is 0.84 ($p<0.0001$), which is slightly lower compared to PEP. On the other hand, the average delay observed is significantly higher than the echo's time resolution. Namely, it is observed that on average the onset of the aortic valve cusps closing

movement is detected 15.48*ms* earlier compared to echocardiography (see table III). This can be attributed to the fact that HS enables the detection of the onset of the aortic valve closing process, while echocardiography enables its detection near the closing click induced by the cusps, i.e. at the end of the dynamic process.

As already mentioned, there is ample evidence that ICG does not enable a precise detection of the onset of the aortic valve opening and closing process [13]. During the opening dynamics, the preferred measurement point is the B-point, which, according to Ermishkin [13], introduces a delay of 3-20*ms* relative to the onset of blood flow. The B-point might not be the only factor contributing to the delay. The sensitivity of the ICG to changing impedance induced by the blood flow during the left ventricle ejection might itself be the origin of the delay.

IV. CONCLUSION

We have investigated the possibility of using heart sounds to accurately measure the main systolic heart time intervals, i.e. the pre-ejection period and the left ventricle ejection time. The working hypothesis was that heart sounds encode clear makers that enable the detection of the opening and the closing of the aortic valve. To evaluate this hypothesis we have conducted a comparative echocardiography-heart sound study on 17 healthy subjects. A heart sound model for the first heart sound was introduced and several features were defined in order to enable the definition of clear markers in the heart sound signal to identify the aortic valve components of the S1 and S2 (the reader is referred to [15] for an algorithm that uses some of these features to automatically measure the systolic time intervals from heart sounds). The achieved results strongly support the view that heart sound can be applied to detect the onset of the aortic valve movement processes. This seems to be a significant result, since other competing approaches for LVET and PEP measurement (e.g. the ICG approach) tend to exhibit biases in determine these moment estimations, leading to possible inaccuracies in cardiac function assessment.

It should be noted that the dataset was collected from a population that is not the typical population with coronary heart diseases (both due to the average age as well as BMI). Hence, it is acknowledged that the study should be pursued with new measurements of patients from the typical target population for heart disease management. This will also enable to extend the available database of HS and Echocardiography with synchronized ICG signals in order to compare more accurately the two measurement principles.

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