31st Annual International Conference of the IEEE EMBS
Minneapolis, Minnesota, USA, September 2-6, 2009

Heart Sounds Based Measures of Cardiac Status for Heart Failure Patient Management

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Abstract— Heart sounds based measurements such as S3 amplitude and systolic timing intervals (STIs) are known to be indicative of cardiac dysfunction. In this paper we investigate the correlation of these measurements from pacemaker device implant locations to echocardiographic hemodynamic metrics of E wave deceleration time (EDT), Ejection Fraction (EF) and Stroke Volume (SV). Simultaneous heart sounds and echocardiography measurements were made in 6 heart failure patients with cardiac resynchronization therapy (CRT) devices prior to CRT activation (baseline) and at 3 and 6 months post-CRT. In N=17 datasets, S3 amplitude was correlated to EDT (r=-0.86, p<0.05). Similarly STIs such as heart sounds based pre-ejection period (HSPEP) was correlated with EF (r = -0.81, p<0.01) and ejection time (HSET) with SV (r = 0.65, p=0.01). Longitudinal analysis in each patient showed consistent changes between % increase in S3 vs. % decrease in EDT (r= -0.83, p<0.01), % change in HSPEP vs. % change in EF (r= -0.80, p=0.03) and % change in SV (r= -0.72, p< 0.01). These results show proof of concept for using pacemaker derived measurements for monitoring HF patients. Further study is needed to determine their efficacy for chronic monitoring of HF patients.

I. INTRODUCTION

Remote monitoring of heart failure (HF) patients has gained increased attention due to its potential to reduce patient hospitalization and slow escalating healthcare costs [1, 2]. The traditional approach of periodic patient follow-up using clinic visits falls short because the patient's HF status can deteriorate in the interval between visits and lead to patient hospitalization. A potential solution to this problem is ambulatory patient monitoring using wearable or implanted sensor technology. Implanted sensors particularly those in cardiac rhythm management devices (such as implantable cardiac defibrillators, ICD, and cardiac resynchronization therapy devices, CRT) could be used for HF patient monitoring and alert clinicians to an impending hospitalization due to worsening (decompensated) HF.

This paper focuses on a novel application of sensors in ICD/CRT devices to monitor heart sounds and cardiac systolic timing intervals (STIs). The four heart sounds (S1, S2, S3, and S4) are vibrations generated by the rapid acceleration or deceleration of blood in the cardiovascular system. We have previously shown that heart sounds, in particular the S3, can be measured using an accelerometer embedded within an ICD [3, 4]. S3 is a vibration generated by abrupt early diastolic filling of the left ventricle (LV). LV diastolic function is normally assessed through echocardiographic measurements of early filling velocity (E-wave), its deceleration time (EDT) and the atrial component of LV filling (A-wave) [4]. In HF, a prominent S3 is a specific sign of elevated filling pressure and suggestive of a restrictive filling pattern and a steep E wave [5]. Since heart sounds are traditionally measured at the cardiac apex, we sought to evaluate the relationship between S3 amplitude, measured at CRT implant locations, and hemodynamic parameters of early filling, specifically the EDT measured using echocardiography. Additionally we also studied changes in S3 and echocardiography parameters at 3 and 6 months post-implant to assess the feasibility of monitoring heart sounds longitudinally from an implanted CRT device.

In addition to heart sounds amplitude, STIs such as Left Ventricular Ejection Time (LVET) and Pre-Ejection Period (PEP), were used prior to the advent of echocardiography to diagnose patients with compromised left ventricular function [6]. STIs have been shown to be correlated with stroke volume and cardiac output [7]. Traditionally, STIs were measured using a time-aligned combination of the carotid pulse, phonocardiogram, and ECG**.** Since our interest is in chronic implanted device measurements of STIs from heart sounds and electrograms, we sought to understand how STIs measured without the aid of a carotid pulse from heart sounds recorded at an implanted device location are correlated to ejection fraction (EF) and stroke volume (SV).

II. DATA

A. *Clinical Study and Data Description*

This clinical study was a single-center feasibility study to longitudinally evaluate heart sounds in patients with implanted CRT devices. Six patients were studied as part of the larger Device Evaluation of Contak Renewal 2 and Easytrak 2 (DECREASE-HF) trial during 3 scheduled follow-up echocardiography exams (baseline, 3 month and 6 month), to yield a total of N=17 datasets. One patient did not return for a 6 month follow-up. A lightweight accelerometer was taped onto the skin surface centered over the implanted CRT device. Echocardiography measurements were

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978-1-4244-3296-7/09/$25.00 ©2009 IEEE

recorded simultaneously with at least 2 minutes of heart sounds data at a sampling rate of 1000 Hz with the patient in a recumbent posture. A surface ECG common to both the echocardiogram and heart sounds was used to time-align the heart sounds waveforms with the LV filling velocity profiles. Algorithms described in Section III. A. were used to measure heart sound based parameters and statistical comparisons described in Section III. B. were used to compare the heart sounds parameters to echocardiographic gold standards.

B. Demographics

The mean age of patients enrolled in the study was 63 years with 4 of 6 being male. Table shows the New York Heart Association (NYHA) heart failure classification at baseline and 6 month follow-ups along with other metrics of patient status such as total body maximum oxygen consumption (VO_{2max}), the Minnesota Living with Heart Failure (MNLWHF) questionnaire score, and LV end systolic volume (LVESV). Patients showed a trend towards improvement in their cardiac status over the course of 6 months. The increase in ejection fractions (EF) showed a clear sign of systolic function improvement.

PT #	NYHA		Vo2max		MNLWHF score		EF		LVESV	
	BL	6-mo	BL	6-mo	BL	6-mo	BL	6-mo	BL	6-mo
1	3	2	8.8	7.5	43	19	19	23	210	176
2	3	1	14.8	17.6	66	12	20	24	344	347
3	3	1	18.0	17.4	77	22	22	34	177	139
4	3	2	13.6		33	40	41	42	112	119
5	2	2			91	9	21	34	147	119
6	2	2	19.2	20.2	56	24	36		66	

Table 1: Subset of the clinical parameters showing improvement in cardiac function over 6 months (BL: baseline).

III. METHODS

A. Algorithm and Measurements

The heart sounds recordings were analyzed using automated algorithms in Matlab®. Figure 1 shows the various steps involved in measuring the heart sound parameters based on a dynamic programming tracking algorithm which is described in detail in [8]. Raw heart sounds recorded using the accelerometer was parsed into individual beats using the ECG Q wave marker. A set of 12 parsed beats was used to generate an average waveform that was then used to make appropriate measurements.

These averaged waveforms were then filtered using appropriate filters to extract the heart sound components of interest. Since the diastolic and systolic heart sounds have different frequency characteristics they were filtered using different filters. For the S1 and S2 a wavelet filter was used. For the S3 a simple bandpass filter was used.

S3 measurements: The S3 measurements were made using the tracking algorithm after filtering the raw waveforms using a bandpass filter with cutoff frequencies at 10 Hz and 60 Hz.

S1 and S2 measurements: Since the S1 and S2 have multiple subcomponents, accurate STI measurements require the separate measurement of timing and amplitudes of the appropriate subcomponent. The S1 is known to be composed of the mitral and aortic components with the mitral component preceding the aortic. Also, the S2 is known to be composed of aortic and pulmonary components. Since we are interested in the LVET and PEP, which are marked by aortic valve opening and closure, we use wavelet filtering, described in Section III. B. to extract the aortic components in both S1 and S2.

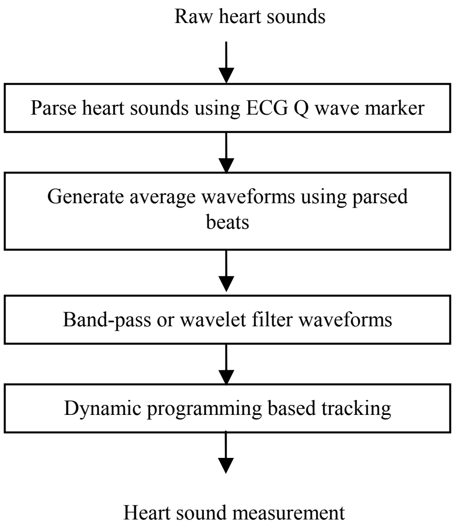

Figure 1: The heart sound detection and tracking algorithm showing the various steps for tracking.

After the waveforms were filtered, windows were setup based on heuristic rules to detect the possible peak candidates for the particular heart sound of interest. While our discussion and Figure 1 depicts S2 detection as an example; in general it applies to any heart sound peak that needs to be measured. The candidate peaks, for each component, were then converted into states by assigning appropriate local scores to them based on the amplitude of the peaks. These states form the basis for the dynamic programming based tracking algorithm as described in [8] which aims to measure the most largest and most consistent peak within each heart sound subcomponent. The heart sound track obtained from the tracking algorithm was next used for statistical comparisons with echocardiography based gold standard data. The HSET was calculated as the time interval between the aortic components of S2 and S1. HSPEP was calculated as the time interval between S1 and the ECG Q wave marker.

B. *Wavelet Filtering*

A continuous wavelet transform (CWT) is used to generate the frequency subbands of each averaged waveform at scales 1 through 64. Figure 2 Panel A shows an example average waveform. Panel B is the CWT of the waveform using a ‘db10’ wavelet. Since we know that the S1 and S2 components have most of their energy in the frequencies between the 30 to 90 Hz, an average of the subbands belonging to those frequencies is generated (Panel C). This process is repeated for all the average waveforms, as part of the wavelet filtering, before the tracking algorithm is applied.

C. *Statistical Analysis*

The S3 amplitude, HSPEP and HSET measured using algorithms in Section III. A. were compared with echocardiography parameters. The S3 amplitude was first (?) normalized by the total signal energy to compensate for variations in acoustic coupling across patients and then averaged over the duration of the echocardiography measurements. Statistical analysis involved correlation analysis of the three heart sound parameters to echocardiography based EDT, SV and EF. Multiple measurements from each patient were assumed to be independent for the purposes of these calculations.

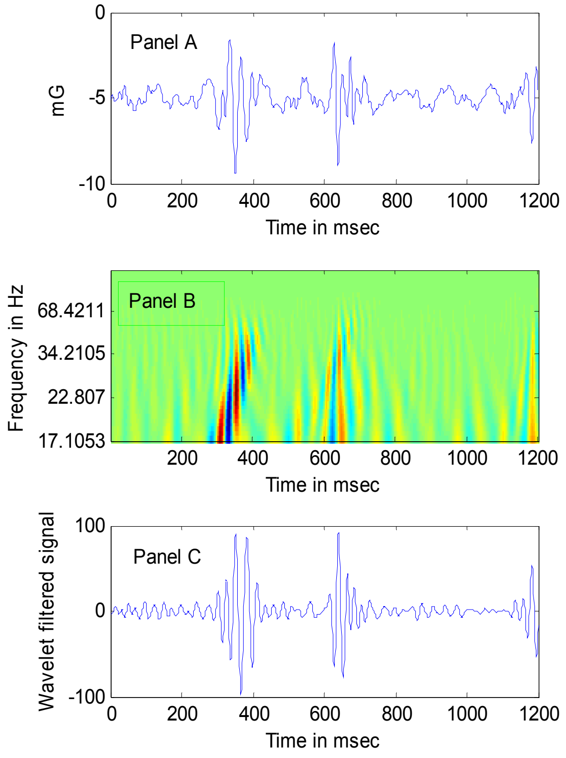

Figure 2: Example wavelet filtering for one waveform.

IV. RESULTS

A. *Third Heart Sound*

On average the time of detected S3 coincided with the time of E-max (mean and stdev of differences = -1.6 ± 46.5 msec.). S3 followed the S2 by 146 ± 27 msec. The normalized S3 amplitude was correlated with the EDT with an R = 0.86 ($p<0.001$) (Figure 3).

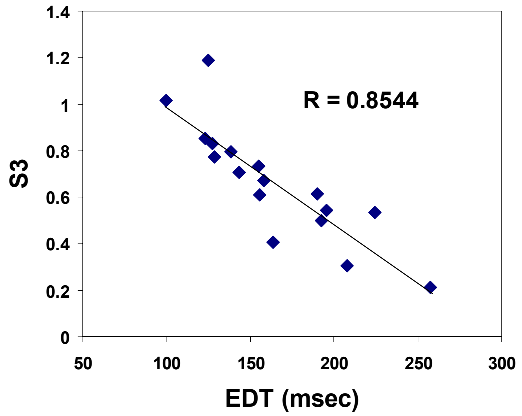

Figure 3: Scatterplot between S3 amplitude and EDT

Larger S3 amplitudes corresponded to shorter EDTs and vice versa. Figure 4 shows the % changes in S3 and EDT at 3 and 6 month follow-ups relative to baseline (before CRT therapy was turned on) for each patient. In this study, longitudinal changes in S3 mirrored the changes in filling characteristics described by EDT (R = -0.83, $p<0.01$). In general improved filling in terms of longer EDT corresponded to reductions in S3 amplitudes.

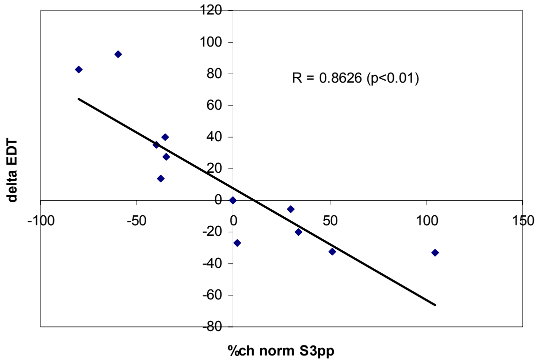

Figure 4: Longitudinal CRT related changes of S3 vs. EDT

B. *Systolic Timing Intervals*

The HSPEP was correlated with EF with an R = 0.80 ($p<0.001$). HSET was found to be correlated with SV with an R = 0.65 ($p<0.001$). These correlations are consistent with previously published relationships between LVET, PEP, SV and EF. Figure 6 shows the % changes in HSPEP and EF at 3 and 6 month follow-ups relative to pre-CRT Baseline for each patient (R = 0.79, $p < 0.01$). These results suggest that both HSPEP and HSET could be used as chronic measures of cardiac systolic performance.

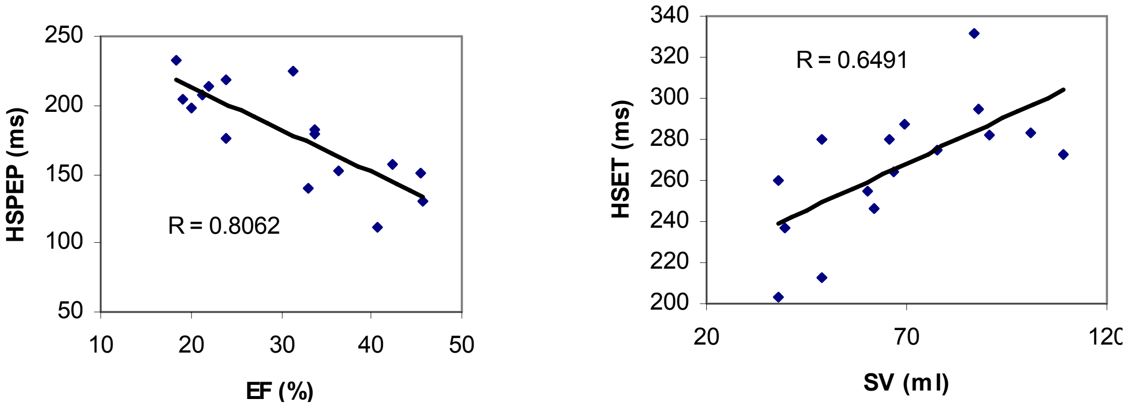

Figure 5: Scatterplots between STIs and echocardiographic gold standards

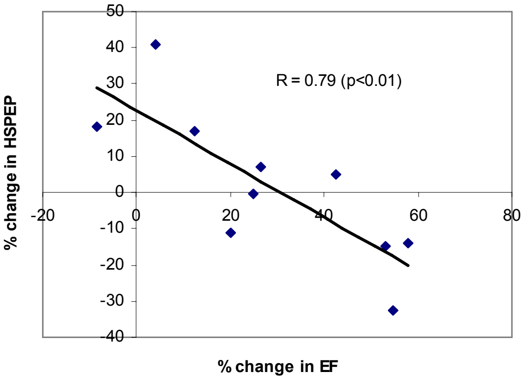

Figure 6: Longitudinal CRT related changes of HSPEP vs. EF

V. DISCUSSION

Traditionally STIs have been measured using a combination of carotid pulse, phonocardiogram and ECG. Additionally both S3 and STIs have been shown to be useful when measured at an apical location. In this paper we have shown that S3 and STIs measured at a CRT device implant location are correlated to well known metrics used to monitor cardiac dysfunction. The STIs are shown to be useful without carotid pulse measurements. Also, these parameters are shown to be correlated to changes in cardiac status measured using echocardiogram at 3 month and 6 month follow-up periods. This is an important result because it demonstrates proof of concept for pectoral measurements of cardiac vibration and timing that could prove to be useful for chronic ambulatory monitoring. The strong correlations in this data set may be attributed to the simultaneous recording of echocardiogram and heart sounds data to eliminate acute hemodynamic variation factors. Signal averaging across a 2-minute period minimizes the effects of marked beat-to-beat amplitude variations in heart sounds. Limitations of this analysis include the small number of patients which limits generalization of these results to all CRT patients. Independence between follow-up measurements was assumed in statistical analysis. Since the reference accelerometer was taped to the skin over the CRT implants, these waveforms were only approximations to the signals expected from a CRT-integrated accelerometer.

VI. CONCLUSION

Despite atypical heart sounds sensor placement at CRT implant locations, in this small sample study, heart sound based parameters were correlated to measures of cardiac status obtained from echocardiographic tests. This analysis supports the feasibility of S3, STI measurements with a sensor integrated into CRT and ICD pulse generators to provide useful hemodynamic information. Further study is needed to evaluate the role of device-based S3 and STIs for ambulatory monitoring and detection of worsening HF and the onset of decompensation.

VII. REFERENCES

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