## EFFECTIVENESS OF A HANDHELD REMOTE ECG MONITOR

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## ABSTRACT Swaroop S. Singh: Effectiveness of a Handheld Remote ECG Monitor (Under the direction of Prof. Henry S. Hsiao)

This present study deals with designing a real-time remote handheld ECG monitoring system and evaluating its potential usefulness in early detection of heart conduction problems. The raw ECG recordings were sent by the handheld monitor (client) to a remote server, which performed an on-line ECG analysis and sent the results back to the client. Real-time feedback provided to the client included display of ECG, results of ECG analysis and alarms (if required).

The objective of this work was to determine its effectiveness in real-time identification of particular pattern preceding ventricular fibrillation. The remote server identified the occurrence of QRS complex and premature ventricular contractions and monitored ECG for ventricular tachycardia and variations in heart rate variability indices. The sensitivity and specificity of the QRS detection to ECG recordings from MIT-Arrhythmia database were 99.34% and 99.31%, respectively. Similarly these parameters of the premature ventricular contraction detection were 87.5% and 91.67%, respectively. The time between alarm and the onset of ventricular fibrillation was measured on ECG recordings where premature ventricular contractions were found to lead to ventricular fibrillation. The remote monitor was able to successfully identify the onset on ventricular fibrillation. Early detection could contribute to better response to an emergency intervention.

HRV indices sensitive to the differences between normal and subjects with congestive heart failure were monitored in real-time. They were heart rate, statistical index RMSSD, total spectral power, high frequency power and the ratio of low frequency to high frequency power (LFP:HFP). The effectiveness of HRV indices was tested on an ECG recording of a sleep study subject, who experienced cardiac arrhythmia. Cyclic changes observed in total spectral power prior to onset of cardiac arrhythmia could be attributed to REM sleep cycles. No other conclusive change in HRV indices was observed.

The monitor's usefulness in predicting long-term prognosis of post-MI subjects was tested on ECG recordings from two subjects made immediately after conclusion of cardiac arrhythmia and during a follow-up visit. Both showed higher RMSSD, total spectral power and LFP:HFP ratio. Personalizing the monitor for each patient further improves its accuracy in measurement of various parameters. To my parents and my better half

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## LIST OF ABBREVIATIONS

- CHF Congestive Heart Failure
- ECG-Electrocardiogram
- HRV Heart rate variability
- LF/HF Ratio Low frequency power to high frequency power
- PDA Personal Desktop Assistant (also referred to as handheld device)
- PVC Premature ventricular contraction
- RMSSD Root mean squared sum of differences
- VT Ventricular Tachycardia

#### CHAPTER 1

#### Introduction

A large number of people need immediate attention when they experience lifethreatening ventricular arrhythmia or angina. Most of the sudden deaths are caused by cardiac arrest, usually resulting from ventricular arrhythmia that occurs as a result of myocardial ischemia. Moreover, many studies attest that rapid response times in prehospital period is key in reducing mortality and dramatically improved patient outcomes [1-3].

Electrocardiogram (ECG) is the most important noninvasive diagnostic tool used for assessing the probability of cardiac event, for stratifying its degree (stable, unstable angina, risk of out-hospital or in-hospital death) and for guiding therapy. Early detection of potentially dangerous cardiac arrhythmia could lead to timely intervention. Significant changes have been reported in the analysis of beat-to-beat intervals of heart rate (heart rate variability) in the period immediately preceding ventricular tachyarrhythmia [4-5]. Such patients may benefit from anti-arrhythmic therapy or intervention. Short-term heart rate variability measures are used for initial screening of all survivors after an acute myocardial infarction [6], prediction of outcomes after myocardial infarction [7] and monitoring of patients after medication and exercise. For monitoring purposes, the Holter based equipment requires clinical supervision and provides no real-time feedback for the patient. Wireless devices provide additional mobility but do not provide adequate real-time monitoring. Handheld devices like Personal Digital Assistants (PDAs) are compact and have increasingly powerful computing capability for complex calculations required for this work. The newer models with features like built-in networking and their integration into the cellular phone has provided the remote monitor access to hospital services. When integrated with a remote processing server, the PDA provides an effective and inexpensive method to monitor real time display of cardiac signals for (i) Normal sinus rhythm (ii) Premature ventricular contractions (PVC) (iii) Ventricular tachycardia and (iv) Changes in heart rate variability indices in normal and in patients affected by cardiac conditions.

#### 1.1 Statement of Problem

In early myocardial ischemia, ventricular fibrillation is often preceded by ventricular tachycardia, which eventually gives way to the ventricular fibrillation [8]. Since the onset of ventricular fibrillation is extremely difficult to pinpoint in many cases [9], it would be useful to design a monitor that accurately detects the onset of ventricular tachycardia. Reducing the time from the detection of "warning" signs of ventricular tachycardia to emergency intervention may prove helpful in preventing the onset of ventricular fibrillation and allow for more rapid delivery of lifesaving interventions. Thus, any clinically useful detector should respond to the runs of tachycardia preceding fibrillation. In other words, the system should exhibit a 'negative time to alarm' compared to the onset of ventricular tachycardia and fibrillation.

The primary objective of this dissertation is to design and measure the effectiveness of the handheld remote ECG monitor, which includes a QRS and PVC detection algorithms. The QRS and PVC detection algorithms were validated against a standard annotated database. The effectiveness of the monitor for detecting the onset of life threatening arrhythmia (ventricular fibrillation) was quantified by measuring the 'negative time to onset' of ventricular fibrillation.

The secondary objective is to determine the usefulness of adding HRV measures to real-time remote ECG monitoring. A number of HRV indices were assessed including heart rate, SDNN, RMSSD, Total spectral power, Low-frequency power, High-frequency power and High frequency power to low frequency power ratio. The sensitivity of these indices to differentiate ECG recordings from normal and subjects with congestive heart failure (CHF) was evaluated. The indices identified to be sensitive in differentiating normal from subjects with CHF were used to determine if they predict the onset of chest pain (arrhythmia) in recording of an older subject during sleep

The tertiary goal is to determine the usefulness of the remote monitor in providing long-term prognosis based on HRV changes. HRV indices calculated from ECG recordings of two subjects made after conclusion of cardiac arrhythmia and a follow-up study done a year later were compared. Changes in HRV indices would provide better assessment of cardiac risk.

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## CHAPTER 2

## Background

The heart is a muscular organ responsible for pumping blood through rhythmic contractions. It receives deoxygenated blood from the venous system and after oxygenation in the lungs the blood is sent back into arterial system. These contractions are associated with electrical activity of the heart and can be detected by surface electrodes.

#### 2.1 Electrical activity of the heart

Electrical stimulation of the heart originates at the sino-atrial (SA) node in the upper section of right atrium. Since the atria are insulated from the ventricles, electrical excitation passes only through the atrioventricular (AV) node. Special tissues conduct electrical excitation from the AV node to the ventricles in sequence from Bundle of His to Bundle branches and finally to Purkinje fibers. The various parts of the electrical conduction system of the heart are shown in figure 2.1.



Figure 2.1. Electrical conduction system of the heart.

Cardiac excitation from the body surface, as electrocardiogram (ECG), by attaching the electrodes to the body surface is monitored. The most common configuration for recording is with electrodes connected to both arms and the left leg (Leads I, II, III). A typical ECG record contains P, QRS and T waves. The P wave is caused by depolarization of the atria, the QRS-complex is produced by depolarization (excitation) of the ventricles and the T wave represents the repolarization of the ventricles. Figure 2.2 shows the typical lead II recording of the ECG, which has the same direction as the axis of the normal heart.



Figure 2.2. Normal sinus rhythm recorded on Lead II

#### 2.2 Premature Ventricular Contraction

In addition to SA node, there are other latent pacemakers, which exist throughout the heart. Regular conduction of electrical impulses from SA node and refractory period of cells reject other electrical impulses except those arriving from SA node. In certain cases, the additional pacemakers interpose additional electrical impulses that generate ectopic beats, which due to their different locations lead to varying behavior. Premature ventricular contraction (PVC) is due to an ectopic cardiac pacemaker located in the ventricle. These are characterized by the premature occurrence of bizarre-shaped QRScomplex (typical QRS width > 120 ms). These complexes are not preceded by a P-wave, and the T-wave is usually large and opposite in direction to the major deflection of the QRS (Figure 2.3). The PVCs may appear in a pattern of bigeminy, trigeminy, or quadrigeminy, which describe their pattern, which occurs every other, every third, or every fourth beat, respectively. These patterns with identical morphologies on a tracing are called monomorphic or unifocal.



Figure 2.3. ECG record with premature ventricular contraction

The PVCs reflect the unwanted spontaneous activity of ventricular pacemaker cells. The suggested mechanisms for these are reentry, triggered activity, and enhanced automaticity [1]. Reentry occurs when an area of one-way block in the Purkinje fibers and a second area of slow conduction are present. During ventricular activation, the area of slow conduction activates the blocked part of the system resulting in an extra beat or leading to paroxysmal tachycardia. These beats are considered to be due to after-depolarizations triggered by the preceding action potential. Enhanced automaticity suggests that an ectopic foci of pacemaker cells exists within the ventricle that has a sub-threshold potential for excitation. The basic rhythm of heart raises these cells to threshold, leading to an ectopic beat.

PVC is one of the most common arrhythmias which can occur in patients with or without heart disease. More than 60% of healthy middle-aged men show PVCs on routine Holter monitoring and is increased to more than 80% in patients with prior myocardial infarction (MI). This is attributed to inadequate stroke volume or to decreased cardiac output caused by effectively halving the heart rate. Prolonged occurrence of these may lead to hypotension. Physical exercise can increase or decrease the PVC rate [2] In young healthy patients without underlying structural heart disease these are not associated with any increased rate of mortality. The early occurrence of PVC in the cardiac cycle (R-on-T phenomenon) of frequency more than 10/hour, with multiple ventricular morphologies, are associated with arrhythmic events and increased mortality rates [1].

#### 2.3. QRS Detection

In an arrhythmic monitoring system, a reliable detection algorithm is of prime importance. Missing a life threatening arrhythmia or false-positive detection may lead to improper therapeutic intervention. In addition to reliability, the speed of detection is an important criterion that depends on the amount of data used to detect arrhythmias [3]. The QRS waveform due to its characteristic shape serves as the basis for the automated determination of the heart rate for classification schemes of the cardiac cycle [4]. In QRS detection algorithms, the detection of this complex and the time taken to achieve this are very important. But detection of QRS-complex – specifically the peak of QRS-complex or R wave due to the time-varying morphology, is a difficult problem. In addition, other sources of noise in a clinical environment such as power line interference, muscle contraction noise, poor electrode contact, patient movement and baseline wandering due to respiration may further degrade the ECG signal [5].

Algorithms for QRS detectors are generally divided into three categories: (1) syntactic, (2) non-syntactic and (3) hybrid. The algorithms based on the syntactic approach are time consuming, due to the need for grammar inference for each class of patterns [6]. Non-syntactic QRS detectors share an algorithmic structure (Figure 2.4) that can be divided into preprocessing or feature extraction stage including linear and non-

linear filtering and a decision stage regarding peak detection and decision logic [7-9]. The algorithms differ with respect to the preprocessing stages, as most of the decision stages are dependent on their results [4]. The detectors generally filter the ECG with a bandpass filter (or matched filter) to suppress P- and T- waves and noise. Thereafter the signal is passed through a nonlinear transformation to enhance the QRS-complex. Finally based on decision rules the presence of QRS-complex in the signal is detected.

In contrast non-linear filtering that takes considerably less time and easily implemented, is a common approach to detect QRS-complex. But the main drawback of these algorithms is that the frequency variation in QRS-complex may overlap with the frequency band of noise, resulting finally in false positive and false negative.



Figure 2.4. Common structure for non-syntactic QRS detectors.

Neural network based algorithms have been superior to classical linear approaches but require a large training dataset [10]. An algorithm based on Hidden Markov methods identifies P- and T-waves in addition to QRS-complex, but are computationally complex even with efficient algorithms [11].

Since the frequency characteristics of the ECG constituents are different, frequency domain parameters have been proposed as an alternative to time domain analysis. Loss of clinically important features, such as duration, amplitude and relative position of the three different waves and the transformation of the waveform into the frequency domain, makes it less attractive for acceptance by clinicians. Another shortcoming is the non-stationary signal. Mutually exclusive time and frequency domain representations of these waveforms fail to reveal the non-stationarity behavior accurately. Hence, there is a need for representation of ECG signals in two dimensions with time and frequency as coordinates. Wavelet transform (WT) is a promising technique for timefrequency analysis. By decomposing signals into elementary building blocks that are well localized both in time and frequency, the WT can characterize the regularity of signals, and can further be used to distinguish ECG waves with serious noise, artifacts and baseline drift.

Wavelet analysis of a signal involves breaking up a signal into shifted and scaled versions of a reference (mother) wavelet. In determining the wavelet decomposition coefficients of a signal, the correlation of the mother wavelet at different shifts and scales with the signal is computed. Hence, the wavelet coefficients represent measures of similarity of the local shape of the signal to the mother wavelet under different shifts and scales. Wavelet transform of time signal at any scale is the convolution of the signal with time scaled daughter wavelet. Scaling and translating the mother wavelet is the mechanism by which the transform adapts the spectral and temporal changes in the signal being analyzed.

Biorthogonal wavelets offer temporal symmetry preventing non-linear phase shift of the transformed signal. In the current problem, the shape of the signal in the time domain is important while reconstruction of the signal is not required and this makes the

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choice of biorthogonal wavelets easier [12]. The singularities (peaks) in the ECG correspond to pairs of modulo maxima across several scales in wavelet transform. The QRS points are detected by comparing the coefficients of the discrete wavelet transform on several scales against fixed thresholds [13]. Figure 2.5 illustrates the QRS detection and the dots on the top are identified by the QRS detector.



Figure 2.5. QRS detection using Wavelet Transform.

#### 2.4. Heart Rate Variability

The heart rate variability (HRV) is a marker of the significant relationship between the autonomic nervous system and cardiovascular mortality [14]. The parasympathetic influence on the heart rate is mediated via release of acetylcholine by the vagus nerve. When parasympathetic nerve is activated, slow diastolic depolarization is initiated. The sympathetic influence on the heart rate is mediated by the release of epinephrine and norepinephrine. The end result is an acceleration of the slow diastolic depolarization. Under resting conditions, the vagal tone prevails and variations in the heart rate are largely dependent on vagal modulation [15]. Association of lethal arrhythmias and signs of either increased or decreased vagal activity contribute in the development of quantitative markers of autonomic activity. The clinical importance of HRV became apparent when this was confirmed as a strong and independent predictor of mortality following an acute myocardial infarction.

The HRV time and frequency measures are derived from normal-to-normal intervals (all intervals from adjacent QRS-complex resulting from sinus depolarization). Lowered HRV was found to precede episodes of atrial fibrillation in patients after coronary artery bypass graft operation and with no structural heart disease [16]. Time-variant algorithms when applied to RR interval data a low frequency (LF) component of HRV power spectra, 1.5-2 minutes before the onset of an ischemic episode was found [17]. Correlation dimensional analysis on RR interval predicted the exact time of occurrence of ventricular fibrillation in a retrospective study [18].

The decreased HRV is a powerful risk stratifier for overall mortality, induced and spontaneous ventricular tachycardia and sudden death following acute myocardial infarction (AMI) [19]. Risk of arrhythmic death was found to be associated with lowered HRV and the presence of ventricular arrhythmia [20]. Low frequency HRV measurement predicted in-hospital complications when measured within 2 days after the AMI [21]. Short-term HRV measures are used in prediction of mortality of patients with chronic heart failure [22]. Frequency domain HRV from short-term recordings (2 to 15 minutes) predicted post-infarction mortality and are used for initial screening of all survivors after an acute MI [19]. Such patients may benefit from anti-arrhythmic therapy or intervention.

The identification of the QRS peak is critical for HRV measurements. Since the modulatory signals from the brain to the heart are embedded as variations in the beat-tobeat intervals of the sinus rhythm, a locally generated ectopic beat may temporarily disrupt neuro-cardiac modulation. Preferentially the short-term recordings, free of ectopy, missing data and noise, should be used as these comply better with the theoretical prerequisite of data stationarity.

#### 2.5. Remote Monitoring

The various studies have shown that remote monitoring from pre-hospital setting results in reduced response time and improved patient outcome [23-25]. Remote monitoring of ECG is used to assess the probability of cardiac event, stratify risk and to guide therapy. The primary attributes of remote monitoring systems are [26]: (a) Recording of key information at the point of care, eliminating errors and duplication of effort, and providing completeness of data, (b) Automation of processes and information sharing, (c) Provision for clinical decision support, (d) Ensuring of secure acquisition and storage of patient data, (e) Provide reliable performance, and (f) Assist patients in management of their own health.

There are different approaches which have been used in application of telemedicine. These include: (1) Single condition disease management, e.g. Cardiac emergency response system implemented by SHL Telemedicine in Israel [27] and (2) Focus on local problems (e.g. Remote consultation/monitoring initiatives in sparsely populated areas of Sweden) [28]. The CSIRO project "Hospital without Walls" in Australia, designed to provide remote monitoring of patient heart rate and activity

information [29]. Remote ECG monitoring, performed from a commercial aircraft [30] or an ambulance [31], has also shown promising results.

The ECG signal recording in a non-hospital setting can be classified as short-term or long-term recording. Short-term measurements (5-15 min) are usually carried out at physician's office or at small clinics. Long term measurements (24-96 hours) are usually made at the patient's home by ambulatory monitors (Holter). The disadvantages of the short-term and long-term recordings are the difficulties in the complete diagnosis and in immediate intervention, respectively. These deficiencies sometime may lead to serious conditions. Holters with DSP chips for ECG analysis can detect cardiac events in realtime and send cardiac report to a monitoring station using standard telephone lines [32]. However such monitoring systems are expensive and do not provide any feedback to the patient about his/her medical condition.

The ECG data are usually transmitted by incorporating Transmission Control Protocol/Internet Protocol (TCP/IP). The TCP is chosen due to its permanent connection channels, data packet checking to ensure that all data are transmitted and error checking is within packets for integrity of data [33]. The TCP/IP encapsulated ECG data are sent over public switched telephone network (PSTN) [34], Cellular technologies incorporating global system for mobile communication (GSM) [35] and time division multiple access (TDMA) [36] standards and broadband networks (DSL/Cable) from the remote patient location to the hospital. The PSTN is the most commonly used medium for ECG transmission due to its ubiquitous presence. Monitoring of infants for sudden infant death syndrome (SIDS) was also implemented using TCP encapsulated data packets over the PSTN [37]. However data sent over the PSTN has a high error rate causing frequent delays. Real-time ECG monitoring systems incorporating the GSM data networks [35] have an advantage of being wireless, but its limited bandwidth leads to significant data loss. Remote web servers are also used to store and display real-time ECG data. Java embedded systems (e.g. Dallas Semiconductor Tiny Internet Interface) are cost effective and provide real-time web-based monitoring [38]. However, these systems do not provide any mechanism to analyze ECG data or provide feedback to the patients.

The handheld devices, like personal digital assistants (PDAs), are small, light, and easy to use with powerful computing capabilities. New generation models have features like built-in networking using Wireless LAN, and its integration into the cellular phone and by these the remote monitor could access to hospital services. The PDAs have been used in the medical community to access online medical databases [39], record patient and clinical training data [40] and send ECG data from the ambulance directly to the hospital [41]. The PDA has also been used to monitor the infants' respiratory in real-time [42] However, at present time, these devices do not possess computing capability or the battery life required to perform real-time ECG analysis. Computer based analysis of ECG for detection of cardiac arrhythmias has been used with considerable success. Innovative signal-processing and analysis techniques in small sized hospitals have also been implemented [43]. The various techniques developed for this purpose may need even faster and more powerful PDA's or implementation purposes.

Considering the present needs, the PDA-based remote monitor is designed to record and monitor ECG and provide real-time feedback for effective monitoring of medication and exercise. Further analysis of ECG recordings can be performed in realtime by a remote processing server.

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## CHAPTER 3

### Effectiveness of a Handheld Real Time Remote ECG Monitor

### 3.1. Abstract

A large number of people need immediate attention when they experience lifethreatening ventricular arrhythmias or angina. Rapid response time in pre-hospital setting has been shown to dramatically improve patient outcomes. In early myocardial ischemia ventricular fibrillation is preceded by runs of ventricular tachycardia. A handheld realtime remote ECG monitor to detect QRS and PVCs and monitor ECG for ventricular tachycardia was designed. The raw ECG recordings were sent by the handheld monitor (client) to a remote server, which performed an on-line ECG analysis and sent the results back to the client. Real-time feedback provided to the client included display of ECG, results of ECG analysis and alarms (if required). The sensitivity and specificity of the QRS detection to ECG recordings from subjects from MIT-Arrhythmia database were 99.34% and 99.31%, respectively. Similarly these parameters of the premature ventricular contraction detection were 87.5% and 91.67%, respectively. The effectiveness of the handheld remote ECG monitor in detection of ventricular fibrillation was quantified by measuring the negative time to onset of ventricular fibrillation. Early detection could contribute to better response to an emergency intervention.

### 3.2. Introduction

Cardiovascular diseases have become an increasing risk to the health of people worldwide who need immediate attention for complications that arise from their coronary heart diseases such as angina, ventricular arrhythmias as well as sudden death. Most of the sudden deaths are caused by cardiac arrest, usually resulting from ventricular tachycardia or fibrillation. Moreover, studies have shown that rapid response time in prehospital setting results in reducing mortality and dramatically improved patient outcomes following cardiac arrest [1-3].

Normal electrical stimulation of the heart originates at the sinoatrial (SA) node in the upper section of right atrium and passes only through the atrioventricular (AV) node and other special conducting tissues (Bundle of His) in sequence and finally to Purkinje fibers in the ventricles. This excitation, monitored at the body surface by electrodes is an electrocardiogram (ECG).

Normal cardiac conduction, resulting from normal sinus rhythm, is due to regular conduction of electrical impulses from SA node and rejection of electrical impulses from other latent pacemakers. The normal electrical stimulation of the heart originates at the sinoatrial (SA) node in the upper section of right atrium and passes only through the atrioventricular (AV) node and other special conducting tissues (Bundle of His) in sequence and finally to Purkinje fibers in the ventricles. This excitation, monitored at the body surface by electrodes is measured with an electrocardiogram (ECG).

In certain cases, additional pacemakers interpose additional electrical impulses that generate ectopic beats, which due to their different locations lead to varying
behavior. A premature ventricular contraction (PVC) is due to an ectopic cardiac pacemaker located in the ventricle, characterized by the premature occurrence of bizarre-shaped QRS-complex (typical QRS width > 120 ms). These widened QRS complexes are not preceded by a P-wave, and the T-wave is usually large and opposite in direction to the major deflection of the QRS (Figure 3.1). The PVCs may appear in patterns of bigeminy, trigeminy, or quadrigeminy, which describe their pattern, which occur every other, every third, or every fourth beat, respectively. Patterns of PVC can also occur in runs of two or more. Runs of two are called a PVC couplet and run of three or more with an elevated heart rate is called ventricular tachycardia.



Figure 3.1 ECG record with premature ventricular contraction

PVC is one of the most common arrhythmias, which can occur in patients with or without heart disease. This is attributed to inadequate cardiac stroke volume or to decreased cardiac output caused by effectively halving the heart rate. Prolonged occurrence of these may lead to hypotension. Physical exercise can increase or decrease the PVC rate [4]. In young healthy patients with underlying structural heart disease, these can lead to angina, ventricular tachycardia or even sudden death. The early occurrence of PVC in the cardiac cycle (R-on-T phenomenon) of frequency more than 10/hour, with multiple ventricular morphologies, are associated with arrhythmic events and increased mortality rates [5].

Remote monitoring of ECG is used to assess the probability of cardiac event, stratify risk and to guide therapy. The ECG signal recording in a non-hospital setting can be classified as short-term or long-term recording. Short-term measurements (5-15 min) are usually carried out at physician's office or at small clinics. Long-term measurements (24-96 hours) are usually made at the patient's home by ambulatory monitors.

The ECG data are usually transmitted by incorporating Transmission Control Protocol/Internet Protocol (TCP/IP). The TCP/IP encapsulated ECG data are sent over public switched telephone network (PSTN) [15,16], Cellular technologies incorporating global system for mobile communication (GSM) [17] and time division multiple access (TDMA) [18] standards and broadband networks (DSL/Cable) from the remote patient location to the hospital. The PSTN is the most commonly used medium for ECG transmission due to its ubiquitous presence. However, data sent over the PSTN has a high error rate causing frequent delays. Real-time ECG monitoring systems incorporating the GSM data networks [17] have an advantage of being wireless, but its limited bandwidth leads to significant data loss. Remote web servers are also used to store and display real-time ECG data. Java embedded systems [19]. Holters with DSP chips for ECG analysis [20] are used as remote servers but are expensive and do not provide any feedback to the patient about his/her medical condition.

Handheld devices, like personal digital assistants (PDAs), are small, light, and easy to use with powerful computing capabilities. and are used in the medical community to access online medical databases [21-22], record patient and clinical training data [23] and send ECG data from the ambulance directly to the a hospital [24]. The PDA has also been used to monitor the infants' respiratory in real-time [25] and stress in adults [26]. Goh et al [27] proposed a PDA based home monitor with on-board hardware based QRS detection. Despite the versatility, this is not suited for detecting variations in the QRS morphologies in different patients due to lack of computing capability or the battery life required to perform real-time ECG analysis.

For a reliable cardiac arrhythmia monitoring system, a remote monitor must not miss a life threatening arrhythmia, causing the patient a lost chance of treatment and must minimize false-positive detection, which may lead to improper therapeutic intervention. In addition to reliability, speed of transmission is critical to early detection of arrhythmia.

Wavelet transforms (WT) based QRS detection is a promising technique for timefrequency analysis of ECG signals [8,9]. Wavelet analysis of a signal involves breaking up a signal into shifted and scaled versions of a reference (mother) wavelet. In determining the wavelet decomposition coefficients of a signal, the correlation of the mother wavelet at different shifts and scales with the signal is computed. Hence, the wavelet coefficients represent measures of similarity of the local shape of the signal to the mother wavelet under different shifts and scales. The QRS points are detected by comparing the coefficients of the discrete wavelet transform on several scales against fixed thresholds [10].

In this study, we evaluate the usefulness of our arrhythmia detection algorithms on ECG recordings transmitted using handheld monitor. Considering the needs of the patient, many of which will be outside the clinical setting, the handheld remote monitor is

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designed to record and monitor ECG, and to provide real-time feedback for effective monitoring of medication and exercise. To show the effectiveness of the remote monitor for real-time applications the time interval between the detection of cardiac arrhythmia and the onset of ventricular fibrillation (negative time to onset) on ECG recordings from Creighton University Ventricular Tachyarrhythmia Database (Cu-DB) is measured.

### 3.3. Methods

### 3.3.1 Local Client

The software design for local client-remote server is shown in Figure 3.2. The ECG data acquired from local clients (computers/handheld devices) was transmitted to a remote server for analysis and storage, which can be used by healthcare provider to assess condition of the patient and for cardiac arrhythmias. The results of analysis are sent back to the client to provide feedback in real-time. An early warning alarm was sounded at local and remote locations in case of ventricular tachycardia. The analyzed results were also available to other remote clients (physicians) to aid in diagnosis.



Figure 3.2 Local client – Remote server model.

The ECG recording was transmitted via a Sony Clie TH-55 running Palm 5.0 with built-in WLAN support. The remote server was a Compaq Presario R3000Z laptop, which was used to analyze and transmit the results to the client. Additional support (booster) files were provided by Mobile VB for running the program on the PDA device. Windows sockets incorporating TCP/IP protocols were used to establish a connection between the remote client and central server. The local client and remote server were part of the campus-wide LAN. The connecting speed of the LAN was 1.54MB/s (T1 line). The client PDA connected to LAN through a wireless adapter. The IP address and port information of the remote server was required for the TCP connection. The server was designed to handle multiple local/remote clients at the same time. Microsoft Visual Basic 6.0 (Microsoft Corp, Redmond, WA) and Mobile Visual Basic (Appforge Inc, Atlanta, GA) software was used to develop the graphical user interface (GUI) and communication (TCP/IP) modules for the client.

3.3.2 Remote Computing Server

Availability of built-in digital signal processing and statistical algorithms has made Matlab the software of choice for developing of the software. The Matlab server was run in a shared mode (multiple client applications) on the server (Figure 3.3).



Figure 3.3. Software model at the remote computation server

The QRS/PVC detection and HRV calculation algorithms were implemented in the Matlab workspace. The results of the analysis were transferred to Visual Basic for display and transmission to client.

## 3.3.3 QRS Detection

# 3.3.3.1 Wavelet Transforms

The continuous wavelet transform (CWT) of signal x(t) is defines as

$$CWT_{x}(b,a) = \frac{1}{\sqrt{|a|}} \int_{-\infty}^{\infty} x(t)g * \left(\frac{t-b}{a}\right) dt$$
(1)

where g(t) is the wavelet function and b and a (b, a  $\varepsilon \Re$ , a $\neq 0$ ) are the translation and dilation parameters respectively. The duration of the mother wavelet g(t) is either compressed or expanded depending on the choice of a. Hence, the CWT can extract both local and global variations of a signal x(t). If x(t) has discontinuities, then the modulus of CWT of x(t),  $|CWT_x(b,a)|$ , exhibits local maxima around the time of occurrence of the discontinuities

The CWT is defined as a dyadic wavelet transform (DWT), if only a is discretized along the dyadic sequence  $2^{i}$  where i = 1, 2, ... The DWT of a signal is then defined as

$$DWT_{x}(b,2^{i}) = \frac{1}{\sqrt{\left|2^{i}\right|}} \int_{-\infty}^{\infty} x(t)g^{*}\left(\frac{t-b}{2^{i}}\right) dt$$
(2)

To cover the entire frequency domain, the DWT should satisfy the relation

$$\sum_{i=-\infty}^{\infty} \left| G(2^{i}\omega) \right|^{2} = 1$$
(3)

where  $G(\omega)$  is the Fourier transform of g(t).

The DWT can reduce the redundancy of each filtered signal so that we can effectively apply the processing algorithm to a small subset of the original signal. Figure 3.4 shows the filter bank for implementing the dyadic discrete wavelet transform decomposition [6]. The notations  $h_1$  are FIR high-pass filters that have coefficients relating to the wavelet coefficients, and  $h_0$  are the FIR low pass filters that have coefficients relating to scaling function coefficients. Each filtered signal is down-sampled thereby reducing the length of the signal by a factor of 2 (Figure 3.4). The signal is reconstructed from  $d_1$ , which contains the highest frequency using IDWT (Inverse DWT). This reconstructed signal, called detail, contains the detail of the high frequencies in the original signal.



Figure 3.4 Multilevel dyadic wavelet analysis filter bank.

Biorthogonal wavelets ('bior2.6') were used as the mother wavelet in the implementation of remote monitor. The scaling and wavelet function of the mother wavelet are shown in Figure 3.5. Biorthogonal wavelets were chosen because they offer temporal symmetry, preventing non-linear phase shift of the transformed signal [28]. In the implementation of remote monitor, an ECG data block of size 512 was reduced to a

32-size data block after wavelet decomposition prior to QRS detection, thus reducing the detection time.



Figure 3.5 Scaling and wavelet functions ('bior2.6')

# 3.3.3.2 QRS Detection/Classification algorithm

The QRS complex appears as a modulus maxima with opposite signs of the wavelet transform. Figure 3.6 shows the absolute reconstructed signal from wavelet levels 1-7.



Figure 3.6 ECG data and reconstructed data from wavelet levels 1-7.

The frequency spectrum of the signal containing the primary energy of the QRS complex is located in the range of 0.1-30 Hz, which is best represented by analysis of reconstructed signal from level 3 (D3) and level 4 (D4) wavelet decomposition [6]. From figure 3.6, it can be seen that QRS complex can also be identified from D3 and D4. D4 was chosen as the number of data points to analyze in D4 (32) was found to be half of data present in D3 (64). The position of the QRS complex was estimated by squaring each data point and applying a moving window integrator [29]. The resulting data was compared to a fixed threshold to locate the local maxima, which were classified as QRS

complex (Figure 3.7). In cases no maxima were found, a search back was initiated with a lowered threshold in the last 70ms of data to locate the missing QRS complex [10].

The ECG data segments were analyzed in blocks of 512. The QRS complex were identified in each segment and care was taken not to count beats occurring at the end of one data and beginning of another segment twice.



Figure 3.7 Flow chart of the QRS detection algorithm. (a) – ECG signal, (b) – Wavelet decomposition at level 4, (c) – Squared and integrated level 4 signal.

Due to the varying morphology of PVCs, designing a general PVC detection algorithm to identify different types of PVCs was found to be very difficult. This inconsistency in performance of PVC detection led to creation of adaptable parameter set (Detection parameters). The parameters were created from a 2 minute annotated ECG data of the patient and were customized for each patient-ECG data. The addition of parameters was found to achieve significant improvement in performance in PVC detection [26]. From figure 3.6, it is seen that D5, D6 and D7 can be used to identify PVC location. Data from level 7 was sparingly used as it was also found to contain noise due to drift.

A global threshold was applied next in order to remove the contribution due to normal QRS complex. The presence of reconstructed wavelet data greater than global threshold indicated the presence of PVC beat. When present, the location is identified by comparing the global maxima in reconstructed levels 5 and 6 (Figure 3.8).



Figure 3.8 Flow chart of PVC detection algorithm. (a) – ECG signal with PVC, (b) – Wavelet decomposition at level 5, (c) – Wavelet decomposition at level 6.

A compromise is often involved in selection of threshold because setting a low threshold minimizes false positives and a high threshold minimizes false negatives. The sensitivity and specificity of the QRS or PVC detection schemes are given by:

Sensitivity = 
$$100 \text{ x} \frac{\text{Beats Detected - False Negative}}{\text{Beats Detected}}$$
 (3)  
Specificity =  $100 \text{ x} \frac{\text{Beats Detected - False Positive}}{\text{Beats Detected}}$  (4)

where, Beats Detected refers to QRS or PVC beats detected, False Negative refers to beats the detector failed to identify and False Positive refers to detecting non-existent beats.

We use modified Lown's grading system [30] to rate arrhythmia severity (Table 1). Cardiac arrhythmias are classified as potentially dangerous or not based on the heart rate and the number and pattern of PVCs present. The monitoring was done for blocks of 512 data points and when arrhythmias were found to be grade 4, an alarm was sounded and sent to the handheld client.

Grade 0	Normal - No PVCs present
Grade 1	Occasional PVCs ( < 30/h)
Grade 2	Frequent PVCs ( $> 30/h$ )
Grade 3	Repetitive PVCs ( A -Couplets, B -Salvos)
Grade 4	$\geq$ 3 PVCs in a row & heart rate > 120bps

Table 3.1. Arrhythmia classification table.

It is very difficult to pinpoint the onset of ventricular fibrillation. Since sustained ventricular tachycardia often leads to ventricular fibrillation, the alarm was sounded on detection of ventricular tachycardia. Negative time to onset [31] was defined as the time between the alarm and the onset of ventricular fibrillation. Negative time to onset was used to determine the effectiveness of a real-time monitor.

# 3.3.4 Data

Ten ECG records were selected randomly from the MIT Normal Sinus Rhythm Database (NSR-DB), five ECG records with unifocal PVCs were chosen from the MIT- BIH Arrhythmia Database (MIT-DB) and four records containing runs of PVCs (ventricular tachycardia) leading to ventricular tachycardia were chosen from the Creighton University Ventricular Tachyarrhythmia Database (CU-DB). Data from NSR-DB had no significant arrhythmia, were of one minute duration, sampled at 100Hz. Data from MIT-DB were of 10 minute duration, and were sampled at 360Hz. ECG recordings from normal and arrhythmic subjects were used to evaluate the QRS and PVC detection algorithms. Data from CU-DB were of 10 minute duration and were sampled at 250Hz. ECG recordings from Cu-DB was used to measure the effectiveness of remote cardiac monitor. All the data chosen was of modified limb II (ML II) and was annotated.

### 3.4 Results

The remote monitor was designed and implemented successfully. Figure 3.9(a)-(b) shows the implementation of the RCAM and remote server. Figure 3.9(a) shows the ECG data displayed on the handheld device in real-time, while remote server performed analysis. The black dots on the remote server application represent the locations of the identified QRS complex.



Figure 3.9 (a) Photograph of handheld device (b) Screenshot of the remote server.

QRS detection algorithm was tested on ECG data from NSR-DB. The number of false positive and false negatives was recorded and the specificity and sensitivity of the QRS evaluated (Table 3.2).

			False		
Filename	<b>QRS</b> Detected	<b>False Positive</b>	Negative	Sensitivity	Specificity
1052	65	0	0	100.00	100.00
1177	103	1	0	100.00	99.03
1184	81	2	0	100.00	97.53
1265	89	0	0	100.00	100.00
1272	58	0	0	100.00	100.00
1273	88	0	0	100.00	100.00
1453	77	0	0	100.00	100.00
1483	91	0	0	100.00	100.00
1773	69	0	0	100.00	100.00
1795	61	0	0	100.00	100.00

Table 3.2. QRS sensitivity and specificity measurements onECG records from NSR-DB data.

QRS and PVC detection algorithms were tested on ECG records with unifocal PVCs from MIT-BIH. Table 3.3 shows the specificity and sensitivity measurements for the QRS and PVC detection algorithms.

	QRS			PVC		
Filename	Detected	Sensitivity	Specificity	Detected	Sensitivity	Specificity
105	839	99.64	98.93	14	50.00	64.29
114	570	99.82	97.72	39	97.44	89.74
116	795	99.75	100.00	28	64.29	100.00
119	662	99.55	98.64	142	98.59	97.18
208	971	96.81	99.59	397	87.91	92.19
221	824	100.00	100.00	163	88.34	88.96

Table 3.3. Sensitivity and specificity measurements by QRS & PVC detectors on ECG records from MITDB.

Negative time to onset was calculated on data from four ECG records of PVC runs leading to ventricular fibrillation. Figure 3.10 illustrates the time available (shaded area) for treatment due to early arrhythmic detection.



Figure 3.10 Negative time measurements



Figure 3.11. A screen-shot of the server application on successful early detection.

## 3.5 Discussion

The handheld monitor has been designed and tested. Critical patients can be monitored remotely and experiences staff at the remote location can monitor and advise for unexpected condition. The effectiveness of the monitor was demonstrated in its ability to detect PVC and ventricular tachycardia, which commonly heralds the onset of angina, acute myocardial infarction, ventricular fibrillation and sudden death. By detecting PVC runs when they occur may provide additional time to prove to be invaluable for emergency intervention for persons with cardiac disease.

Handheld device with WLAN capability provides mobility required during transport and exercise. This portability is the key to successful monitoring of mobile patients. Real-time telemonitoring was achieved by wireless technology. Constant use of WLAN adapter on the client greatly increases the power consumption of the device limiting it for short duration real-time ECG measurements. However, in cases of patient transport, which is often completed in 20 minutes, this mobile unit is very useful.

Today, the handheld devices are moderately priced and are becoming increasingly powerful. With minimal additional hardware to acquire and filter the ECG data, the monitor can provide a cost-effective solution for a remote home monitor. The handheld monitor is very user-friendly and required minimal user training. Software updates can easily be made to ECG detection and analysis algorithms without affecting the client unit. The presence of a graphical user interface unit on the client providing a real-time display is very useful feature when the user feels uncomfortable and requires a quick diagnosis. Most of the systems available today are very bulky and without wireless communication capability and thus, not efficient for continuous monitoring of a mobile patient. In an earlier study [24] we had designed and implemented a handheld remote infant respiratory monitor. The handheld remote ECG monitor, designed on infant monitor framework incorporates modules for a more comprehensive ECG analysis and a more detailed feedback to the client.

GSM-based systems are often limited by cost effectiveness of expensive data link, limited data transfer rate and possible electromagnetic interference with mobile phones. Taking that into account, we have used WLAN technology, which offers a practical and flexible means of transmitting data. WLANs emit low intensity radio waves, which has been found acceptable for hospital use and has been implemented in ICU and radiology examination rooms [32]. WLAN also incorporates encryption and authentication mechanisms for client access to remote server, making it hard to hack to intercept data from network. In our study, we have used a single ECG channel for monitoring and analysis. At present, the WLAN standard (802.11b) can support data transfer rates of 10MB/s and can easily handle additional ECG data channels. Addition of additional data channels can improve the performance of QRS and PVC detectors. The new 802.11g WLAN standard promises to further increase the data transfer rate to 54MB/s, paving the way for addition of more parameter for real-time remote monitoring.

The ideal location for the server is in a medical center, where ECG and results (if abnormal) can be verified as soon as possible. To further facilitate remote monitoring, we have developed remote client application for medical staff's handheld devices. This provides remote access to the patient's ECG and aids in assessment of patient's status. In some cases, deteriorating trends can be identified and emergency procedures can be implemented efficiently.

Real-time monitoring studies done earlier [26,32] have acquired and analyzed ECG data for arrhythmia at client location. The disadvantage of this design is that dedicated hardware based detection needs to be implemented for individual clients or no feedback is provided to the client. Another approach has been to send the data for analysis, but no feedback was provided to the client. A software based detection scheme is more adaptable and easier to implement and modify for varying client ECG morphology. Feedback is important for a symptomatic patient when no medical staff is available nearby.

The good performance of QRS detector makes it reliable for monitoring normal heart rate after exercise or follow up monitoring after medication or rest. The performance of the QRS detector is slightly lower in presence of PVCs and is comparable to algorithms used for off-line analysis [29]. Additional parameters have been used in detection of PVCs [26]. Detection parameters have been found to improve the performance or PVC detector. At the present time, the creation of parameters is not automated. The stored data can be used for a more a more comprehensive off-line analysis at a later time.

### 3.6 Conclusions

In this paper, we have illustrated the implantation of a handheld remote monitor. The handheld remote monitor satisfies all requirements expected of a remote monitor [7]. In addition to being cost-effective, it provides an instantaneous feedback to the user regarding his current cardiac condition. The remote monitor is ideally suited for monitoring normal daily activities like heart rate after exercise or medication. The detection parameters help customizes the PVC detector to reduce the number of false positives. The effectiveness of the monitor was successfully demonstrated on four ECG datasets having PVC runs leading to ventricular fibrillation. This increase in response time in combination with a portable ECG monitor can eventually lead to increased patient survival.

At the present time, the display resolution and battery life of the handheld device are limited. The maximum display allowed is 320x160 pixels. This limits the details of the ECG being displayed. The short battery life limits its use to short duration ECG measurements. In the future, on a new generation mobile computer, a better display and faster computing power to perform analysis on the client may be possible. At the server computation level, the PVC detector was tested only on unifocal premature ventricular contractions. Additional detection schemes may be designed for multiform premature ventricular contractions and other arrhythmias.

In the future, ultra-portable laptops with full-fledged communication, display and longer battery life will eliminate the limitations imposed by a handheld device.

# 3.7 References

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## CHAPTER 4

# Evaluation of Heart Rate Variability Indices to Predict Cardiac Event Using a Real Time Handheld Remote ECG Monitor

# 4.1 Abstract

A retrospective study on ECG recordings of patients during cardiac arrest has showed significant changes in Heart rate variability indices prior to the onset of cardiac arrhythmia. Early detection of the changes in HRV indices would increase response time for timely medical intervention. The handheld remote ECG monitor detects the occurrence of QRS complex and calculates short-term HRV indices from ECG recordings. The sensitivity and specificity of the QRS detection to ECG recordings from subjects from MIT-Arrhythmia database were 99.34% and 99.31%, respectively. Differences in HRV indices were assessed on ECG recordings from normal and subjects with congestive heart failure. Time domain indices heart rate, SDNN and RMSSD and frequency domain indices total spectral power, low frequency power, high frequency power, and low frequency to high frequency power ratio were found to be sensitive to differentiate between the two groups. These HRV indices were monitored for changes on an ECG recording of a sleep study subject who experienced acute chest pain. The total power spectrum exhibited a cyclic pattern, which could be attributed to REM sleep cycles. No other significant change in HRV indices was observed.

# 4.2. Introduction

HRV is a marker of the significant relationship between the autonomic nervous system and cardiovascular mortality [1]. The parasympathetic influence on the heart rate is mediated via release of acetylcholine by the vagus nerve. When parasympathetic nerve is activated, slow diastolic depolarization is initiated. This slowing of cardiac contraction allows the coronary vessels to dilate and in blood flow to the working cardiac cells. The sympathetic influence on the heart rate is mediated by the release of epinephrine and norepinephrine. The end result is an acceleration of the slow diastolic depolarization, which lessens the time for the coronary vessels to fill and possibly leading to decrease in blood flow to the working cells.

Under resting conditions, the vagal tone prevails and variations in the heart rate are largely dependent on vagal modulation [2]. Sympathetic mediators appear to exert their influence over longer time periods and are reflected in the low frequency power (LFP) of the HRV spectrum. In contrast, vagal mediators exert their influence more quickly on the heart, and principally affect the high frequency power (HFP) of the HRV spectrum. Thus, at any point in time, the LFP:HFP ratio can serve as proxy for the sympatho-vagal balance.

The clinical importance of HRV became apparent when it was confirmed as a strong and independent predictor of mortality following an acute myocardial infarction. Lowered HRV was found to precede episodes of atrial fibrillation in patients after coronary artery bypass graft operation and with no structural heart disease [3]. Time-variant algorithms when applied to RR interval data a low frequency (LF) component of HRV power spectra, 1.5-2 minutes before the onset of an ischemic episode was found

[4]. Correlation dimensional analysis on RR interval predicted the exact time of occurrence of ventricular fibrillation in a retrospective study [5]. Low frequency HRV measurement predicted in-hospital complications when measured within 2 days after the AMI [6]. Short-term HRV measures are used in prediction of mortality of patients with chronic heart failure [7].

Ventricular tachyarrhythmias (VTAs) have a circadian rhythm with increasing frequency during early morning and early evening [8]. Diurnal variation is also found in HRV. Higher LFP occurs in daytime and higher HFP during night [9,10]. An inverse circadian rhythm is seen in patients with a morning VTA peak. Some studies have reported significant changes in HRV in the period immediately preceding a VTA [11,12]. Huikuri et. al. [13] found significant reduction in heart rate (HR), very low frequency power (VLFP), LFP and HFP in post-MI patients who developed cardiac arrest one hour prior to onset of VTA. Shusterman et. al. [14] noted an increase in heart rate, fall in LFP and LFP:HFP ratio prior to onset of VT in post-MI patients. Other studies have shown a rise in VLFP and decline in HFP [16] and a rise in LFP:HFP ratio [11,17]. These results strongly suggest an alteration in the interaction between the sympathetic and parasympathetic nervous system prior to onset of VTAs. The effect on HRV variables is likely to be heterogeneous and affected by individual patient characteristics.

In episodes of cardiac failure, ventricular fibrillation is almost always preceded by a run of ventricular tachycardia, which eventually gives way to the ventricular fibrillation. The onset of ventricular fibrillation is extremely difficult to pinpoint in many cases. The addition of HRV to remote monitoring of patients with cardiomyopathy and vascular heart disease will aid in early detection of potentially dangerous cardiac arrhythmias.

In a previous study [18], we presented a handheld remote monitor to record and monitor ECG. The sensitivity and specificity of the QRS detection to ECG recordings from MIT-Arrhythmia database were 99.34% and 99.31%, respectively. Similarly, these parameters of the premature ventricular contraction detection were 87.5% and 91.67%, respectively. The time between alarm and the onset of ventricular fibrillation was measured on ECG recordings where premature ventricular contractions were found to lead to ventricular fibrillation. The remote monitor was able to successfully identify the onset on ventricular fibrillation. In this study, we apply HRV techniques on data from available databases to determine which HRV indices discriminate ECG recording from normal subjects form ECG recordings of subjects with congestive heart failure. These indices would be monitored in real-time to predict the onset of cardiac arrhythmia on ECG recordings of a sleep study subject. The subject had prior history of cardiac arrhythmias and had complained of chest pain during the study.

### 4.3. Methods

### 4.3.1 Remote Client

The ECG data acquired from local clients (computers/handheld device) was transmitted to a remote server for analysis and storage. ECG data was monitored to assess condition of the patient and for cardiac arrhythmias. The results of analysis were sent back to the client to provide feedback in real-time. An early warning alarm was sounded at local and remote locations in case of potentially dangerous cardiac arrhythmia.

### 4.3.2 Remote Computing Server

At the remote server, communication modules in Visual Basic 6.0 (Microsoft Corp, Redmond, WA) receive ECG data from the client. QRS complex were detected and HRV indices computed using Matlab (The Mathworks Inc., Natik, MA). The results were sent back to the client (Figure 4.1). Detailed information on the design and implementation of client and remote server can be found in Chapter 3 [18].



Figure 4.1. Software model at the central computation server

# 4.3.3 QRS Detection

The automated detection of QRS complexes is important to cardiac disease diagnosis. A good performance of an automatic ECG analyzing system depends heavily upon the accurate and reliable detection of QRS complexes.

Wavelet transforms (WT) are currently being used in various signal processing fields as well as for a diversity of biomedical signal processing applications. By decomposing signals into elementary building blocks that are well localized in time and frequency, the WT can characterize the local regularity of signals. The feature can be used to distinguish ECG waves from serious noise, artifacts and baseline drift. A QRS detector based on biorthogonal wavelet was implemented. Biorthogonal wavelets enable detection of QRS complex as an extrema, simplifying the QRS detection algorithm. The QRS detector also detected premature ventricular contraction beats. Detailed information on the design and implementation of QRS and PVC detection algorithms can be found in [18].

# 4.3.4 Heart Rate Variability

Short term HRV (5 minute) duration was chosen for time and frequency domain HRV measurements.

4.3.4.1 Time Domain Measurements

(i) SDNN - Standard deviation of the NN interval (SDNN) [19],

$$SDNN = \sqrt{\frac{1}{N-2} \sum_{n=2}^{N} (\delta(n) - \overline{\delta})^2}$$
(1)

where  $\overline{\delta}$  is the average NN signal from N beats,

$$\overline{\delta} = \frac{1}{N-1} \sum_{n=2}^{N} \delta(n)$$
<sup>(2)</sup>

The scaling factor is N-2 because there are N-1 intervals in the record and one degree of freedom is used to estimate the mean NN interval. SDNN reflects all the cyclic components responsible for the variability in the period of recording.

(ii) RMSSD - Square root of the mean squared differences of successive NN intervals.

RMSSD = 
$$\sqrt{\frac{1}{N-2} \sum_{n=3}^{N} [\delta(n) - \delta(n-1)]^2}$$
 (3)

# 4.3.4.2 Frequency Domain Measurements

Power spectral density analysis was used to provide basic information of how power (i.e. variance) distributes as a function of frequency. The frequency indices calculated from short-term recordings are:

- (i) Total spectral power (TP) Power in 0.001-1.5 Hz range.
- (ii) Very Low Frequency (VLFP) Power in 0.001-0.04 Hz range
- (iii) Low Frequency (LFP) Power in 0.04-0.15 Hz range
- (iv) High Frequency (HFP) Power in 0.15-0.4 Hz range
- (v) Normalized low frequency:  $LF_{norm} = 100 \text{ x} \frac{LF}{TP VLF}$  (4)
- (vi) Normalized high frequency:  $HF_{norm} = 100 \text{ x} \frac{HF}{TP VLF}$  (5)

(vii) LFP:HFP – Low to high frequency power ratio averaged every 5 minutes

Measurements of VLFP, LFP and HFP were made in absolute units (ms<sup>2</sup>), but LFP and HFP may also be measured in normalized units (norm.) which represents the relative value of each component in proportion to the total power minus the VLFP component.

The NN data sequence was obtained after removal of ectopic and missing beats. The presence of ectopics or missed beats can corrupt the frequency domain measurements because of the broad-band frequency content of the impulse-like artifact [20]. In the continuous ECG record, QRS complexes (RR intervals) were detected using wavelet-based QRS detector [21]. ECG data segments containing more than 10% PVCs were discarded. Missing and ectopic beats varying by more than 12.5% were removed. The resulting gaps were filled with an average value computed in the local neighborhood of the missing beat. With this filtering technique, temporary changes in the RR interval sequence, representing missing or ectopic beats were removed and more stationary data

were obtained. A linear detrend was applied to the resulting NN interval data. To make NN interval dataset regularly sampled at 2Hz by a moving window curve-fitting algorithm. The mean value of the data is subtracted from individual NN data. Power spectral density (PSD) estimation was done using 512-sample FFT by Welsh's periodogram method. Each data segment was divided into 8 sub-segments that overlapped on each other for 50% of their lengths. For each sub-segment, the data were weighted with a Hanning window and the periodogram estimated using fast Fourier transform algorithm. The PSD was obtained by averaging the periodograms and then rescaling to take into account the power loss due to windowing. The spectral power present in VLF, LF and HF bands was estimated. Figure 4.2 illustrates the process to estimate the HRV temporal and spectral estimates.



Figure 4.2. Flow chart summarizing individual steps in HRV analysis

4.3.5 Data

Five ECG records were selected from the normal sinus rhythm database (NSR-DB), five records were selected from the BIDMC congestive heart failure database (CHF-DB) and a three hour ECG recording from a subject with prior history of cardiac arrhythmias at the School of Nursing, University of North Carolina at Chapel Hill were used. The records from NSR-DB were of 30 minutes duration each and were sampled at 100 Hz. The records from CHF-DB were of 30 minutes duration each and were sampled at 250 Hz. This database contained long-term ECG recordings from subjects with severe

congestive heart failure. The subject was an 84-year-old white female. The subject reported chest pain during this study, which was relieved with rest. The three-hour recording was 45 minutes prior to the onset of cardiac arrhythmia. The standard lead II ECG data was sampled at 250 Hz.

# 4.4 Results

The sensitivity and specificity of the QRS detector on normal ECG recordings and ECG recordings with PVCs present is shown in Table 4.1. Detailed information can be obtained from Chapter 3 [18].

Normal ECG		ECG with PVCs		
Sensitivity	Specificity	Sensitivity	Specificity	
100.00	99.03	99.64	98.93	
100.00	97.53	99.82	97.72	
100.00	100.00	99.75	100	
100.00	100.00	99.55	98.64	
100.00	100.00	96.81	99.59	
100.00	100.00	100	100	

 Table 4.1. Sensitivity and Specificity measurements of QRS detection on normal and arrhythmic ECG recordings.

The heart rate variability indices were computed in 5 minute intervals. A comparison of the averaged time-domain measurements shows an increase in HR and a decrease in RMSSD (Figure 4.3) in ECG recordings from normal and subjects with congestive heart failure.



Figure 4.3. Comparison of HR and RMSSD.

The power spectrum of data from normal ECG recordings and that from ECG recordings from subjects with congestive heart failure is shown in Figures 4.4(a)-(b). Data from a normal ECG recording has higher concentration of spectral power in HF range, while a CHF ECG recording have higher concentration of power in VLF and LF range.



Figure 4.4(a). Power spectrum of a normal ECG recording.



Figure 4.4(b). Power spectrum of a CHF ECG recording.

A breakdown of spectral power into TP, VLFP, LFP and HFP is shown in figure 4.5(a). The total spectral power in CHF ECG recordings was much lower than that of normal ECG. An increase in VLFP(norm), LFP(norm) and LFP:HFP ratio and a decrease in HFP was observed in CHF ECG recordings.


Figure 4.5(a). Comparison of total spectral power and normalized spectral components.



Figure 4.5(b). Comparison of LFP:HFP ratio.

A comparison of time and frequency domain HRV indices is shown in Table 4.2. Student's t test (95% CI) was used to compare the differences between ECG recordings from CHF and normal subjects. Among time indices, HR and RMSSD showed significant differences and among frequency domain indices, Total power, HFP and LFP:HFP showed significant differences.

Index	CHF	Normal	P Value
Heart Rate	88.09	72.96	<.001
SDNN	145.39	164.99	0.245
RMSSD	181.41	239.74	0.003
LFP	2269.28	2653.86	0.606
HFP	2225.36	6401.52	<.001
ТР	6048.34	10499.32	0.023
LFP:HFP	0.74	0.46	0.002

Table 4.2: Summary of differences between various HRV indices

A 180-minute ECG segment recorded 45 minutes prior to onset of chest pain was analyzed. The heart rate variability indices were monitored in five-minute intervals. HR showed no significant change over the three-hour period (Figure 4.6). Dashed (reference) line represents the mean value of HR measured during a follow-up a year later.



Figure 4.6. Variation in HR over 36 5 minute time points.

RMSSD decreased from an increase 195 minutes prior to onset of chest pain (Figure 4.7). No significant variation was observed 180 minutes prior to arrhythmia.



Figure 4.7. Variation in RMSSD 45 minutes prior to chest pain.

The total spectral power oscillated in a cyclic pattern, repeating every 70 minutes (Figure 4.8) in the three-hour period.



Figure 4.8. Total spectral power at various time-points prior to chest pain. No significant trend was observed in the variation of HFP(norm) and in LFP:HFP ration (Figures 4.9, 4.10)



Figure 4.9. HFP(norm) at various time-points prior to chest pain



Figure 4.10. Variation of LFP:HFP ratio prior to chest pain.

#### 4.5 Discussion

The handheld monitor using HRV indices to detect onset of cardiac arrhythmias in real-time was designed and tested. Trends in HRV indices of patients with pre-existing cardiac conditions can be remotely monitored. Early detection of changes in time and frequency domain indices could prove invaluable in early intervention.

Among HRV indices to monitor, RMSSD was strongly recommended by a consensus committee because it determines heart rate variability from differences between successive beats and is indicative of high frequency power [1]. The differences in HRV indices among ECG from normal and CHF subjects was in agreement with an earlier study [31]. Among the frequency indices, TP, HFP and LFP:HFP ratio were found to separate the ECG recordings from normal and CHF subjects. The TP reflects the change in the variance of the heart rate, while the LFP:HFP ratio reflects the sympathovagal balance. Higher values of LFP:HFP ratio, accompanied by higher heart rate could

indicate higher sympathetic activation in subjects with congestive heart failure. Very low frequency power accounts for long-term regulation mechanisms (probably thermoregulation, to the rennin-angiotensin system and other factors). These mechanisms cannot be satisfactorily resolved by short-term analysis.

It was not surprising that the subjects with congestive heart failure differed from the sleep study subject. The subject under study patient at the School of Nursing had no recent history of cardiac problems and chest pain resolved with no intervention. No significant trend in HRV indices was observed prior to onset on cardiac arrhythmia. The decrease in RMSSD (high-frequency component) could indicate a decrease in parasympathetic activation. The variation in LFP was found to be identical to that of the total spectral power (Figure 4.11). Studies have shown sympathetic domination during sleep [22] and TP and LFP were found to be significantly higher during REM cycle [23]. Villa et. al. [24] showed age to be factor in variation of HRV indices during sleep. The variations observed in TP and LFP could be attributed to the sleep state of the subject at the time of ECG recording.



Figure 4.11. Variation in low frequency and total spectral power measured 45 minutes prior to chest pain.

The maximum error in identification of R wave in Wavelet based QRS detector was 20ms when raw ECG data is sampled at 250Hz, 13.8ms when sampled at 360 Hz and 10ms when sampled at 500Hz. The effect of RR error was minimized by choosing an effective resampling algorithm. The variation in spectral components of the subject was found to be very subjective and depends on patient age and prior cardiac history [25].

#### 4.6. Conclusions

Reed et. al. [25] suggested that merely a change in heart rate variability indices, rather that the magnitude or nature of change, facilitates the development of ventricular tachyarrhythmias. Detection of the change in heart rate variability measures would provide an effective method for early detection of arrhythmias.

A number of factors (like age, posture, sleep, exercise, etc) might be responsible for the change in heart rate variability indices. Our data were obtained during the course of a sleep study. Possibly, the changes detected are influenced by other activities. The relationship between changes in monitoring indices during sleep needs to be investigated further.

It was observed that knowledge of resting value of indices improves interpretation of changes in HRV measures. Availability of prior cardiac history is also helpful in determining of the risk posed by arrhythmia. Further examination of more cases is needed to be done.

# 4.7 References

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## CHAPTER 5

# Development of a Handheld Remote ECG Monitor to Assess Cardiac Risk Based on Changes in Heart Rate Variability

#### 5.1 Abstract

Heart rate variability has been shown to be a powerful risk stratifier for overall mortality, induced and spontaneous tachycardia and sudden death in patients following acute myocardial infarction. Short-term ECG recordings made from home or clinics using remote monitor will provide good assessment of cardiac risk as indicated by changes in HRV indices. The usefulness of monitoring changes in HRV to assess cardiac risk using a handheld remote ECG monitor was evaluated. The handheld remote ECG monitor detected the occurrence of QRS complex and calculated short-term HRV indices from ECG recordings. The sensitivity and specificity of the QRS detection to ECG recordings from subjects from MIT-Arrhythmia database were 99.34% and 99.31%, respectively. Changes in HRV indices of ECG recordings of two subjects after a cardiac event and during follow-up recording made a year later were compared. A significant increase in RMSSD, total spectral power and the ratio of low frequency power to high frequency power was observed.

#### 5.2. Introduction

Post MI patients with recurring chest pain and arrhythmia may require periodic monitoring of heart rate variability (HRV) indices to determine cardiac risk. HRV indices calculated from short-term ECG recording can also be used in initial screening of subjects for arrhythmic risk, or as a possible candidate for cardioverter fibrillators. Shortterm HRV indices are also used to monitor changes in the sympatho-vagal balance after medication and exercise.

The electrocardiogram (ECG) is the most important noninvasive diagnostic tool used for assessing the probability of cardiac event, for stratifying its degree (stable, unstable angina, risk of out-hospital or in-hospital death) and for guiding therapy. The duration between adjacent R waves in a normal ECG (sinus rhythm) is termed as normal-to-normal (NN) interval. Heart rate variability (HRV) is the measurement of the variability of NN intervals.

Decreased HRV is a powerful risk stratifier for overall mortality, induced and spontaneous ventricular tachycardia and sudden death following acute myocardial infarction (AMI) [1]. Risk of arrhythmic death was found to be associated with lowered HRV and the presence of ventricular arrhythmia [2]. Low frequency HRV measurement predicted in-hospital complications when measured within 2 days after the AMI [3]. Short-term HRV measures are used in prediction of mortality of patients with chronic heart failure [4]. Frequency domain HRV from short-term recordings (2 to 15 minutes) predicted post-infarction mortality and are used for initial screening of all survivors after an acute MI [1]. HRV based estimators were also used analyze and estimate surgical procedures [5]. Such patients may benefit from anti-arrhythmic therapy or intervention.

Earlier studies [6-8] have shown that remote monitoring from pre-hospital setting results in reduced response time and improved patient outcome. Remote monitoring of ECG is used to assess the probability of cardiac event, stratify risk and to guide therapy. Remote ECG monitoring, performed from a commercial aircraft [9] or an ambulance [10], has also shown promising results. Short-term ECG recordings are sent over public switched telephone network (PSTN) [11], Cellular technologies incorporating global system for mobile communication (GSM) [12] and time division multiple access (TDMA) [13] standards and broadband networks (DSL/Cable) from the remote patient location to the hospital. These devices send ECG data for quick assessment and storage. No analysis is performed on the data nor is feedback provided to the user.

The handheld devices, like personal digital assistants (PDAs), are compact and easy to use with powerful computing capabilities. The PDAs have been used in the medical community to access online medical databases [14], record patient and clinical training data [15] and send ECG data from the ambulance directly to the hospital [16]. However, at present time, these devices do not possess computing capability or the battery life required to perform real-time ECG analysis. Innovative remote signalprocessing and analysis techniques in small sized hospitals have also been implemented [17].

Short-term ECG recordings (15-30 min) can be made at home, physician's office or at small clinics. HRV measures derived from these measurements can be used to identify patients at risk or assess changes after medication or rest. Incorporating monitoring of HRV indices in handheld remote monitor would aid in better assessment of the cardiac condition.

#### 5.3. Methods

#### 5.3.1 Remote Client

The ECG data acquired from local clients (computers/handheld device) was transmitted to a remote server for analysis and storage. ECG data was monitored to assess condition of the patient and for cardiac arrhythmias. The results of analysis were sent back to the client to provide feedback in real-time. An early warning alarm was sounded at local and remote locations in case of potentially dangerous cardiac arrhythmia.

#### 5.3.2 Remote Computing Server

At the remote server, communication modules in Visual Basic 6.0 (Microsoft Corp, Redmond, WA) receive ECG data from the client. QRS complex were detected and HRV indices computed using Matlab (The Mathworks Inc., Natik, MA). The results were sent back to the client (Figure 5.1). Detailed information on the design and implementation of client and remote server can be found in [20].



Figure 5.1. Software model at the remote computation server

The QRS/PVC detection and HRV calculation algorithms are implemented in the Matlab workspace. The results of the analysis are transferred to Visual Basic for display and transmission to remote client.

# 5.3.3 QRS Detection

The automated detection of QRS complexes is important to cardiac disease diagnosis. A good performance of an automatic ECG analyzing system depends heavily upon the accurate and reliable detection of QRS complexes. A QRS detector based on biorthogonal wavelet was implemented. Premature ventricular contraction beats were also identified and their locations stored. QRS information along with heart rate was sent back to the remote monitor. Detailed information on the design and implementation of QRS and PVC detection algorithms can be found in Chapter 3 [18].

#### 5.3.4 Heart Rate Variability

Short-term HRV (5-minute) duration was chosen for time and frequency domain HRV measurements.

- 5.3.4.1 Time Domain Measurements
- (i) SDNN Standard deviation of the NN interval (SDNN) [19],

$$SDNN = \sqrt{\frac{1}{N-2} \sum_{n=2}^{N} (\delta(n) - \overline{\delta})^2}$$
(1)

where  $\overline{\delta}$  is the average NN signal from N beats,

$$\overline{\delta} = \frac{1}{N-1} \sum_{n=2}^{N} \delta(n)$$
<sup>(2)</sup>

The scaling factor is N-2 because there are N-1 intervals in the record and one degree of freedom is used to estimate the mean NN interval. SDNN reflects all the cyclic components responsible for the variability in the period of recording.

(ii) RMSSD – Square root of the mean squared differences of successive NN intervals.

$$RMSSD = \sqrt{\frac{1}{N-2} \sum_{n=3}^{N} [\delta(n) - \delta(n-1)]^2}$$
(3)

#### 5.3.4.2 Frequency Domain Measurements

Power spectral density analysis was used to provide basic information of how power (i.e. variance) distributes as a function of frequency. The frequency indices calculated from short-term recordings are:

- (i) Total spectral power (TP) Power in 0.001-1.5 Hz range.
- (ii) Very Low Frequency (VLFP) Power in 0.001-0.04 Hz range
- (iii) Low Frequency (LFP) Power in 0.04-0.15 Hz range
- (iv) High Frequency (HFP) Power in 0.15-0.4 Hz range

(v) Normalized low frequency: 
$$LF_{norm} = 100 \text{ x} \frac{LF}{TP - VLF}$$
 (4)

- (vi) Normalized high frequency:  $HF_{norm} = 100 \text{ x} \frac{HF}{TP VLF}$  (5)
- (vii) LFP:HFP Low to high frequency power ratio averaged every 5 minutes

Measurements of VLFP, LFP and HFP were made in absolute units (ms<sup>2</sup>), but LFP and HFP may also be measured in normalized units (norm.) which represents the relative value of each component in proportion to the total power minus the VLFP component. The NN data sequence was obtained after removal of ectopic and missing beats. The resulting gaps were filled with an average value computed in the local neighborhood of the missing beat. A linear detrend and applied and resulting data was sampled at 2Hz a moving window curve-fitting algorithm. Power spectral density (PSD) estimation was done using 512-sample FFT by Welsh's periodogram method. The spectral power present in VLF, LF and HF bands was estimated. The details of the implementation of HRV are given in Chapter 4 [20].

#### 5.3.5 Data

The ECG recordings from two subjects (subjects A and B) with their one-year follow-up ECG recording were selected. The ECG recordings were made during a sleep study at School of Nursing, The University of North Carolina at Chapel Hill, Chapel Hill, NC. ECG data segment from 'Subject A' taken after cardiac arrhythmia was 10 minutes long and second segment of the ECG recording taken a year later was of 30 minute duration. The first segment of the ECG recording taken from 'Subject B' was 30 minute long and was taken after the conclusion of cardiac arrhythmia. The second segment of the ECG recording taken a year later. Both subjects no longer had chest-pain or arrhythmias in their follow-up recordings. ECG data collected was the standard lead II sampled at 250 Hz.

# 5.4 Results

The sensitivity and specificity of the QRS detector on normal ECG recordings and ECG recordings with PVCs present is shown in Table 5.1. Detailed information can be obtained from Chapter 3 [18].

Normal ECG		ECG with PVCs	
Sensitivity	Specificity	Sensitivity	Specificity
100.00	99.03	99.64	98.93
100.00	97.53	99.82	97.72
100.00	100.00	99.75	100
100.00	100.00	99.55	98.64
100.00	100.00	96.81	99.59
100.00	100.00	100	100

Table 5.1. Sensitivity and Specificity measurements of QRS detection on normal and arrhythmic ECG recordings.

*Subject A*: Five-minute HRV measurements were calculated on the two data segments. The mean HR was lower in the follow-up (64 vs. 59) and RMSSD (Figure 5.2) showed an increase in the follow-up recording.



Figure 5.2. RMSSD after arrhythmia and during follow-up.

Among the frequency domain measurements, the total spectral power (Figure 5.3) and the LFP:HFP ratio was found to be higher in the follow-up visit.



Figure 5.3. Total spectral power and LFP:HFP ratio after Arrhythmia and during follow-up in Subject A.

An increase in normalized low frequency power was observed in a follow-up visit (0.50 vs. 0.56) and an identical decrease was observed in the normalized high frequency (0.50 vs. 0.44).

*Subject B*: Five-minute HRV measurements were calculated on the two data segments. The mean heart rate was found to be slightly lower during the follow-up (65 vs. 56) and RMSSD (Figure 5.4) showed an increase in the follow-up recording.



Figure 5.4. RMSSD after arrhythmia and during follow-up.

Among the frequency domain measurements, the total spectral power (Figure 5.5) and LFP:HFP ratio was found to be higher during the follow-up visit.



Figure 5.5. Total spectral power and LFP:HFP ratio after arrhythmia and during follow-up in Subject B.

An increase in normalized LF power was observed in follow-up visit (0.56 vs. 0.49) and a similar decrease was observed in the normalized high frequency (0.51 vs. 0.44). The changes in both subjects are summarized in Table 5.2. The highlighted indices

show a statistically significant increase when compared to recordings made after cardiac arrhythmia.

	Subject A	Subject B
Heart Rate	↓ (14%)	↓ (7%)
RMSSD	↑ (21%)	↑ (24%)
VLF (norm)	↑ (39%)	↓ (33%)
LF (norm)	↑ (14%)	↑ (12%)
HF (norm)	↓ (13%)	↓ (12%)
<b>Total Power</b>	$\uparrow$ (31%)	↑ (22%)
LF/HF	$\uparrow$ (30%)	$\uparrow$ (23%)

Table 5.2. Summary of changes during follow-up visit.

#### 5.5 Discussion

Low HRV as early as 24 hour after acute MI has been shown to be useful predictor of cardiac mortality and aids in early risk stratification and therapeutic management of patients [21]. HRV indices have also been used to assess changes in sympatho-vagal influence after administration of nitroglycerine [22] and aprindine [23]. Tsuji et. al. [24] showed the estimation of ambulatory HRV indices from a community based population significantly associated with risk of cardiac event. Short-term HRV indices could also help in identifying congestive heart failure patients, who might benefit from implantable cardioverter fibrillators as a bridge to heart transplant.

Both subjects showed an increase in sympathetic and parasympathetic activation as reflected an increase in the LFP:HFP ratio and RMSSD. The increase in total spectral power in both subjects is usually indicative of improved prognosis as shown in an earlier study [20]. The prognosis was found to be highly subject-dependent and general trends cannot be used to make prognosis.

# 5.6 Conclusions

The predictive value of heart rate variability from short-term recordings is ideally suited for identification of patients with cardiac risk and as a follow-up monitor after medication and exercise. Short-term ECG recordings made from local handheld client at home or small clinics will provide additional impetus for regular cardiac assessment. An individualized criterion for HRV indices was found to provide a better prognosis. For each particular subject we have found only indicative evidence for this and further research needs to be done to substantiate this aim.

# 5.7 References

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#### CHAPTER 6

#### Conclusions

A handheld remote ECG monitor was designed and successfully tested. The handheld remote ECG monitor satisfies all requirements [1] expected of a remote monitor and in addition provided real-time display of ECG and analyzed results. The monitor provides an instantaneous feedback to the user regarding his current cardiac condition. The effectiveness of the monitor was demonstrated on four ECG recordings from the Cu-Tachyarrhythmia database, which have PVC runs leading to ventricular fibrillation. The remote monitor was successfully able to predict the onset of ventricular fibrillation. This increase in response time can lead to timely intervention.

Earlier studies [2-4] suggest that a change in HRV indices, rather that the magnitude or nature of change, facilitates the development of ventricular tachyarrhythmias. Short-term HRV indices were incorporated into the cardiac monitor with the goal of detecting changes in HRV indices, which might enhance early detection capability of the remote ECG monitor. Time domain measures, Heart rate and RMSSD and frequency domain measures TP, HFP and the ratio of LFP:HFP ratio were found to differentiate between the groups. The usefulness of HRV indices to identify early onset of arrhythmia was tested on an ECG recording made of subject during a sleep study. The subject had experienced acute chest pain, which resolved after rest. HRV indices

monitored did not show any significant changes to indicate the onset of arrhythmia. Changes in TP may be attributed to increased sympathetic activity during REM sleep. Further examination of more cases is needed to be done to measure the usefulness of HRV indices in real-time monitoring.

HRV indices have been used in predicting mortality and arrhythmic complications [5]. Short-term HRV indices can be used in initial screening of subject for arrhythmic risk, possible candidate for cardioverter fibrillators and monitor changes in the sympathovagal balance after exercise and medication. Short-term recordings made from remote home or clinics using remote monitor will provide additional impetus for regular monitoring of HRV indices. Remote monitor would make regular HRV monitoring easy and changes in HRV indices after activity or medication can be effectively monitored in patients with pre-existing heart conditions. Changes in HRV indices of ECG recordings of two subjects after a cardiac event and during follow-up recording made a year later were compared. Both subjects showed an increase in RMSSD and total spectral power indicating improved prognosis. This further strengthens the case for personalizing the criteria for individual heart rate variability measures for every subject to provide a more accurate prognosis. For each particular subject we have found only indicative evidence for this and further research needs to be done to substantiate this aim.

The remote monitor has showed good potential for clinical applications. However, HRV indices, though monitored for non-clinical applications, have not been validated for real-time clinical applications. We had shown short-term HRV indices monitored by remote monitor has the potential for real-time applications and can also be used to assess cardiac risk. Display of ECG recording and analyzed results on the client in real-time reduces the stress on the subject and in some cases provides an early alarm.

# 6.1 References

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# Appendix

# **Related Publications**

- 1. Singh SS, Hsiao HS. Internet based infant monitoring system. *Proceedings of 1st joint BMES/EMBS Conference Serving Humanity, Advancing Technology.* IEEE Press. 1999;674.
- 2. Singh SS, Hsiao HS. Infant telemonitoring system. *Proceedings of 25th Annual Conference of IEEE Engineering in Medicine and Biology Society*. IEEE Press. 2003;1354-57
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- 6. Singh SS, Hsiao HS and Carlson B. Development of a Handheld Remote ECG Monitor to Assess Cardiac Risk Based on Changes in Heart Rate Variability. In Preparation.

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