

# Analysis of Non-Invasively Recorded His-Purkinje Signals from Patients with Myotonic Muscular Dystrophy

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## Abstract

*This study presents several new approaches to analyze the non-invasively recorded His-Purkinje system (HPS) signals from patients with myotonic muscular dystrophy. A high resolution electrocardiogram based on signal averaging to improve the signal-to-noise ratio (SNR) is a well established means to record HPS potentials. These new approaches used methods to temporally and spectrally separate the HPS potentials from the P wave potentials. These included both physiologically based and signal processing based schemes. Separating or shifting the P wave from the HPS potentials using heart rate dependent averaging and the addition of several highpass filtering methods proved somewhat, but not totally successful. In the group of patients with sequential recordings over a period of two years the progression of their muscular dystrophy may also be seen in the heart as well. This may then produce noticeable progressive trends or changes in their HPS waveforms over time. The most noticeable changes found in this study were temporal changes and morphological changes of the HPS activity of these patients over time.*

## 1. Introduction

Methods for noninvasively recording His-Purkinje system (HPS) potentials were developed 30 years ago and were based upon signal averaging to improve the SNR [1-2]. A significant factor limiting the clinical usefulness of this approach has been the temporal overlap of atrial and HPS signals.

This study presents several new approaches to analyze the signal averaged HPS potentials from patients with myotonic muscular dystrophy (MMD). Patients with MMD often have significant cardiac involvement as part of this disease and are now recognized as having high incidences of heart block as well as sudden cardiac death. [3]. By documenting HPS characteristics non-invasively and repeatedly over a period of time it may be possible to identify those characteristics which may predict complete heart block and the subsequent need for pacemaker

therapy. Others have looked at HPS signals in patients with Chagas disease, another progressive disease in the HPS, in an attempt to similarly quantify progression to heart block[4].

The new approaches for HPS enhancement proposed in this study were primarily developed to temporally and spectrally separate the HPS from the P wave potentials. These included both physiologically and signal processing based schemes. Separating the P wave from the HPS potentials was done by using heart rate dependent averaging [5]. The highpass filtering methods used varying filter orders, types, and corner frequencies. One aim of the signal processing techniques was to apply filters and preserve the PR segment authenticity for precise signal measurement in the time domain. This approach required accurate identification of the QRS onset which served as a temporal pivot point to fold or create the mirror image of the PR segment. Hence both forward time and reverse time highpass filters were used enhance the HPS signals.

## 2. Methods

### 2.1 Data collection

The patient data were acquired with a belt-worn, battery operated digital data acquisition system, the Altair 6632. This data acquisition system records three simultaneous channels of high-resolution ambulatory ECGs with a 10 mV peak-to-peak dynamic range and stores the data with 16 bits of amplitude resolution. This system samples each channel at 1000 Hz and has an analog bandwidth between 0.05 and 500 Hz. This high resolution mode collected 20 minutes of data prior to reverting to a lower sampling rate for 24 hours.

Seven standard, disposable ECG electrodes were attached to the patients' upper torso in an anatomically orthogonal configuration. These are bipolar X, Y, and Z leads commonly used in high resolution ECG work.

Data were collected from a 350 patients enrolled in the Arrhythmias in DM1 Study which is a multi-center

registry designed to follow these patients and to determine their arrhythmic outcome. Data were collected from 23 centers from adult patients. The Institutional Review Board at Indiana University and the at each participating site approved the study. An informed consent was obtained from each patient. Data were collected from 350 patients with 68 patients have a second study at one year follow up and 5 patients having a third study at the two year follow up.

## 2.2 Signal averaging and filtering

Standard approaches to signal average the ECG were performed [6] with emphasis on identifying the HPS signals within the PR segment. Figure 1 shows an example of the normal gain XYZ leads in the left panels with the vertical lines delineating the PR segment. The right panels show the same leads after averaging with a noise reduction to less than  $0.3 \mu\text{V}$  [6] and a horizontal scale expansion of 4X and vertical scale expansion of about 40X. The vertical lines delineate the same region of the PR segment.

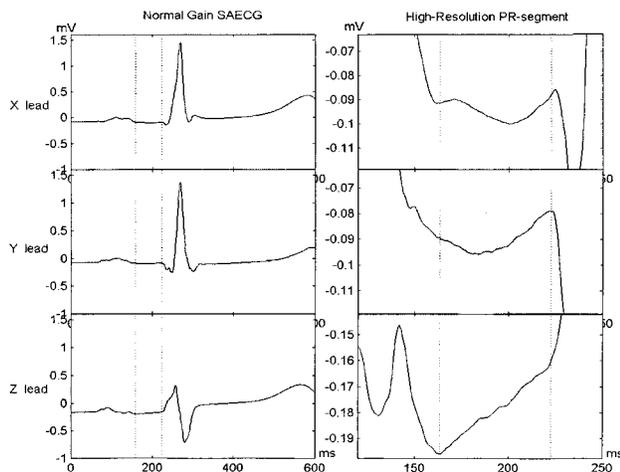


Figure 1. A normal gain ECG of the XYZ leads on the left and a high resolution version of the same signals after signal averaging on the right.

The ramp like feature in PR segment is a typical presentation of the HPS activity[7]. Highpass filtering has usually been applied in an effort to accentuate the higher frequency components and yield a point at which the HPS onset could be determined. This study in its thesis form [8] also examined the role of filter types, filter order, and filter frequency on HPS waveforms in an effort to identify a “best” group of settings. As would be expected there was no optimal group of settings.

## 2.3 Heart rate based signal averaging

One approach for separating the atrial activity from the HPS activity is to average separate ensembles where the preceding RR interval is within two clearly defined ranges. Figures 2 and 3 shows the plot of the RR intervals and its respective histogram in the two top panels. In figure 2 the patient has an almost uniform RR distribution ranging between 500 and 800 ms. There are well over 200 beats in each bin of the histogram. The middle panels show the low resolution and high resolution signal averaged X lead with the RR interval between 550 and 700 ms. The bottom panels show the same set of recordings with the RR interval between 750 and 900 ms. The main difference in Figure 3 is the highpass filtering in the right sided panels and different RR interval ranges.

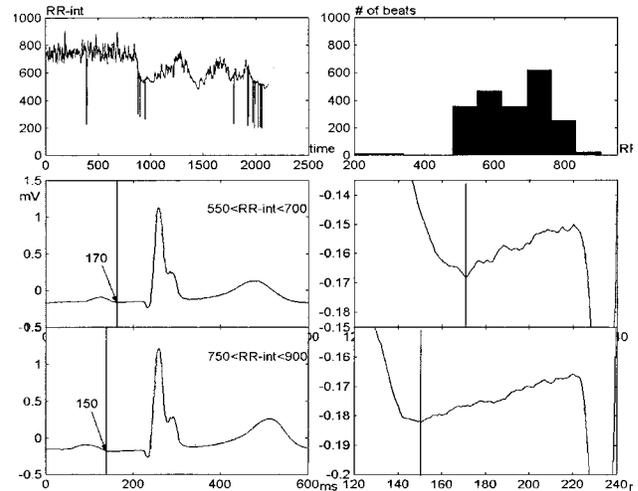


Figure 2. A plot of RR interval versus beat number (left) and the resulting histogram with 100 ms bins (right).

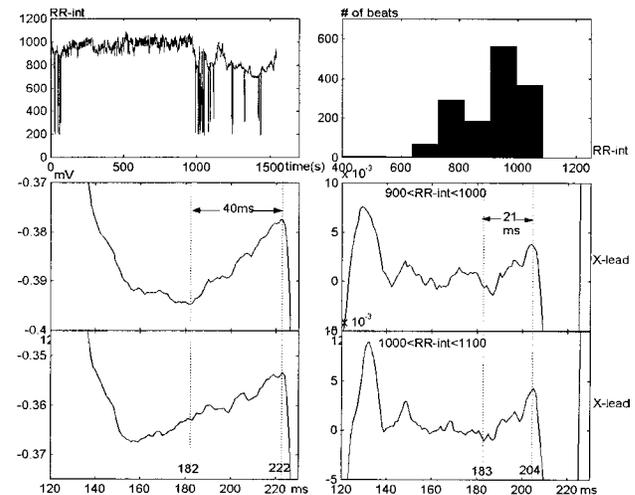


Figure 3. Heart rate dependent averaging. The X leads on the right are highpass filtered.

## 2.4 Fold and filter

Another approach for limiting the overlap of atrial and HPS signals is to minimize the affects of filter phase shifting. The time sense of the digital filter can play an important role in separating a low level signal from an adjacent high amplitude signal. In the case of the HPS signal, the signal of interest is temporally bounded by the P wave and the QRS complex. Hence there would be no advantage in filtering in either the forward time sense (P wave contamination) or the reverse time sense (QRS complex contamination.) Figure 4 shows the unfiltered ECG in the top trace. The middle trace shows P wave contamination in the PR segment when forward time filtering was used. The bottom trace show the QRS complex contamination after reverse time filtering.

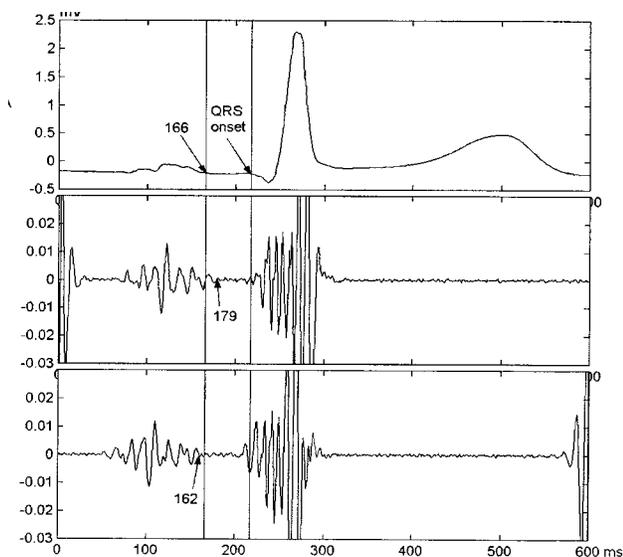


Figure 4. Example of both forward time filtering (middle trace) and reverse time filtering (bottom trace). The PR segment is contaminated by the P wave (middle) and by the QRS complex (bottom).

The solution proposed in this study to limit the effects of these filters was to “fold” the signal around the QRS onset point. This point was chosen since it has not been a difficult point to determine using straightforward slope detection techniques. Once the signal is folded then a reverse time filter is used. This eliminates QRS contamination as well as P wave contamination of the PR segment. Additionally, signal folding limits digital filter artifacts in the PR segment since the spectral components of the folded signal remain constant in frequency. This signal processing sequence is shown in Figure 5. The top trace is the original signal average lead. The second trace is the signal truncated at the QRS onset point. The third trace is the folded signal and the bottom trace is the highpass filtered signal.

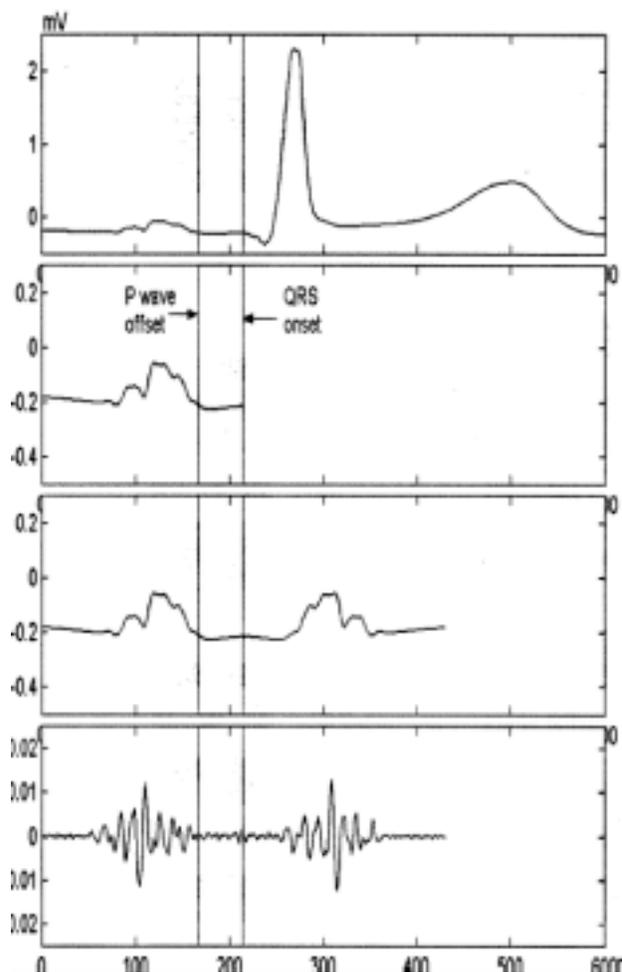


Figure 5. The “folded” and filtered method used to preserve PR segment authenticity.

## 3. Results

In general the data collected from the patients in the first 20 minute high resolution portion of the data record were amenable to signal averaging with approximately 1500 to 2000 beats per record. However, in the case of the heart rate based averaging this short data record proved to be a significant limitation since most of the patients did not exhibit a significant distribution of RR intervals with enough beats for a low noise average.

Another significant aspect of the study when looking for disease progression were the follow-up studies. Unfortunately, at the time of this study only five patients had three follow-up studies in a two year period. Figure 6 demonstrates examples of a temporal change in the HPS waveform over time in the top row of traces. There appears to be a progressive lengthening in the HPS waveform from 21 ms to 31 ms. The bottom row of traces demonstrates a morphological change in the HPS

waveform. The waveform changes from a negative ramp in the first study to an almost isoelectric waveform in the second study to a positive waveform in the third study.

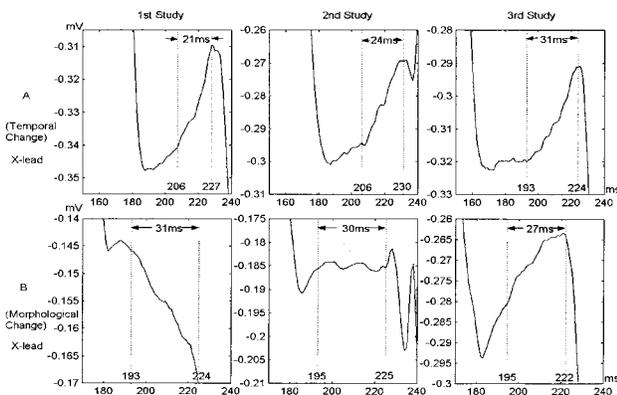


Figure 6. Changes in the HPS waveform from two patients with three studies over a two year period.

#### 4. Conclusions

Re-visiting the recording technology for the HPS signals in the context of progressive muscle disease proved to be valuable in light of the modern technology of continuous digital data acquisition and modern computing tools. The clinical results are incomplete with more effort needed to study and compare the follow up studies. Eventually there will be some clinical end points such as heart block in this group of patients and these data and the new tools used for analysis may provide the necessary insights needed to quantify progression of heart disease in MMD patients.

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