Effects of Cardiac Resynchronization Therapy on the First Heart Sound Energy

Ask S Jensen¹, Samuel E Schmidt¹, Johannes J Struijk¹, John Hansen¹, Claus Graff¹, Jacob Melgaard¹, Tanveer A Bhuiyan¹, Kasper Emerek², Peter Søgaard²

¹Aalborg University, Aalborg, Denmark
²Aalborg University Hospital, Aalborg, Denmark

Abstract

Introduction: The first heart sound (S1) carries information about ventricular function which may be clinically useful in optimization of cardiac resynchronization therapy (CRT). We developed a method of measuring the effects of CRT on S1 energy.

Methods: For 10 patients with activation induced heart failure (age 64±8.4 years), the heart sound was recorded synchronously with the three lead ECG. Two recordings were made with the pacemaker turned off and on, respectively. An automated method was used for beat segmentation and alignment, and a median ECG beat was calculated. ECG beats were aligned to the median, and heart sound beats were aligned to the ECG. An envelope of the median heart sound was calculated using the absolute Hilbert transform, and the energy of the S1 envelope in a 0.2s interval was calculated. Statistical analysis was carried out using the Wilcoxon signed-rank test.

Results: Activation of the pacemaker resulted in an increase in S1 energy of 419.6±623.4%. This was statistically significant with p<0.01. Out of ten cases, the energy increased by >40% in nine and >74% in eight. In the single remaining case there was a -4.5% reduction.

Conclusion: CRT causes clinically relevant change in S1 energy, and methods of real-time measurement may be useful in CRT optimization.

1. Introduction

Approximately 25% of subjects with heart failure display a widening of the QRS complex, which is associated with dyssynchrony of cardiac electric activity, discoordinate contraction, and a 1.7-fold higher risk of worsened failure and sudden cardiac death [1]. Mechanically dyssynchronous contraction caused by electrical disorder wastes cardiac work and energy and results in reduced stroke volume and cardiac output and increased end-systolic wall stress [2].

A common treatment of cardiac dyssynchrony, which reduces the risk of adverse outcomes in well selected patients, is cardiac resynchronization therapy (CRT) using an implantable pacemaker for biventricular pacing [3]. However, the benefit of CRT treatment varies greatly among patients. Between 25-40% of treated patients see no benefit [2], and the variability in effectiveness is affected by the type of conduction abnormality and mechanical dysynchrony, the location of pacing, and the timing of pacing stimuli. Optimization of ativoventricular and interventricular delays for the individual patient is important as this has significant acute hemodynamics effect and can improve clinical condition and exercise tolerance. [4]

Optimization of CRT requires practical measures of treatment efficacy. Outcomes are strongly related to mechanical dyssynchrony, for which QRS duration is only an indirect indicator [1]. Consequently, the standard method used for optimization is echocardiographic evaluation of cardiac function [4]. However, echocardiography is expensive, time consuming, and highly operator dependent with relatively few clinicians routinely carrying out CRT optimization.

For these reasons, alternative practical measures of mechanical cardiac function in CRT optimization would be welcome.

The first heart sound (S1) arises due to closure of the atrioventricular valves which is a product of ventricular contraction. Consequently, we hypothesized that the S1 signal energy reflects dyssynchrony of the ventricular contraction.

We developed a system for recording and automated analysis of the heart sound in order to measure S1 energy. We used this system to investigate the effects of biventricular pacing in patients with activation induced heart failure. The results show that CRT has substantial acute effect on S1 energy in these patients.

2. Methods and materials

This study included 10 patients (age 64±8.4 years, eight male) with activation induced heart failure already in treatment with CRT.
2.1. Data acquisition

Data acquisition was carried out immediately prior to routine evaluation of CRT efficacy and evaluation of the need for pacemaker reprogramming. The heart sound was recorded using a microphone placed at the left sternal border in the 4th intercostal space, synchronously with the three lead ECG, all at a sample rate of 5000 Hz. With the patient in the supine position, two consecutive recordings of one minute duration or more were obtained with the pacemaker turned on and off respectively. The microphone was attached using an adhesive patch.

2.2. ECG-based segmentation

The heart sound energy was calculated based on the mean of a number of included heart sound beats. The heart sound beats were identified and aligned using the R-peaks in the synchronously recorded ECG signal as follows.

ECG lead I or II was selected for use in the analysis, and 50 Hz power-line noise was removed using a IIR notch zero phase (forward-backward) filter. The mean value of the ECG was subtracted.

An automated algorithm was used to detect if the pacemaker was active. This was done by dividing the signal into segments using two different window lengths and comparing peaks detected in the segmented signals. The longer window was 3 seconds, while the shorter was 0.1 second. In each segment, the maximum of the absolute signal was identified, and the median peak value was calculated for each window length. If the median peak value using the longer window was more than twice the amplitude of the median peak value using the short window, the pacemaker was detected as being active. This identified pacing, as pacing resulted in a relatively large pulse in the ECG with each beat, which was present in every long window segment but only in a small minority of short window segments.

An initial estimate of the RR interval was calculated from the ECG. First, low frequency drift was removed using a Butterworth high pass filter. The autocorrelation function was calculated and the lag between 0.6 and 2.0s which resulted in the maximal autocorrelation was accepted as an estimate of the RR interval.

Local peak values in the ECG were then identified in overlapping signal segments with window duration equal to 120% of the estimated RR interval and moving in steps of 25% of the window length. The ECG signal was bandpass filtered in order to emphasize R waves and decrease T waves using a Butterworth bandpass filter. Duplicate peaks were removed. In order to fine tune the location of identified peaks, the location of each peak was adjusted using a smoothed ECG signal. The peak signal value was identified in a window of 100ms around previous peak location estimates. A final pass was made to ensure that any located peaks with a distance between them too short to be real resting rate RR intervals were removed. Any peaks with extreme amplitude (more than twice the median peak amplitude in the smoothed signal) were also removed.

Finally, the locations of the identified ECG peaks were adjusted by aligning each beat to the median ECG beat. An interval centered on each peak was extracted, and the median signal of these segments was calculated. Each segment was then aligned by calculating the time lag resulting in maximal autocorrelation.

Figure 1. A representative example of the effects of pacing on S1 energy. Top row: Heart sound without and with pacing. Bottom row: heart sound envelope without and with pacing. The gray area indicates the interval of the envelope extracted for calculation of energy.
2.3. Removal of noisy beats

Following beat detection and alignment, beats with either noisy ECG or noisy heart sound recordings were rejected. The ECG beat for each included R wave was extracted using a window of 1s duration with the R peak located at 250ms. The error between each beat and the median beat was calculated as the root of the residual sum of squares. A threshold for beat rejection was set as the 75th percentile error value multiplied by a fixed factor. Beats with an error score above this threshold were rejected, see Figure 2.

![ECG Noise Rejection](image)

![HS Noise Rejection](image)

![Aligned S1](image)

Figure 2. The results of signal alignment and noisy beat removal. A: Histograms indicating distribution of noise calculated for each ECG and HS beat. The dashed lines indicate the rejection threshold. B: S1 of included heart sound beats of a recording following alignment.

Rejection of noisy beats for heart sound followed similar principles but included additional steps. First, an initial rejection of beats with extreme noise was carried out. This could occur if the patient was talking during a segment of the recording. The envelope of the signal was calculated as the absolute value of the Hilbert transform. The integral of each envelope was calculated, and the rejection threshold was set using a similar method as for the ECG.

The median heart sound beat was calculated based on beats extracted in identical intervals to those in the ECG. In each beat, the locations of S1 and S2 were identified using the envelope. The two greatest envelope peaks were identified with a minimal distance of 150ms and not located near the start or end of the beat. These corresponded to S1 and S2 peaks. An interval of 300ms centered on S1 was extracted. Median heart sounds were calculated, and S1 errors between each beat and the median beat were calculated as for the ECG. The rejection threshold was set using a similar method as for the other signals, see Figure 2.

2.4. Data analysis

Analysis of the S1 energy was carried out using a mean heart sound beat calculated from all included beats. An example of the aligned S1 used to calculate the median is shown in Figure 2. The envelope of the mean beat was calculated and the S1 peak located as before. An interval of 200ms centered on the S1 peak was extracted, and the S1 energy was calculated as the sum of squared envelope values within this interval, see Figure 1. The S1 energy change induced by turning on the pacemaker relative to S1 energy without pacing was calculated. As the data were not normally distributed, statistical analysis was carried out using the nonparametric Wilcoxon signed-rank test. A significance level of $\alpha=0.01$ was used.

2.5. Materials

Synchronous data acquisition was carried out using an IX-228 data acquisition unit (Iworx Systems, Dover, NH, USA). The ECG was recorded using standard ECG electrodes, and the heart sound was recorded using a CadScor microphone (Acarix, Kgs. Lyngby, Denmark). The data was recorded using the LabScribe2 (Iworx Systems) acquisition software and exported to MatLab (Mathworks, Natick, MA, USA). All data analysis and statistical testing were carried out in MatLab.

3. Results

The results for relative values of S1 energy change are shown in Figure 3. Following the removal of noisy beats, an average of 132 beats was included in the analysis for each recording (with two recordings for each patient). The mean and standard deviation of S1 energy change induced by turning on the pacemaker was $419.6 \pm 623.4\%$, while the median was 194%. The statistical test indicated that this was strongly significant with $p=0.004$. In nine out of ten cases, turning on the pacemaker resulted in an increase in S1 energy of $>40\%$, and in eight of ten cases the increase was $>74\%$. In one case there was...
4. Discussion

The data acquisition procedures and signal processing methods which were applied resulted in well aligned ECG and heart sound beats. The number of beats included after rejection of noisy beats was sufficiently great to allow reliable and accurate calculation of representative mean beats. Based on representative mean beats, signal features could be calculated.

The results indicate that in patients with activation induced heart failure, ventricular pacing reliably results in an acute and considerable increase in S1 energy. As the S1 sound arises from the closure of the atrioventricular valves, this indicates that the increased S1 energy reflected increased ventricular contractility induced by CRT.

References


Address for correspondence.
Ask Schou Jensen.
Aalborg University
Fredrik Bajers Vej 7
9000 Aalborg, Denmark.
ask@hst.aau.dk.