Evaluation of 12-Lead Electrocardiogram Reconstruction Methods for Patient Monitoring

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Evaluation of 12-Lead Electrocardiogram Reconstruction Methods for Patient Monitoring

Evaluatie van 12-afleidingen electrocardiogram reconstructiemethoden voor patiëntbewaking

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Contents

1

Introduction

Background

With the introduction of coronary care units in the late 1950s, electrocardiogram (ECG) monitoring devices were developed to facilitate rapid response to life-threatening arrhythmias in patients with acute myocardial infarction (Julian, 1987; Fye, 1994). Since then ECG monitoring has become widely available in other hospital units, such as intensive care environments, ambulatory telemetry units, operating theatres, and emergency rooms. Starting with basic single-lead registration, ECG monitoring goals have expanded to the detection of complex arrhythmias, identification of prolonged QT intervals, and ST-segment/ischemia monitoring (Drew *et al.*, 2004).

For these extended purposes, multilead ECG monitoring has become a requirement. In recent years, patient monitoring equipment has been developed to facilitate the simultaneous registration and analysis of all leads of the standardized 12-lead ECG. Figure 1.1 contains the electrode placements of the 12-lead ECG on the chest and abdomen.

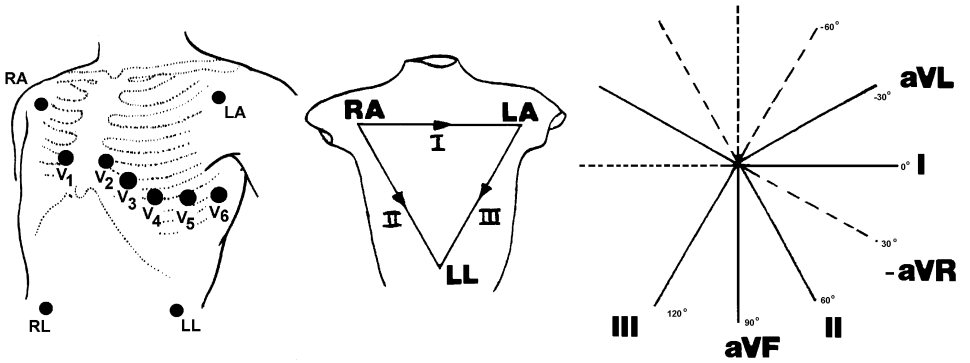
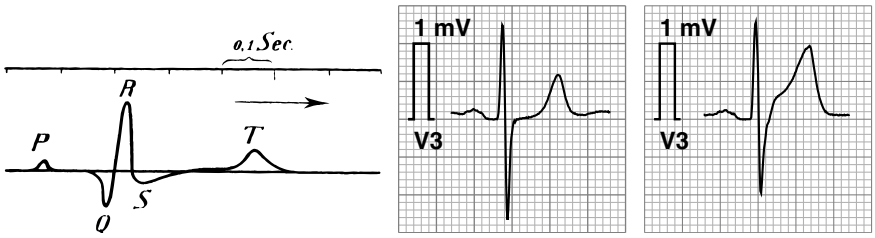


Figure 1.1: Electrode positions of the 12-lead ECG system using proximal placement (Mason-Likar) of electrodes RA, LA, RL, and LL. The left torso depicts all 10 required electrode positions. The torso (middle) and hexial reference diagram (right) depict the leads I, II, III and augmented leads aVR, aVL, and aVF in the frontal plane.

The 12-lead ECG system consists of six frontal plane leads (I, II, III, aVR, aVL, and aVF) and six chest leads (V_1-V_6). Three frontal plane leads are bipolar leads (I, II, and III) and three are augmented leads (aVR, aVL, and aVF). Of these six frontal plane leads, only two leads need to be known to calculate the remaining four. In practice, most ECG equipment only stores leads I and II to save space without loss of information. The remaining leads can be calculated by the equations in 1.1.

$$\begin{aligned} III &= II - I \\ aVR &= -\tfrac{1}{2}(I + II) \\ aVL &= I - \tfrac{1}{2}II \\ aVF &= II - \tfrac{1}{2}I \end{aligned} \tag{1.1}$$

In the 1930s, Wilson *et al.* (1932) introduced a so-called central terminal which made it possible to measure unipolar chest leads. By connecting a 5 kΩ resistor to each terminal of the limb electrodes (RA, LA, and LL), the Wilson central terminal is defined by WCT = $\frac{1}{3}(RA + LA + LL)$. With this reference central terminal, six unipolar chest leads



(a) ECG Complex (b) Rest (c) Ischemia

Figure 1.2: Diagram of an ECG complex with the characteristic P, Q, R, S, and T waves illustrated by Einthoven (1902) (a). The ST segment is located between the end of the S wave (J point) and the start of the T wave. The second ECG complex (b) shows lead V3 of a patient at rest and the right figure (c) shows an abnormal ECG complex with ST elevation during an ischemic episode.

were defined by the American Heart Association (1943). These chest leads were intended as exploratory leads and followed the right to left atria and ventricles. Nowadays, the six chest leads can be obtained simultaneously, but contain redundant information (Lux *et al.*, 1995; Kors and van Herpen, 2002).

An illustration of a single heartbeat with the characteristic P, Q, R, S, and T waves is presented in Figure 1.2a. The P wave and QRS complex reflect the electrical activation of the respective atria and ventricles. The segment between the QRS offset and the end of the T wave reflects the return to the electrical resting state, known as repolarization. The ST segment is a transition from the end of the S wave (J point) to the start of the T wave. Elevation of the ST segment is a distinctive characteristic of myocardial ischemia and injury. Figures 1.2b and 1.2c contain an example of an ECG complex of the same patient prior (b) and during an ischemic episode (c).

Continuous multilead ST-segment monitoring devices have been developed to measure, display, and compare ST-T changes in real-time (Krucoff *et al.*, 1988; Dellborg *et al.*, 1991) for the evaluation of patients with acute coronary syndromes. The most important applications of these devices include: (1) assessment of reperfusion, prolonged ischemia, or re-ischemia after thrombolytic therapy (Veldkamp, 1996; Klootwijk, 1998), (2) detection of reocclusion during and after percutaneous coronary intervention, and (3) detection of transient myocardial ischemia in patients with acute coronary syndromes (Akkerhuis *et al.*, 2001; Pelter *et al.*, 2002).

Continuous ECG registration problems

Long-term, continuous, 12-lead ECG and ST-segment monitoring is often difficult in daily practice. Patient management and the nursing burden is increased in order to maintain a high-quality recording and to reduce false alarms. Several problems related to patient monitoring can be identified:

First, registration of one or more leads may be of low quality because of problems related to the attachment of electrodes. For example, as a result of patient movement, lead wires may not be firmly attached to the electrodes and may distort the recorded

signals. Other sources of noise artifacts may include those caused by muscle movement or poor skin preparation (Schijvenaars, 2000).

Second, certain ECG leads may not be available at all. For example, during and after cardiac surgery often electrodes V_1 and V_2 cannot be attached. Furthermore, when a patient is transferred to a telemetry department, only a limited set of electrodes is available.

Third, patients may turn on their left or right side, which may have a profound effect on QRS and ST-segment measurements (Adams and Drew, 1997; Jernberg *et al.*, 1997), and may lead to false alarms. Moreover, most diagnostic ECG programs assume that the patient is in supine position. This need not be true during continuous monitoring in an intensive care unit.

Fourth, the ECG of an intensive care patient may have been recorded with different extremity electrode positions than the routinely recorded resting ECG (Sevilla *et al.*, 1989; Krucoff *et al.*, 1994; Norgaard *et al.*, 2000). As a result of these different electrode placements, ECG variations may occur in the extremity leads, such as (dis)appearing Q waves, changes in R and ST amplitudes, and shifts in the frontal QRS axis.

Lead reconstruction

Reconstruction of leads may help to address these problems during continuous ECG monitoring. Most lead reconstruction techniques are aimed at synthesizing unavailable or noisy ECG leads by making use of the (inherent) redundancy of information in the 12-lead ECG (Cady, 1969; Levkov, 1987; Lux *et al.*, 1995).

Based on the assumption that cardiac electrical activity can be represented by a dipole model, it is sufficient to measure three orthogonal leads. Over the last 60 years, vectorcardiographic (VCG) lead systems have been based on this assumption with the Frank lead system being the most widely used. The vectorcardiogram has been used for diagnostic interpretation (Kors *et al.*, 1990), exercise testing (Simoons *et al.*, 1975), and continuous ST monitoring (Dellborg *et al.*, 1991). The VCG to 12-lead ECG conversion by Dower's transformation (Dower *et al.*, 1980) has shown that the 12-lead ECG can be reconstructed in good approximation. Therefore, fewer selectively chosen leads may still contain enough diagnostic information to represent the full 12-lead ECG.

Several investigators have reconstructed the VCG by taking a subset of the 12-lead ECG: II, V_2, V_6 (Kors *et al.*, 1986), aVF, V_2, V_6 (Bjerle and Arvedson, 1986) and I, II, V_2 (Kors *et al.*, 1990). Earlier work also concentrated on synthesizing the 12-lead ECG from the Frank VCG (Dower *et al.*, 1980; Smith *et al.*, 1975). Recently, Dower *et al.* (1988) introduced a modified Frank VCG consisting of only five electrodes (EASI), from which the 12-lead ECG can be derived. The other way around, synthesizing the VCG from the 12-lead ECG, has also been explored (Levkov, 1987; Edenbrandt and Pahlm, 1988). Almost all of these methods use a general transformation matrix. The disadvantage of a general transformation matrix is that the reconstructed ECG may not be valid for all patients.

To overcome differences among patients, patient-specific transformation matrices have also been used, first by Cady (1969), followed by Scherer *et al.* (1989). This method requires a reference 12-lead ECG for each patient and calculations of a transformation matrix for each individual patient.

Overview

The aims of this thesis were to investigate, develop, and clinically validate lead reconstruction algorithms using reduced lead sets of the 12-lead ECG and to address continuous ECG registration problems which may occur as a result of changes in body position and differences between standard versus monitoring lead configurations.

Part I: ECG reconstruction

The first part of the thesis (Chapters 2, 3, and Appendix A) describes the design and evaluation of the ECG reconstruction methods based on subsets of the leads. The following questions were asked during the design and evaluation phase:

1 *How many leads and which lead subset should be used for accurate reconstruction of the 12-lead ECG?*
The questions of how many and which leads to use are addressed in Chapter 2. The reconstruction method is described and is evaluated on a large data set of 10-second, 12-lead ECGs. For each 12-lead ECG, precordial leads were systematically removed. These absent precordial leads were reconstructed with the remaining limb and precordial leads. Reconstruction performance was assessed by correlation coefficients and root mean square errors between the original and reconstructed leads.

2 *Which method is preferred: general or patient-specific reconstruction?*
The study in Chapter 2 contains a comparison of general coefficients based on a learning set and patient-specific coefficients calculated from a previously recorded 12-lead ECG of the same patient.

3 *How accurate are derived lead systems over time?*
Chapter 3 presents a study which investigates whether the general and patient-specific reconstruction methods are influenced by time. For this purpose, ECG registrations from a 24-hour ischemia monitoring study were used and split in an equally-sized learning and test set. General and patient-specific reconstruction coefficients were computed and applied on the ECGs in the test set at various time instants during the recording period.

Part II: Clinical evaluation

The second part of the thesis, comprising Chapters 4-6, presents three validation studies in which the general and patient-specific reconstruction methods are applied in a clinical setting. The following issues were considered for clinical validation and application:

4 *How accurate are the reconstruction methods in a clinical setting?*
In Chapter 4, the general and patient-specific reconstruction methods are validated in recordings of patients undergoing a percutaneous coronary intervention procedure. During these procedures balloon inflations were performed, which may cause ischemia and ST-T changes on the ECG. Accuracy is assessed on the ST differences between the original and reconstructed leads.

5 *Application of a reduced lead set for pre-hospital triage*
In Chapter 5, the general reconstruction method is applied to pre-hospital decision making on patients with symptoms of acute myocardial infarction. In this setting, a reduced number of electrodes and easy to find locations may save time.

6 *Comparison of different derived 12-lead methods*
Chapter 6 describes a study which compares the general and patient-specific reconstruction methods with a widely used commercially available reduced lead system, the EASI system. The 12-lead ECG and the three reduced lead systems (EASI, general, and patient-specific) are simultaneously recorded during PCI procedures. Accuracy between the methods and the original registration is assessed with correlation coefficients, root mean square errors, and ST-segment differences prior and during balloon inflations.

Part III: Patient monitoring

In the last part of the thesis (Chapters 7 and 8) methods for detection and correction of ECG-variations caused by body position changes and different electrode placements are investigated.

7 *ECG variations caused by body position changes*
Chapter 7 presents methods to detect and correct for body position changes which may occur during long-term ECG monitoring. Using a data set of known body positions and the 12-lead ECG, a detector is presented. A body position correction method with general and patient-specific reconstruction techniques is also evaluated.

8 *Correction of ECG variations due to non-standard electrode positions*
The standard limb lead placement of the 12-lead ECG at the wrists and ankles is often not applied in continuous ECG monitoring environments. Instead, the limb electrodes are often placed at the Mason-Likar positions (Mason and Likar, 1966). However, these electrode changes may produce changes on the registered ECG as compared to an ECG recorded with standard positions, making serial comparison difficult or even impossible. Chapter 8 presents a study to quantify the effects of these alternative electrode placements and evaluates a detection and correction method.

Discussion, summary, and conclusions

A discussion of these investigations, conclusions, and recommendations for future work are presented in Chapter 9.

Part I

ECG Reconstruction

2

Minimal Lead Sets for Reconstruction of 12-Lead Electrocardiograms

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Reprinted from *Journal of Electrocardiology;33: 163–166,*

As part presented at ISCE 2000, Yosemite, CA, USA

Abstract

Background

It may not always be possible to record all precordial leads of the standard 12-lead electrocardiogram (ECG). Especially in monitoring situations, a minimal lead set from which the 12-lead ECG can be reconstructed, would be valuable. In this study we assessed how well absent precordial leads could be synthesized from the remaining leads of the 12-lead ECG.

Methods

A total of 2372 diagnostic 12-lead ECG recordings were obtained from subjects with chest pain suggestive of acute myocardial infarction. The Modular ECG Analysis System was used to compute representative average beats. The recordings were divided into a learning set and a test set. We considered all lead sets with one or more precordial leads removed, but always including limb leads I and II. Using the learning set, general reconstruction coefficients were computed to synthesize the missing precordial leads in each lead set. Performance of the synthesis was assessed by correlation coefficients between the original and the reconstructed leads. Also, patient-specific reconstruction coefficients were derived for each ECG in the test set and correlations were determined.

Results and conclusions

High correlation coefficients were found with both reconstruction techniques. For different sizes of lead sets, the best patient-specific reconstructions had higher correlation values than the general reconstructions. For example, when two precordial leads were excluded, the best patient-specific median correlation was 0.994 compared to 0.963 for the best general reconstruction correlation. General reconstruction allows synthesis of two or three excluded precordial leads in good approximation. When patient-specific reconstruction can be applied, a minimal lead set including the limb leads and only two precordial leads suffices.

Introduction

Recording all leads of the standard 12-lead electrocardiogram (ECG) may be impractical or even impossible. In critical care or emergency situations, a continuous 12-lead ECG monitoring device may not always be available. In intensive care situations, electrodes might fall off, sometimes unnoticed because of time-demanding other activities. Some electrodes also need to be removed when diagnostic tests such as echocardiograms or X-rays are required. It may also be impossible to place electrodes because bandages or drains occupy the electrode position.

It is well-known that the eight independent leads of the 12-lead ECG contain redundant information (Cady, 1969; Lux *et al.*, 1995). It should therefore be possible to reconstruct the 12-lead ECG accurately from a subset of leads. In this study, we want to assess for all lead subsets how well the 12-lead ECG can be reconstructed and which subset of a given size is best.

Methods

Study population

From January 1992 until April 1994, 2484 subjects with chest pain suggestive of myocardial infarction in the Rotterdam municipal area were evaluated by the general practitioner and subsequently referred to the hospital for specialized cardiological care (Grijseels, 1996; Grijseels *et al.*, 1996). A 10-second, diagnostic 12-lead ECG was recorded on the spot.

A total of 2484 ECGs were digitally recorded with a small portable battery-powered computer ECG device (Sicard P+, Siemens Elema, Sweden). The ECG electrodes were mounted on a rubber mat with the extremity electrodes positioned at the shoulder and abdomen to ensure rapid placement of electrodes.

The digital 10-second ECG recordings were analyzed with the Modular ECG Analysis System (van Bemmel *et al.*, 1990). ECGs with electrode reversals and recording problems were excluded (n=112). Representative average beats were computed for every included ECG. For further analyses, samples were taken from the QRS-T interval of each lead. The QRS-T interval was selected because this time interval represented information (such as a possible Q wave, the ST segment, and T wave) that was important to synthesize correctly.

ECG reconstruction

The remaining 2372 recordings were divided into a learning set and test set of equal size. We considered all lead sets with one or more precordial leads removed. The independent limb leads I and II were always included. Thus, a total of 62 lead sets were examined.

We differentiated between a general, population-based synthesis and a patient-specific synthesis. Reconstruction coefficients were derived by linear regression. We also synthesized leads with patient-specific reconstruction coefficients that were derived for each recording separately.

Reconstruction accuracy was evaluated on the test set. A reconstructed lead was synthesized for each missing lead in a particular lead set. To quantify the degree of similarity between the original and synthesized lead, we computed Pearson's correlation coefficient. For each case, a performance measure was computed by averaging the correlation coefficients of the reconstructed leads. The median of these averaged correlations for a particular lead set was used to determine the best among lead sets of a given size.

Results

Median (inter-quartile range) correlation results of all lead subsets for general and patient-specific reconstruction methods are shown in Figure 2.1. High performances were obtained with lead sets missing one or two precordial leads. Table 2.1 contains the best lead subsets of a given size.

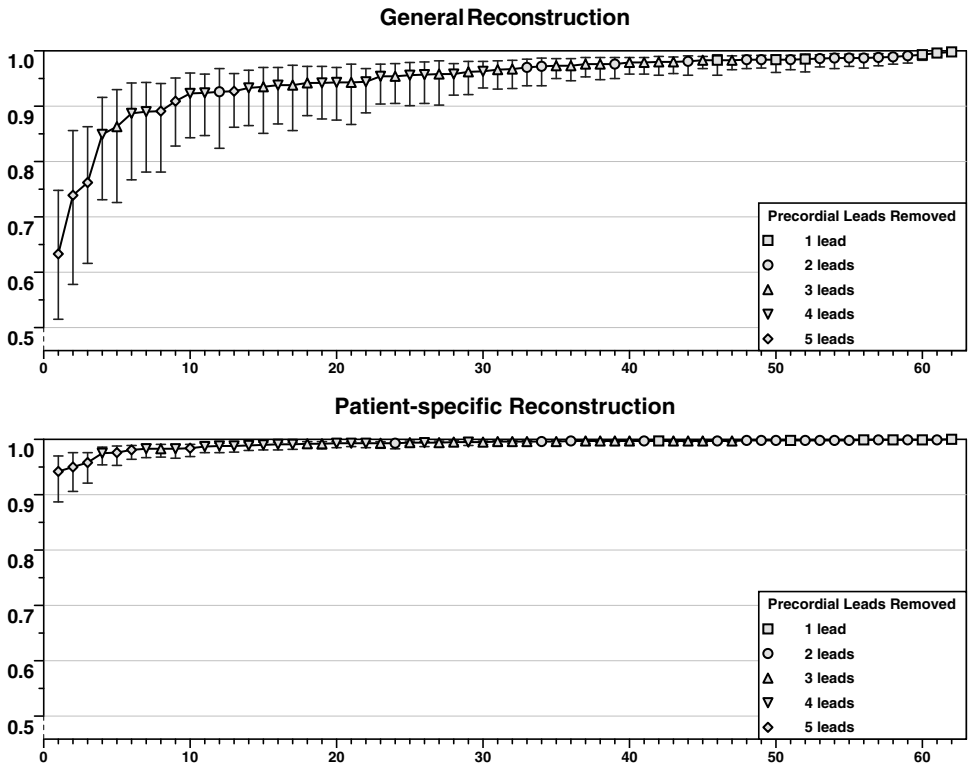

Figure 2.1: Median (inter-quartile range) correlation coefficients of 62 lead sets with one or more precordial leads removed for general (top) and patient-specific reconstruction (bottom).

General synthesis performed overall lower than the patient-specific. There was no difference between the synthesis methods in lead sets of a given size, except for the lead sets with two leads removed. In this case, the second best lead set of one reconstruction method was the same as the best lead set of the other. Overall, differences in correla-

Table 2.1: Correlations and leads of the best lead subsets of a given size of general and patient-specific reconstructions.

Number of Precordial Leads Removed	Correlation *		Lead Set	
	General	Patient-specific	General	Patient-specific
1	0.995 (0.986 – 0.998)	0.999 (0.999 – 1.0)	I, II, V_1, V_2, V_3, V_4, V_6	I, II, V_1, V_2, V_3, V_4, V_6
2	0.988 (0.966 – 0.994)	0.999 (0.997 – 0.999)	I, II, V_1, V_2, V_4, V_6	I, II, V_1, V_2, V_4, V_6
3	0.977 (0.952 – 0.988)	0.997 (0.994 – 0.999)	I, II, V_1, V_3, V_5	I, II, V_1, V_3, V_5
4	0.964 (0.934 – 0.979)	0.994 (0.988 – 0.996)	I, II, V_2, V_5	I, II, V_2, V_5
5	0.912 (0.858 – 0.950)	0.978 (0.964 – 0.988)	I, II, V_2	I, II, V_2

** Correlation values denote median (inter-quartile range)*

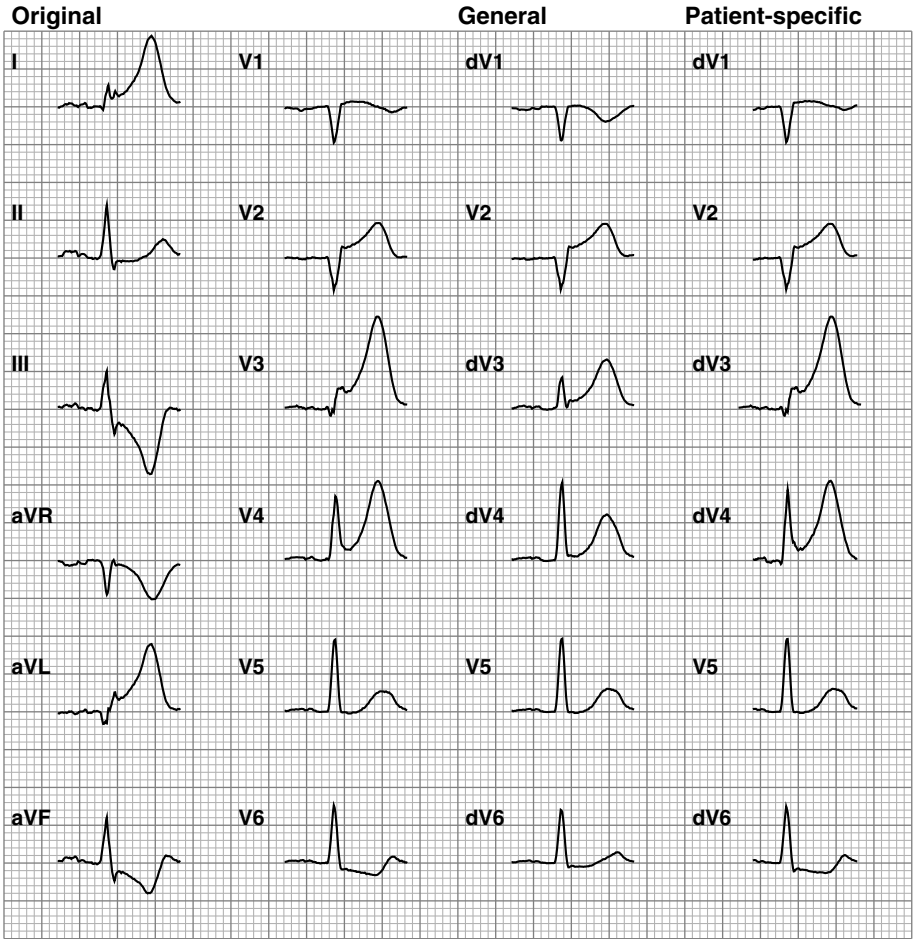

Figure 2.2: Example of general and patient-specific reconstruction of leads V_1, V_3, V_4, and V_6 with a lead subset of I, II, V_2, and V_5.

tion between lead sets of the same size were small. However, this difference gradually increased in lead sets containing fewer precordial leads.

For general reconstruction, a performance decrease was observed when more than three precordial leads were removed. For the patient-specific method, a similar decrease was seen after removal of more than four precordial leads.

An example of general and patient-specific reconstruction is shown in Figure 2.2. The first and second columns contain the averaged beats of the original 12-lead ECG recording. In the third and fourth column, the precordial leads V_1, V_3, V_4, and V_6 have been reconstructed from the lead subset I, II, V_2 and V_5. In this example, the general reconstruction performance was 0.946, while the patient specific reconstruction performance was 0.987.

The reconstruction and evaluation procedure was repeated again with samples of the QRS interval instead of the whole QRS-T interval, but this led to a slight decrease in performance.

Discussion

In this study, missing leads can be reconstructed in good approximation. With general reconstruction coefficients, performance of lead sets with two or three missing precordial leads remained high, while near perfect correlations were found when only one precordial lead was excluded. When patient-specific reconstruction was used, a lead set including the limb leads and only two precordial leads appeared sufficient.

Patient-specific reconstruction has an overall higher performance than general reconstruction. However, patient-specific reconstruction may not always be possible, because it requires a baseline 12-lead ECG from which the reconstruction coefficients can be calculated.

General reconstruction is only valid if the used precordial electrodes are placed on the standard electrode positions. With patient-specific reconstruction, this requirement may be less strict. A valid reconstruction is still likely if the remaining electrodes stay on the same position as to when the baseline ECG was taken.

The patient-specific 3-lead set (I, II, and V_2) recommended by Scherer *et al.* (1989) for 12-lead ECG reconstruction was also the best lead set in our general and patient-specific synthesis. However, we saw a substantial increase in performance between a 3-lead set and a 4-lead set in general and patient-specific reconstruction. For both methods, the best set with four leads contained a left- and right-precordial lead. In another investigation (Cady, 1969), leads V_2 and V_6 were recommended, while in this study V_2 and V_5 had the best performance results.

A different approach of dealing with the impracticalities imposed by the 12-lead ECG system is to use a lead system that requires fewer and more conveniently located electrodes. One such lead system is the EASI lead system (Dower *et al.*, 1988), which uses a 3-lead (five electrodes) configuration of which three electrode positions have been based on the Frank lead system. A derived 12-lead ECG can be calculated from the three EASI leads and empirically obtained reconstruction coefficients (Dower *et al.*, 1988). Drew *et al.* (1999) have shown that the diagnostic information in the derived and original 12-lead ECG is comparable, even though there is still individual variation between the lead signals (Levkov, 1987). The best minimal lead sets in this study use only a few more electrodes (seven electrodes) than the EASI lead system, but all limb leads and at least one precordial lead still remain original. However, further investigation is needed to evaluate both lead set strategies in a similar setting, possibly during simultaneous registration.

In this study, we did not investigate the accuracy of patient-specific reconstruction over time. Scherer *et al.* (1989, 1992) emphasize that their coefficients remain valid, but it is unknown if synthesis performance is maintained during interventions or events such as thoracic surgery and ischemic episodes. Furthermore, the reconstruction coefficients are also sensitive to the quality of the baseline ECG recording. Noisy leads may have a detrimental effect on subsequent reconstruction.

Conclusion

Reconstruction of missing precordial leads in the 12-lead ECG is possible based on the redundant information that is available in the remaining leads. The precordial leads of the 12-lead ECG can still be accurately synthesized with general reconstruction coefficients when two or three precordial leads are removed. Patient-specific reconstruction yields high performances even with four precordial leads removed, but requires a full 12-lead baseline ECG.

3

Reconstruction of the 12-Lead Electrocardiogram from Reduced Lead Sets

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Reprinted from *Journal of Electrocardiology;37:11-18,*

As part presented at the ESC 2002, Berlin, Germany

Abstract

Background

In clinical practice, continuous recording of all leads of the 12-lead electrocardiogram (ECG) is often not possible. We wanted to assess how well absent, noisy, or defective leads can be reconstructed from different lead subsets and how well lead reconstruction performs over time.

Methods

A data set of 234 24-hour ECG recordings was divided into an equally sized training and test set. Precordial leads were systematically removed, and for all lead subsets including the limb leads and at least one precordial lead, the absent leads were reconstructed using general and patient-specific reconstruction templates. Reconstruction performance was measured by correlation between the original and reconstructed leads over the QRS and T waves, by average and maximum absolute ST differences, and by agreement when a clinical decision rule was applied. Reconstruction performance over time was evaluated at baseline, at 20 minutes, and 1, 6, 12, and 24 hours after the start of each recording.

Results

Reconstruction accuracy was high (correlation ≥ 0.932, average ST difference ≤ 30 μV, agreement $\geq 94.9\%$) with general reconstruction for lead sets with one or two precordial leads removed but was less satisfactory when more leads were missing. Patient-specific reconstruction performed well when up to 4 precordial leads were removed (correlation ≥ 0.967, average ST difference ≤ 26 μV, agreement ≥ 95.7 %). Patient-specific reconstruction performance initially slightly decreased and then stabilized over time but remained much better than general reconstruction after 24 hours.

Conclusion

Accurate reconstruction of the 12-lead ECG from lead subsets is possible over time. General reconstruction allows reconstruction of one or two precordial leads, whereas up to four leads can be reconstructed well using patient-specific reconstruction.

Introduction

Continuous monitoring of the 12-lead electrocardiogram (ECG) is a practical, sensitive, noninvasive tool for detection and quantification of myocardial ischemia and infarction (Klootwijk *et al.*, 1997; Drew and Krucoff, 1999; Thygesen *et al.*, 2000). However, recording of all leads of the standard 12-lead electrocardiogram may be cumbersome, impractical, or even impossible. For example, electrodes may need to be removed when certain diagnostic tests such as echocardiograms are required. If bandages or drains occupy the electrode positions, it will be impossible to record the corresponding leads. In telemetry situations, only a subset of leads is currently recorded because of practical and technical limitations. Moreover, electrodes may fall off, sometimes unnoticed because of time-demanding other activities.

Reconstruction of the 12-lead ECG in these situations is desirable particularly for continuous ischemia monitoring and may be possible by making use of the redundant information in the eight independent leads of the 12-lead ECG (Cady, 1969; Lux *et al.*, 1995; Nelwan *et al.*, 2000). In this study, we assessed how well the 12-lead ECG can be reconstructed from different lead subsets and how well lead reconstruction performs over time.

Methods

Data set

Experiments were done on a data set consisting of 236 continuous 12-lead ECG recordings from patients enrolled in the PURSUIT ECG ischemia monitoring study (PURSUIT Trial Investigators, 1998). In summary, patients were eligible if they presented within 24 hours of an episode of ischemic chest pain (>10 minutes) and had transient ST-segment elevation (>50 μV), transient or persistent ST-segment depression (>50 μV), T-wave inversion (>100 μV), or elevation of the creatine kinase-MB fraction above the upper limit of normal. The study protocol excluded patients with persistent (>30 minutes) ST-segment elevation and those with ECG abnormalities interfering with ST-segment interpretation, such as left bundle branch block, third-degree atrioventricular block, persistent arrhythmias, or pacemakers. There were no restrictions regarding age.

Patients were monitored for 24 hours with a continuously updated 12-lead ECG recording system (Mortara Instruments, Milwaukee, WI). The extremity electrodes were placed in monitoring positions at the Mason-Likar locations (Mason and Likar, 1966). The system computed median ECG complexes of the 12 leads every 20 seconds, and an ECG was stored every five minutes.

Electrocardiographic processing

The ECG recordings were manually scanned and edited for artifacts and detection errors. Two recordings were excluded because of recording problems in one or more leads. The remaining 234 recordings contained 5796 hours of data. The median duration of a recording was 24 hours with an inter-quartile range of 10 hours. For each recording, median complexes were obtained at baseline, at 20 minutes, and 1, 6, 12, and 24 hours after the start of the recording.

Lead reconstruction

We generated all lead subsets of the eight independent ECG leads (I, II, V_1-V_6), always including limb leads I and II, and at least one precordial lead. Thus, a total of 62 different reduced lead sets were evaluated.

The ECG recordings were randomly divided into a learning set and a test set of equal size. For each lead subset, general reconstruction coefficients to synthesize the absent leads were derived from the baseline ECGs in the learning set using linear regression (Levkov, 1987; Nelwan *et al.*, 2000). These coefficients were subsequently applied to the ECGs of the test set. Patient-specific coefficients were derived from each baseline ECG in the test set. These reconstruction coefficients were applied to the ECGs at baseline, 20 minutes, and 1, 6, 12, and 24 hours after the start of the recording.

ECG analysis

For each lead subset, reconstruction accuracy of the missing leads was evaluated on three different levels. First, overall waveform similarity for each ECG was assessed by averaging, over the reconstructed leads, the correlations between the originals and their reconstructions. The correlations were based on all samples in the QRS-T complex.

Second, reconstruction accuracy was determined for a clinically important measurement, the amplitude of the ST segment at 60 milliseconds after the J point (ST_{60}). We determined the average of the absolute differences between the original and reconstructed ST_{60} amplitudes. In addition, the maximum absolute difference at ST_{60} was determined.

Third, reconstruction accuracy was assessed at the diagnostic level. We applied a clinically accepted decision rule for detection of myocardial ischemia and evolving myocardial infarction (Thygesen *et al.*, 2000) to the original ECG and to the reconstructed ECG and determined the agreement defined as the percentage number of cases in which decisions concurred. The decision rule holds true when two or more contiguous leads show ST elevations of ≥ 200 μV in leads V_1, V_2, or V_3, or ≥ 100 μV in the other leads (Thygesen *et al.*, 2000).

Results

The median (inter-quartile range) of maximum ST_{60} deviation of the baseline ECGs was 105 (70–145) μV in the learning set and 100 (67–188) μV in the test set. Six ECGs in the learning set and eight ECGs in the test set were found positive according to the decision rule (Thygesen *et al.*, 2000) at baseline.

Tables 3.1-3.3 show the median and range of the general and patient-specific results of lead subsets of a given size on the baseline recordings of the test set. Patient-specific reconstruction performed better than general reconstruction. For general reconstruction, median correlations of 0.932 or higher were obtained for lead subsets with one or two precordial leads removed; considering the best lead subsets, removal of even three precordial leads yielded similar high correlations. With patient-specific reconstruction, lead subsets with four precordial leads removed had median correlation coefficients of 0.967. The best lead subset with five precordial leads removed still had a correlation of at least 0.921.

The average and the maximum absolute ST-amplitude differences for general reconstruction were about twice as high as the differences for patient-specific reconstruc-

Table 3.1: Median (range) correlation results of general and patient-specific reconstruction methods on the baseline ECGs of the test set (n=117), for lead sets with an increasing number of precordial leads removed.

Number of Precordial Leads Removed	Correlation Coefficient	
	General	Patient-specific
1	0.988 (0.966 – 0.995)	0.999 (0.994 – 0.999)
2	0.978 (0.932 – 0.988)	0.998 (0.991 – 0.999)
3	0.965 (0.844 – 0.977)	0.995 (0.980 – 0.997)
4	0.938 (0.807 – 0.964)	0.989 (0.967 – 0.994)
5	0.854 (0.642 – 0.912)	0.964 (0.921 – 0.978)

Table 3.2: Median (range) ST_{60} differences of general and patient-specific reconstruction methods on the baseline ECGs of the test set (n=117), for lead sets with an increasing number of precordial leads removed.

Number of Precordial Leads Removed	Absolute ST_{60} Difference (μV)			
	General		Patient-specific	
	Average	Maximum	Average	Maximum
1	15 (10 – 19)	15 (10 – 19)	7 (6 – 9)	7 (6 – 9)
2	16 (13 – 30)	32 (18 – 40)	8 (7 – 11)	12 (10 – 16)
3	20 (16 – 48)	31 (28 – 78)	10 (8 – 24)	17 (13 – 57)
4	24 (18 – 51)	43 (34 – 89)	13 (9 – 26)	24 (18 – 45)
5	37 (26 – 48)	66 (46 – 93)	24 (16 – 33)	47 (29 – 64)

tion. By and large, general reconstruction results for a lead subset of a given size were comparable with patient-specific results for a subset with two more precordial leads removed. For example, using general reconstruction, the average absolute ST difference for lead subsets with two precordial leads removed had a median (range) of 16 (13–30) μV, whereas patient-specific reconstruction for lead subsets with four leads removed gave differences of 13 (9–26) μV.

For the clinical decision rule, high to very high median agreements were obtained for any lead subset of a given size using both general and patient-specific reconstruction. In lead subsets with less than five precordial leads removed, the best lead subsets of a given size had a maximum agreement of 100%, regardless of the reconstruction method.

The best lead subsets with the highest correlation of a given size are presented in Table 3.4. The same subsets were almost always the ones with the lowest average and maximum absolute ST difference. When only one or two precordial leads were removed, several subsets showed a performance almost identical to the best subset. The second

Table 3.3: Accuracy results of general and patient-specific reconstruction methods on the baseline ECGs of the test set (n=117), for lead sets with an increasing number of precordial leads removed.

Number of Precordial Leads Removed	Accuracy (%)	
	General	Patient-specific
1	100 (95.7 – 100)	100 (99.1 – 100)
2	100 (94.9 – 100)	100 (97.4 – 100)
3	96.6 (94.9 – 100)	99.1 (95.7 – 100)
4	95.7 (91.5 – 100)	98.3 (95.7 – 100)
5	94.5 (93.2 – 96.9)	96.4 (94.1 – 99.1)

Table 3.4: Best lead subsets of a given size based on the highest average correlations found in the baseline ECG recordings of the test set.

Number of Precordial Leads Removed	Best Lead Set	Correlation	
		General	Patient-specific
1	I, II, V_1, V_2, V_3, V_4, V_6	0.995 (0.986 – 0.998)	0.999 (0.999 – 1.0)
2	I, II, V_1, V_2, V_4, V_6	0.988 (0.966 – 0.994)	0.999 (0.997 – 0.999)
3	I, II, V_1, V_3, V_5	0.977 (0.952 – 0.988)	0.997 (0.994 – 0.999)
4	I, II, V_2, V_5	0.964 (0.934 – 0.979)	0.994 (0.988 – 0.996)
5	I, II, V_2	0.912 (0.858 – 0.950)	0.978 (0.964 – 0.988)

Note: Correlation values denote median (inter-quartile range)

best lead set with three precordial leads removed was the other set with non-adjacent precordial leads (V_2, V_4, V_6), performing nearly as well as the best lead set (V_1, V_3, V_5). In lead sets with four precordial leads removed, the combination of V_2 and V_6 was second best, whereas in lead sets with five precordial leads removed, V_2 performed clearly better than other leads.

Performance of general and patient-specific reconstruction over time was evaluated on the test set for the best lead sets presented in Table 3.4. Figure 3.1 shows a typical example of lead reconstruction at baseline and after 24 hours using lead subset I, II, V_2, and V_5. Note the better performance of patient-specific reconstruction as compared to general reconstruction, both in a global sense and in preserving the ST elevations after 24 hours.

Figure 3.2 presents medians and inter-quartile ranges of the average correlation between the original and reconstructed leads at baseline and at 20 minutes, 1, 6, 12, and 24 hours. Similarly, Figures 3.3 and 3.4 present medians and inter-quartile ranges of the

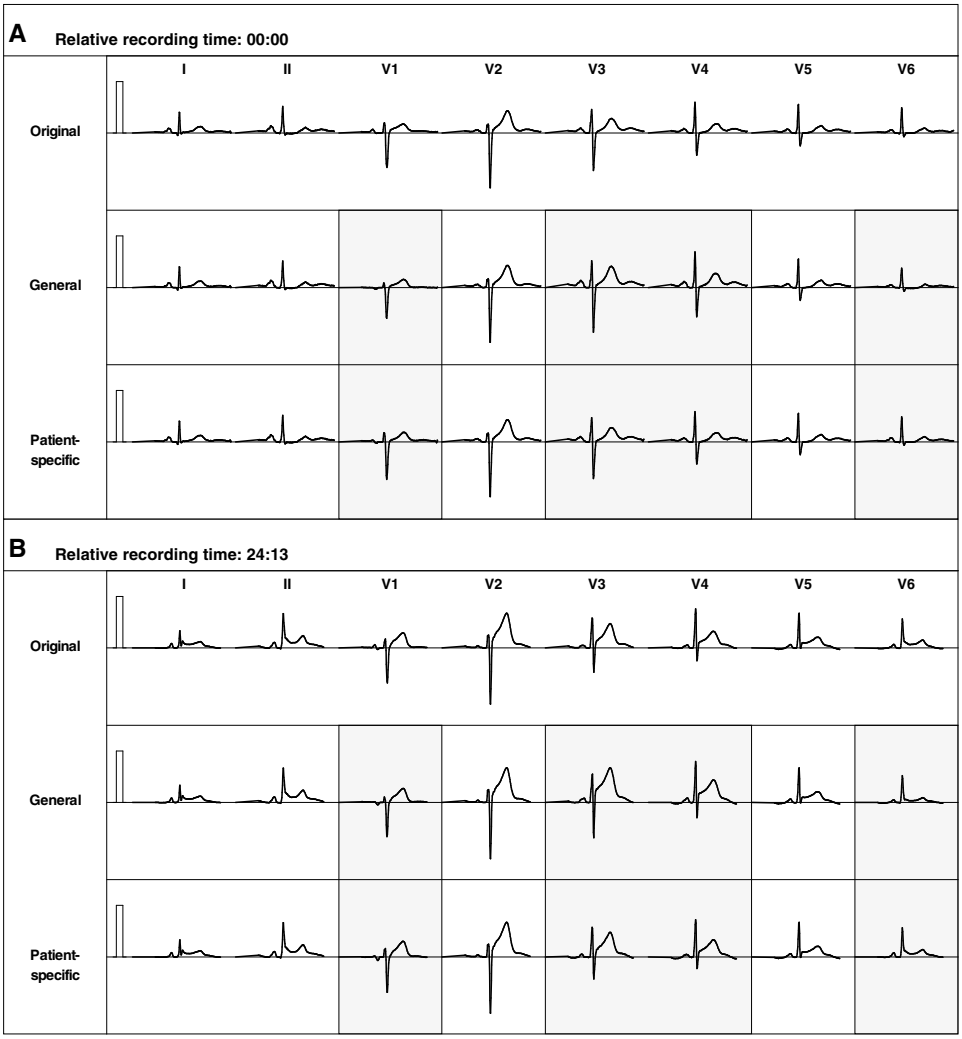

Figure 3.1: Example of general and patient-specific reconstruction of ECG leads at baseline (a) and after 24 hours (b) using lead subset I, II, V_2, and V_5. Shaded areas mark the leads that were reconstructed.

average and maximum absolute ST-amplitude differences, respectively. Patient-specific reconstruction performed better than general reconstruction over the whole recording period. General reconstruction remained at the same level over time, while patient-specific reconstruction showed some decrease in performance. Figures 3.2b, 3.3b and 3.4b suggest an initial worsening of performance, which stabilizes after a few hours. A possible explanation is that the first ECG was used to compute the patient-specific coefficients and may have yielded higher correlations than ECGs at a later time. Additional inspection of the correlations at all time instants (data not shown) revealed large variations between neighboring time instants and showed an overall stabilizing pattern.

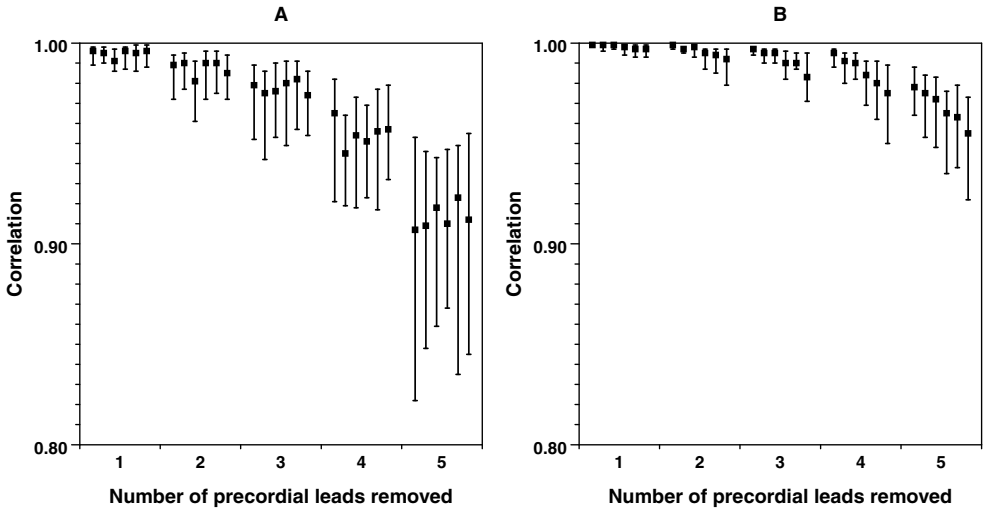

Figure 3.2: Median (inter-quartile range) of the average correlations between original and reconstructed waveforms using general reconstruction (a) and patient-specific reconstruction (b) of the best lead sets (cf. Table 3.4). For each lead set, bars indicate results at baseline, and at 20 minutes, and 1, 6, 12, and 24 hours after baseline (from left to right).

The decision rule for detection of ischemia and evolving infarction (Alpert *et al.*, 2000) was also applied for each lead subset on the ECGs over time. For lead subsets with up to three precordial leads removed, average agreement was 99.8% (range 99.1–100) regardless of reconstruction method. Overall, agreement remained. For lead subsets with four and five leads removed, average agreement using general reconstruction was 95.9% (91.9–100) and 94.3% (92.3–94.9), respectively. For patient-specific reconstruction, average agreement was 98.1% (96.6–100) and 97.3% (94.9–99.1).

Discussion

In this study, we investigated how well the 12-lead ECG can be reconstructed from different lead subsets. Both general and patient-specific reconstructions were evaluated on a well-defined set. General reconstruction allows accurate reconstruction of one or two missing precordial leads, while up to three to four precordial leads can be reconstructed well by patient-specific reconstruction parameters. Reconstruction of the 12-lead ECG over time remained accurate using general and patient-specific reconstruction. In all cases, patient-specific reconstruction performance was better than general reconstruction performance.

Practical application

ECG reconstruction can be used in the field of continuous monitoring (intensive care, telemetry or step-down intermediate care), where it can be integrated in clinical practice by the nurse or technician with minimal effort. For general reconstruction, electrodes can be placed on the well-known 12-lead positions except for those leads that need to

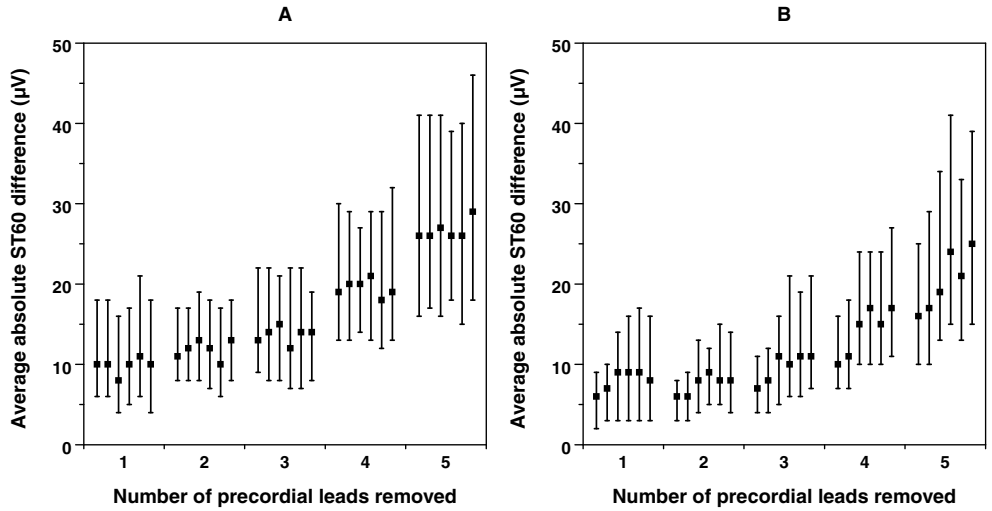

Figure 3.3: Median (inter-quartile range) of the average absolute ST_{60} difference between original and reconstructed waveforms using general reconstruction (a) and patient-specific reconstruction (b) of the best lead sets (cf. Table 3.4). For each lead set, bars indicate results at baseline, and at 20 minutes, and 1, 6, 12, and 24 hours after baseline (from left to right).

be reconstructed. By using a previously recorded ECG, patient-specific coefficients can be computed and reconstruction can be improved. From a technical point of view, the reconstruction algorithms require less than a few milliseconds with modern equipment and can easily be implemented by vendors of medical equipment.

Lead reconstruction

Our findings of the general reconstruction corroborate with previous investigations (Cady, 1969; Scherer *et al.*, 1989; Drew *et al.*, 2002). In our study, the best 4-lead subset consisted of leads I, II, V_2, and V_5. Cady (1969) found the best performance for leads V_2 and V_6, which was second best in our study. Our best 3-lead subset consisted of I, II, and V_2, which was also recommended by Scherer *et al.* (1989). However, 4-lead subsets performed substantially better than 3-lead subsets, both using general and patient-specific reconstruction.

The 5-lead subsets with the highest reconstruction performances were clearly better than other sets of the same size. A possible explanation for these results is that these subsets form a quasi-orthogonal set of leads, representing the vectorcardiographic X, Y, and Z leads that describe the heart vector. Previous work has shown that the 12-lead ECG can be reconstructed from the vectorcardiogram in good approximation (Kors *et al.*, 1986; Bjerle and Arvedson, 1986).

In a previous preliminary investigation (Nelwan *et al.*, 2000), we applied 12-lead reconstruction techniques on 10-second ECGs from subjects with chest pain suggestive of myocardial infarction. Performance was assessed by morphology correlation coefficients only. Results are comparable to those obtained for the baseline ECGs in the present study. When we used the general reconstruction coefficients from the other study (Nel-

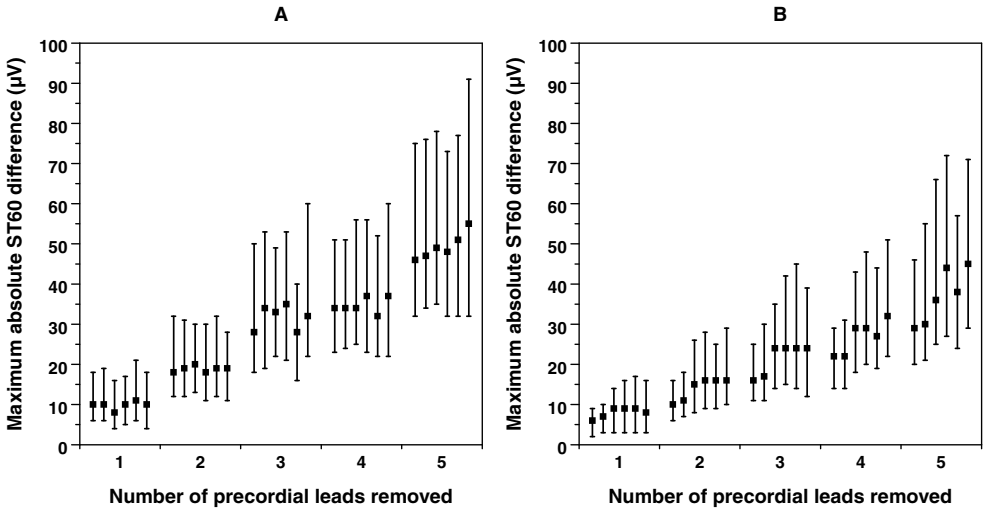

Figure 3.4: Median (inter-quartile range) of the maximum absolute ST_{60} difference between original and reconstructed waveforms using general reconstruction (a) and patient-specific reconstruction (b) of the best lead sets (cf. Table 3.4). For each lead set, bars indicate results at baseline, and at 20 minutes, and 1, 6, 12, and 24 hours after baseline (from left to right).

wan *et al.*, 2000) to reconstruct the ECGs in our current data set, similar performance results were found.

General versus patient-specific reconstruction

Patient-specific reconstruction is clearly superior over general reconstruction, but requires the availability of a 12-lead baseline ECG from which the reconstruction coefficients can be computed. This would make patient-specific reconstruction particularly attractive in situations in which some leads of the 12-lead ECG are temporarily unavailable. General reconstruction, on the other hand, can always be applied but is more vulnerable to changes in electrode placement. Since differences are known to exist between standard limb leads derived from electrode positions on the ankles and wrists, and those from monitoring positions, (Pahlm *et al.*, 1992; Krucoff *et al.*, 1994) this would require separate sets of general reconstruction coefficients for each configuration. Patient-specific coefficients on the other hand would yield a valid reconstruction irrespective of configuration, provided that the extremity electrodes are located on the same position as when the baseline ECG was obtained.

Lead reconstruction over time

While general reconstruction remained at a similar performance level over 24 hours, patient-specific reconstruction was affected by time. A possible explanation is that postural changes, modifying the location of the electrodes relative to the heart, may have caused the patient-specific reconstruction to perform less well. General reconstruction would be less vulnerable to this effect as the general reconstruction coefficients were de-

rived from a large set of ECGs, with variability between individuals that surpasses the variation induced by changes in posture. One should also consider that the decrease in performance is rather small. For example, the median of the maximum absolute ST difference increases from 30 μV at baseline to 44 μV 24 hours later (Figure 3.4b), a change that will be difficult to notice for a human observer.

Study limitations

The data set in this study was limited to a group of patients with unstable angina pectoris. The presented techniques can be applied on additional data sets containing other abnormalities to determine their robustness. In this respect, the stable results when the reconstruction coefficients derived from another data set (Nelwan *et al.*, 2000) were applied to our current set, are encouraging.

Another limitation is that we focused on continuous ischemia monitoring and did not include the P wave in our performance assessment. This would be a point of further investigation, possibly necessitating the derivation of a separate set of reconstruction coefficients for the P wave only.

Conclusion

Accurate reconstruction of the 12-lead ECG from lead subsets is very well possible. General reconstruction allows one or two precordial leads to be reconstructed well, whereas patient-specific reconstruction allows reconstruction of up to four leads. Patient-specific reconstruction performance initially slightly decreases and then stabilizes over time, but still performs better than general reconstruction after 24 hours.

Part II

Clinical Evaluation

4

Assessment of Derived 12-Lead ECGs using General and Patient-Specific Reconstruction Strategies at Rest and During Transient Myocardial Ischemia

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Abstract

Background

Twelve-lead ST-segment monitoring is a widely used tool for capturing focal ischemia and transient intermittent episodes. However, continuous registration of all 10 electrodes is often impractical in clinical settings. This study investigated the accuracy of 2 derived 12-lead strategies that required 6 electrodes, including all limb leads, and 2 precordial leads by using population-based (generalized) and individualized (patient-specific) reconstruction coefficients to derive the additional 4 precordial leads.

Methods

A total of 26880 simultaneous digital conventional, generalized, and patient-specific 12-lead ECGs were monitored over 112 hours in 39 patients during percutaneous coronary intervention, including 159 balloon occlusions in 63 arteries, to test accuracy at rest and during ischemia. Occlusion duration was 78 seconds (range 42 to 96) in the left main coronary in 2 patients, the left anterior descending artery in 15, the right coronary artery in 10, the circumflex artery in 2, and graft segments in 5 patients.

Results and conclusions

Average summated 12-lead ST deviation over the study population at baseline was 377 μV (range 104 to 1718), which increased at peak ischemia to an average of 1086 μV (range 282 to 4099). Median absolute differences at peak ischemic ST deviation were 25 μV in lead V_1, 0 μV in lead V_2, 35 μV in lead V_3, 34 μV in lead V_4, 0 μV in lead V_5, 11 μV in lead V_6, and 114 μV for summated 12-lead ST deviation with the generalized method and 7 μV in lead V_1, 4 μV in lead V_2, 1 μV in lead V_3, 5 μV in lead V_4, 4 μV in lead V_5, 9 μV in lead V_6, and 83 μV for the summated 12-lead ST deviation with the patient-specific method. Limb leads (I, II, III, aVR, aVL, and aVF) were identical in all patients. Thus, generalized and patient-specific methods derived from 12-lead electrocardiography using actual limb and 2 precordial electrodes accurately derived the additional chest leads at rest and during ischemia. These approaches appear to be more practical than conventional 10-electrode monitoring, yet preserve high accuracy.

Introduction

Twelve-lead ST-segment monitoring is a widely used, noninvasive tool for detection and quantification of focal ischemia and temporally intermittent episodes (Klootwijk *et al.*, 1998; Drew and Krucoff, 1999; Johanson *et al.*, 2001). However, continuous registration of all leads may not always be practical in clinical settings. Derived 12-lead strategies that require fewer electrodes may decrease patient management and costs and provide better access to the left precordium when resuscitation or cardiac tests such as echocardiograms are required. This study assessed the accuracy of simultaneous recording of the actual 12-lead electrocardiogram and two derived 12-lead strategies at rest and during known ischemia from percutaneous coronary intervention (PCI). In the first strategy, all limb leads and precordial leads V_2 and V_5 were directly recorded, and the absent precordial leads V_1, V_3, V_4, and V_6 were derived from a set of population-based coefficients. The second strategy used the directly recorded limb leads and two precordial leads selected from the baseline 12-lead electrocardiogram recorded at rest for each patient. The absent four precordial leads were derived with patient-specific coefficients.

Methods

Patient selection

Patients at the Durham VA Medical Center (Durham, North Carolina, USA) who had been scheduled to undergo percutaneous coronary intervention (PCI) gave informed consent to undergo continuous 12-lead electrocardiogram (ECG) monitoring during and after their PCI procedure. PCI procedures were performed in the usual fashion without significant modification for this protocol. Coronary stenting, antiplatelet therapy, and anticoagulation therapy were performed according to institutional standards in all patients.

ECG monitoring

Monitoring was started at least 30 minutes before the first contrast injection and continued at least 30 minutes after the final contrast injection. Ten electrodes were positioned on Mason-Likar (ML) compatible monitoring locations (Mason and Likar, 1966) prior to the PCI procedure. Radiolucent electrodes allowed ECG monitoring to continue throughout the PCI procedure without interfering with fluoroscopy. Signal quality was visualized on a dedicated Siemens 7000 monitor (Siemens Medical Systems, Danvers, Massachusetts, USA) paired with a laptop personal computer for data collection and a review tool (CRS, Thoraxcentrum, Rotterdam, The Netherlands (Nelwan *et al.*, 1996)). The overall system acquired high-fidelity 12-lead ECGs at 500 Hz, from which average complexes were continuously calculated on a beat-by-beat basis using an incremental updated moving average filter.

Measurements were done by a computer program (Siemens Medical Systems). The system provided the user with a 12-lead average complex every 15 seconds over the entire monitoring period. In addition, the system contained a tool to export an isolated 10-second, 500-Hz, 12-lead ECG strip. This export tool was used to isolate six baseline electrocardiograms (before PCI) that were sent to the Rotterdam ECG laboratory for derivation of patient-specific matrices, thus blinding the Rotterdam group to other information from the monitoring session (see data flow diagram in Figure 4.1).

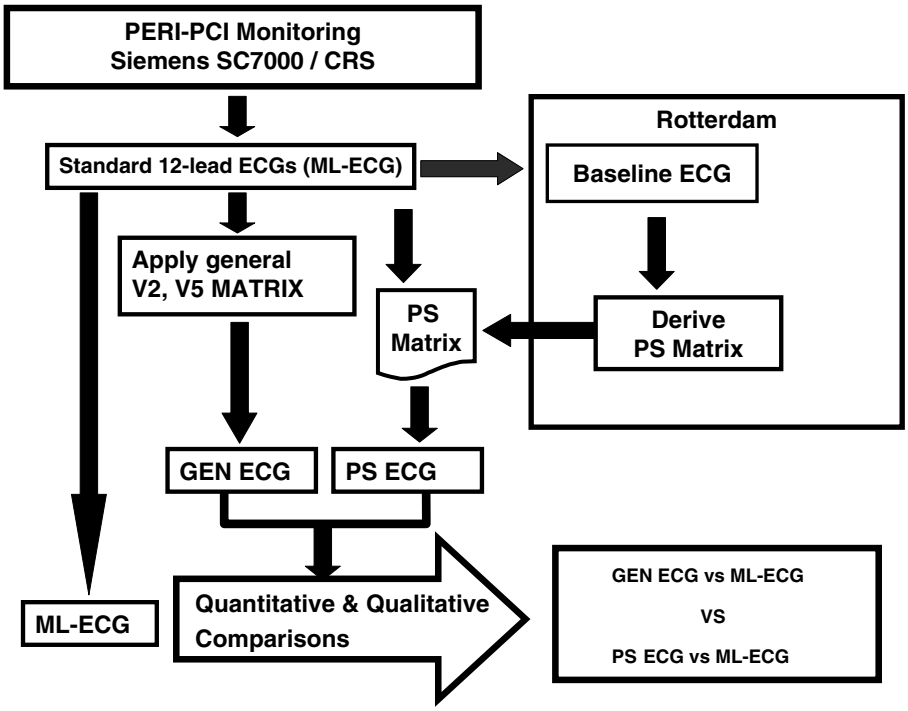

Figure 4.1: Data flow diagram of the data collection, reconstruction process, and performance comparisons.

Electrocardiographic derivation

Two kinds of derived electrocardiograms were constructed: a general electrocardiogram (GEN ECG) and a patient-specific electrocardiogram (PS ECG). These two strategies used all torso limb leads and two precordial leads and comprised a subset of the conventional 12-lead electrocardiogram. The generalized ECG derivation used limb leads I and II and precordial leads V_2 and V_5 in all procedures and derived leads V_1, V_3, V_4, and V_6. A derived lead V_1 (dV_1) was synthesized using the linear combination of $dV_1 = c_{11}I + c_{21}II + c_{31}V_2 + c_{41}V_5$. The coefficients c_{11} to c_{41} were computed using multiple linear regression from a large, independent ECG database that included normal and ischemic findings on electrocardiograms (Nelwan *et al.*, 2000). Leads V_3, V_4, and V_6 were synthesized in a similar manner. The patient-specific ECG derivation strategy used the patient's baseline ML electrocardiogram to select the pair of precordial leads that had the highest morphologic correlation. Patient-specific coefficients were computed to derive the remaining four precordial leads.

Electrocardiographic analysis

For each patient, quantitative and qualitative ECG analyses were performed in three steps: (1) ML ECG selections, (2) general ECG versus ML ECG analysis, and (3) patient-

specific ECG versus ML ECG analysis. All ST-segment measurements were digitally measured at 60 ms after the J point for each lead and summated over all 12 leads.

Superimposition scanning of the actual 12-lead electrocardiograms recorded before, during, and after PCI was performed at the Duke Core Laboratory with CRS software. For each patient, electrocardiograms "before PCI" and during "peak ischemia" were selected. An electrocardiogram before PCI was defined as a ML electrocardiogram that was representative of the patient at rest, subsequent to the "baseline" electrocardiograms (which were sent to Rotterdam) and just before the first contrast injection. An electrocardiogram at peak ischemia was defined as a ML electrocardiogram during PCI occlusion that showed maximum deviation of the summated ST-segment levels relative to the ST-segment levels before PCI. ST-segment levels were electronically forwarded as ASCII files to the statistician for use in quantitative analyses.

CRS software was used to analyze patient-specific versus ML electrocardiograms to determine the limb leads and two precordial leads for each patient monitoring session as determined from the patient-specific matrix. Waveform and ST-level measurements for these leads were identical to those for the ML electrocardiogram. The application used the patient-specific matrix to derive the additional four precordial leads for each electrocardiogram over the course of the monitoring session. Superimposition scanning of the patient-specific ECG waveforms on the corresponding ML ECG waveforms allowed direct visual qualitative comparisons of all recorded electrocardiograms. For quantitative comparison, digital ST levels at 60 ms after the J point for every lead for each of the patient-specific electrocardiograms before PCI and at peak ischemia were electronically forwarded as ASCII files to the statistician for analysis. Generalized ECG versus ML ECG analysis was conducted identically to the patient-specific ECG versus ML ECG analysis using limb leads plus leads V_2 and V_5; leads V_1, V_3, V_4, and V_6 were derived from the general reconstruction coefficients.

Thus, simultaneous electrocardiograms from identical lead positions, using conventional versus derived waveforms, with patients serving as their own controls, were used for all quantitative analyses and qualitative comparisons.

Quantitative analysis

Absolute differences between ML ECG levels and generalized or patient-specific ST levels were tested as continuous variables. A dichotomous variable threshold for clinically significant differences between ST levels in any lead on a ML electrocardiogram versus a generalized or patient-specific electrocardiogram was set at > 50 μV, which is the approximate width of an ink line on an electrocardiogram or a line width of two pixels on an average 17-inch computer monitor.

Statistical analysis

All data were archived using coded patient study numbers at the Ischemia Monitoring Core Laboratory, and all statistical analyses were completed at the Duke Clinical Research Institute (Durham, North Carolina). Subjects' baseline characteristics were summarized in terms of counts and percentages for categorical variables and as medians and inter-quartile ranges for continuous variables. Data were correlated using patients as their own controls. Differences in ST deviation between the ML and patient-specific electrocardiograms (D_1) and between the ML and generalized electrocardiograms (D_2) were

computed for each lead. D_1 and D_2 were tested for similarity with Wilcoxon's signed rank test. This distribution-free test allowed us to make inferences regarding the median of the differences between the two ECG analysis methods and control for non-normality in the data and matched pairs. A dichotomous variable was also created to evaluate the number of times D_1 or D_2 was > 50 μV for each lead. McNemar's χ^2 test for dependent proportions was used to determine whether these proportions were similar. A p-value < 0.05 was considered statistically significant.

Results

A total of 26880 electrocardiograms were acquired over 112 hours of monitoring in 39 patients during PCI procedures, including 159 balloon occlusions in 63 coronary arteries. Patients were men, with an average age of 66 years, average weight of 92 kg, and average height of 178 cm. Median duration of coronary occlusion by balloon inflation was 78 seconds (range 42 to 96). In two patients, PCI was performed during evolving myocardial infarction, and each had a sustained coronary occlusion for > 30 minutes. Peak ischemia occurred on electrocardiograms during occlusion of the left main coronary in two patients, the left anterior descending artery in 15 patients, the right coronary artery in 10 patients, the circumflex artery in two patients, and vein graft segments in five patients. In five patients, PCI did not cross a long-term total occlusion or PCI was not performed, so contrast injections with transient ST changes were analyzed. Average summated 12-lead ST deviation over the population before PCI was 377 μV (range 104 to 1718), which increased at peak ischemia to an average of 1086 μV (range 282 to 4099).

Quantitative analysis

Table 4.1 presents absolute ST-level differences for each lead and summated over 12 leads for electrocardiograms before PCI and during peak ischemia. Differences between ML and generalized electrocardiograms were compared with differences between ML and patient-specific electrocardiograms. There were no differences in the limb leads, because the actual limb leads were used for all derivations. Leads V_2 and V_5 were also identical for ML and generalized comparisons, with only leads V_1, V_3, V_4, and V_6 being reconstructed. For the patient-specific electrocardiogram across these 39 patients, the frequency and distribution of the precordial leads used for reconstruction were 31% for lead V_1, 41% for lead V_2, 46% for lead V_3, 33% for lead V_4, 44% for lead V_5, and 5% for lead V_6. Differences on average were 5 μV for patient-specific versus ML electrocardiograms and 26 μV for ML versus generalized electrocardiograms. Comparisons across leads V_1, V_3, and V_4 favored the patient-specific versus ML electrocardiogram over the generalized versus ML electrocardiogram and the comparison for lead V_6 was statistically equivalent. Differences for leads V_2 and V_5 were only 4 μV. Although relevant from a technical standpoint in a digital ECG environment, average differences of 4 to 35 μV are unlikely to be clinically significant.

Table 4.2 presents comparisons of the incidence of patients in whom any lead varied from ML by > 50 μV for electrocardiograms before PCI or at peak ischemia. Leads V_1, V_3, and V_4 were superior for patient-specific electrocardiograms, with no difference in lead V_6.

Table 4.1: Quantitative absolute differences in ST levels (μV) before percutaneous coronary intervention (pre-PCI) and at balloon inflation (n=39) for general and patient-specific reconstructions.

Group *	I	II	III	aVR	aVL	aVF	V_1	V_2	V_3	V_4	V_5	V_6	SUM
Before PCI													
General (μV)	0	0	0	0	0	0	10	0	13	13	0	6	49
							(5–19)	(0–0)	(7–26)	(4–24)	(0–0)	(3–13)	(29–72)
							(1–67)	(0–0)	(0–127)	(1–110)	(0–0)	(0–33)	(14–282)
Patient-specific (μV)	0	0	0	0	0	0	3	2	1	4	1	6	36
							(0–11)	(0–14)	(0–12)	(0–17)	(0–8)	(2–15)	(24–63)
							(0–25)	(0–36)	(0–81)	(0–51)	(0–79)	(0–35)	(9–219)
p-value	–	–	–	–	–	–	<0.001	<0.001	0.003	0.009	<0.001	0.95	<0.21
Peak													
General (μV)	0	0	0	0	0	0	25	0	35	34	0	11	114
							(9–33)	(0–0)	(8–79)	(15–49)	(0–0)	(5–20)	(65–180)
							(0–215)	(0–0)	(1–427)	(2–478)	(0–0)	(1–158)	(14–1112)
Patient-specific (μV)	0	0	0	0	0	0	7	4	1	5	4	9	83
							(0–23)	(0–19)	(0–20)	(0–31)	(0–25)	(3–24)	(47–172)
							(0–127)	(0–169)	(0–141)	(0–139)	(0–201)	(0–158)	(6–436)
p-value	–	–	–	–	–	–	0.004	<0.001	<0.001	<0.001	<0.001	0.99	0.12

** Data are reported as median values for all leads (25th to 75th percentiles) (range).*
SUM = average summated 12-lead ECG ST deviation.

Table 4.2: Number of patients with absolute differences > 50 μV in any lead before percutaneous coronary intervention and at balloon inflation (n=39) for general and patient-specific reconstructions.

Group	I	II	III	aVR	aVL	aVF	V_1	V_2	V_3	V_4	V_5	V_6	SUM
Before PCI													
General	0	0	0	0	0	0	1 (3%)	0	5 (13%)	4 (11%)	0	0	6 (15%)
Patient-specific	0	0	0	0	0	0	0	0	2 (5%)	1 (3%)	1 (3%)	0	2 (5%)
p-value	–	–	–	–	–	–	0.68	1.0	0.44	0.44	0.68	1.0	0.25
Peak													
General	0	0	0	0	0	0	5 (13%)	0	12 (31%)	9 (23%)	0	2 (5%)	18 (46%)
Patient-specific	0	0	0	0	0	0	3 (8%)	5 (13%)	5 (13%)	5 (13%)	4 (10%)	3 (8%)	17 (44%)
p-value	–	–	–	–	–	–	0.68	0.04	0.21	0.39	0.09	0.94	0.98

SUM: average summated 12-lead ECG ST deviation.

Tables 4.3 and 4.4 present absolute ST differences and incidence of differences $> 50\ \mu V$ for peak ischemia with respect to occlusions in the left anterior ascending artery and other locations. For occlusions not in the left anterior descending artery, generalized and patient-specific electrocardiograms were nearly identical.

Qualitative analysis

Visible qualitative differences that underestimated or overestimated P, QRS, ST, and T waves for generalized and patient-specific electrocardiograms at baseline, before PCI, at peak ischemia, and over the entire course of monitoring were examined on a superimposed display of the derived and actual electrocardiograms for each patient. Occasional morphologic changes were observed, although the clinical significance of these minor observations was unclear. Importantly, on no electrocardiogram did derivation produce significant shifts in fiducial points important to ST-segment level determinations.

Discussion

This study demonstrates the accuracy with which ST-segment levels from a 12-lead electrocardiogram before and during transient ischemia can be reconstructed from a 6-electrode set. In patient-specific and general variations of the algorithm, limb leads and two of the standard precordial leads are used, thus decreasing the need to record the four absent precordial leads. In the two variations, patient-specific waveform elements are used to augment the accuracy of the derived leads.

In the generalized strategy, standard precordial leads V_2 and V_5 are used for all ECG recordings, in contrast to the patient-specific strategy, when leads other than V_2 and V_5 may be selected, depending on the actual spatial location of key waveform elements. In the patient-specific strategy, a 12-lead electrocardiogram is mandatory before monitoring because it is used to assess the range of derivations across all possible pairs of precordial waveforms, with two precordial leads selected for each patient based on the best overall correlation between the actual electrocardiogram and the four derived precordial waveforms.

The concept of 12-lead ECG monitoring derived from only six electrodes placed on the patient represents an important logistical advantage to bedside integration and feasibility for clinical use. The accuracy of the ECG reconstruction is critical to patient management and to widespread acceptance. Current studies have reported that derived 12-lead electrocardiograms contain more information about ischemia than do traditional cardiac care unit leads such as leads V_1 and II, (Drew *et al.*, 1996) but whether any derived 12-lead electrocardiogram reproduces the 12-lead electrocardiogram sufficiently and accurately to be clinically useful, remains controversial.

The assessment of derived ECG accuracy has important technical elements. In previous reports that assessed two or three recording devices cycling independently (Drew *et al.*, 1997; Krucoff *et al.*, 1993), ischemia from a rapidly moving source (e.g. coronary occlusion) during PCI may appear differently on different devices simply due to a 10- to 20-second difference in timing from one device to another. In this protocol, the derived electrocardiograms were created with a subset of leads from fully archived 12-lead electrocardiograms, thus allowing comparison of truly simultaneous actual and derived ECG waveforms and truly using patients as their own simultaneous controls. Further, even

Table 4.3: Quantitative absolute differences in ST levels (μV) at balloon inflation: LAD (n=13) and non-LAD (n=26) coronary occlusions for general and patient-specific reconstruction.

Group *	I	II	III	aVR	aVL	aVF	V_1	V_2	V_3	V_4	V_5	V_6	SUM
Before PCI													
General (μV)	0	0	0	0	0	0	27	0	81	38	0	13	166
Patient-specific (μV)	0	0	0	0	0	0	9	2	0	29	7	7	95
p-value	–	–	–	–	–	–	0.02	0.02	0.002	0.24	0.02	0.80	0.09
Peak													
General (μV)	0	0	0	0	0	0	24	0	26	24	0	10	91
Patient-specific (μV)	0	0	0	0	0	0	6	4	4	2	2	14	75
p-value	–	–	–	–	–	–	0.09	<0.001	0.04	<0.001	<0.001	0.94	0.54

** Data are reported as median values.*
SUM: average summated 12-lead ECG ST deviation.

Table 4.4: Number of absolute differences > 50 μV at balloon inflation: LAD (n=13) and non-LAD (n=26) coronary occlusions for general and patient-specific reconstructions.

Group	I	II	III	aVR	aVL	aVF	V_1	V_2	V_3	V_4	V_5	V_6	SUM
Before PCI													
General	0	0	0	0	0	0	0	3 (23%)	1 (8%)	4 (31%)	1 (8%)	1 (8%)	6 (46%)
Patient-specific	0	0	0	0	0	0	2 (15%)	0	8 (62%)	6 (46%)	7	0	10 (77%)
p-value	–	-	–	–	–	–	0.39	0.20	0.03	0.68	0.68	0.68	0.25
Peak													
General	0	0	0	0	0	0	3 (12%)	2 (8%)	4 (15%)	1 (4%)	3 (12%)	2 (8%)	11 (42%)
Patient-specific	0	0	0	0	0	0	3 (12%)	0	4 (15%)	3 (12%)	0	2 (8%)	8 (31%)
p-value	–	–	–	–	–	–	1.0	0.39	1.0	0.68	0.20	1.0	0.59

SUM: average summated 12-lead ECG ST deviation.

if the ST-segment waveform is accurately derived, the location of measurement points such as 60 ms after the J point may be adversely affected if the derived QRS interval or other fiducial points in the waveform are inaccurate. In this study, visual superimposition of the entire derived waveform onto the simultaneous actual waveform was used to inspect not only the electrocardiograms analyzed quantitatively but also all electrocardiograms in the monitoring session. This qualitative superimposition also allowed the core laboratory to observe any other obvious inaccuracies in the non-ST-segment waveform components.

The two reconstruction strategies performed very well in non-ischemic and ischemic electrocardiograms and during coronary occlusions in the left anterior descending artery and elsewhere. Although statistically significant differences in this model were detectable at the microvolt level when comparing digital electrocardiograms of single leads, differences greater than the threshold of 50 μV were rare.

This study has several limitations. First, the total patient number was small. However, using patients as their own simultaneous controls provides considerable statistical power with which to assess accuracy. Second, this study used an arbitrary threshold of 50 μV as the cutoff for accuracy assessments. This threshold represents a measurement range equivalent to the width of the ink line on a printed electrocardiogram. Although reasonable for this kind of algorithm assessment, effects on implementation strategies, such as programmable alarm thresholds in a monitored patient care setting, remain unclear.

Conclusion

Generalized and patient-specific methods derived from 12-lead electrocardiograms using actual limb and two precordial leads accurately derive the absent four precordial electrodes at rest and during ischemia. These approaches appear to be more practical than conventional 12-lead monitoring and preserve high accuracy.

5

Efficacy of a Reduced Lead Set for Pre-Hospital Triage of Thrombolytic Strategies

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Abstract

Background

In emergency care situations, recording all leads of the 12-lead ECG is often not possible due to technical or organizational restrictions. The recording of a reduced lead set and subsequent synthesis of the absent leads might be a solution to these problems. The aim of this study was to evaluate the efficacy of a reduced lead set containing leads I, II, V_2, and V_5.

Methods

We used a data set of 2260 10-second, 12-lead ECGs from patients with chest pain suggestive of acute myocardial infarction (AMI). The ECGs were recorded by the ambulance personnel prior to hospitalization. The data set was split in a training set of 1435 ECGs and a test set of 825 ECGs. Reconstruction coefficients were derived by linear regression from the learning set. Performance was evaluated between the actual and reconstructed leads using correlation coefficients and average and maximum absolute ST differences. We applied a decision rule for initiation of pre-hospital thrombolysis and a detection rule for AMI to the original and reconstructed ECGs. Accuracy was determined by percentage agreement and Cohen's kappa was computed to correct for chance agreement.

Results

The overall median (inter-quartile range) correlation coefficient was 0.985 (0.971–0.992). The median absolute ST difference was 25 (16–45) μV with a maximum difference of 49 (29–88) μV. The median performance results of each reconstructed lead were for correlation: V_1 0.983 (0.960–0.993), V_3 0.953 (0.877–0.980), V_4 0.980 (0.954–0.991), and V_6 0.986 (0.967–0.994). Median ST differences were for V_1 20 (9–41) μV, V_3 38 (16–78) μV , V_4 23 (11–45) μV, and V_6 13 (6–26) μV. For the pre-hospital decision rule, accuracy was 0.987 with a kappa of 0.880. The accuracy of the AMI detection rule yielded 0.981 with a kappa of 0.941.

Conclusions

The findings in this study show that high overall agreement, correlation, and small ST differences have been obtained. In emergency situations where a 12-lead ECG cannot be recorded because of technical or organizational restrictions, a reduced lead set can be considered.

Introduction

Early diagnosis, risk stratification, and initiation of treatment are of importance for patients with chest pain suggestive of acute coronary syndromes and may result in reduction of mortality and final infarct size (Boersma *et al.*, 1996; Grijseels *et al.*, 1996). The 12-lead ECG is an important noninvasive tool for diagnosing acute myocardial infarction in patients with chest pain and an increasing number of emergency medical services are being equipped with and are trained to use a 12-lead ECG recorder. Depending on local regulations, the 12-lead ECG may be evaluated by a cardiologist using facsimile transmission or by a computer program.

However, there are several practical considerations. First, a 12-lead ECG requires ten electrodes and wires. A reduction in the number of electrodes may save time. Furthermore, there may not always be room in the ambulance for a separate 12-lead ECG recorder. An integrated solution with a defibrillator would be ideal, but not all defibrillators can record all 12 leads.

Recording of a reduced subset of leads and subsequent synthesis of a full 12-lead ECG may provide a solution to these problems. The goal of this study was to evaluate the efficacy of a reduced lead set consisting of leads I, II, V_2, and V_5. This lead subset has previously been shown to give excellent results in a patient monitoring setting (Nelwan *et al.*, 2004b).

Methods

Study population

The data set for this study was based on the REPAIR study (Boersma *et al.*, 1996; Grijseels *et al.*, 1996; Bouten *et al.*, 1990). REPAIR was used for the development and evaluation of a computer-assisted decision algorithm for early initiation of thrombolytic therapy in the pre-hospital setting. Between 1992 and 1994, 2641 patients in the municipality of Rotterdam with chest pain suggestive of myocardial infarction were evaluated by their general practitioner, who then asked for ambulance assistance and hospital admission. After arrival of the ambulance, a 12-lead ECG was recorded by the ambulance personnel and interpreted by a computerized analysis system.

A final diagnosis was made by the treating cardiologist, and was based on the admission and discharge ECGs, recurrence of symptoms, laboratory findings, and autopsy results. These results were also provided to the general practitioner, who used the information for further patient management.

Electrocardiographic processing

In 365 patients, an ECG could not be recorded or stored due to technical failure or unsuitable circumstances on the spot. In 16 patients, the ECG was left out of the analysis because of reversed leads or pacemaker rhythms. The remaining 2260 ECGs were split into a training set (n=1435) and a test set (n=825). All ECGs were processed by the Modular ECG Analysis System (MEANS) (van Bemmel *et al.*, 1990). The program MEANS computes for each of the 12 leads a representative averaged beat from which ECG measurements are derived. MEANS has been extensively evaluated by the developers (van Bemmel *et al.*, 1990) and by others (Willems *et al.*, 1991).

Reconstruction method

Leads III, aVR, aVL, and aVF can be calculated from leads I and II without error. Lead V_1 can be approximated by $c_{11} * I + c_{21} * II + c_{31} * V_2 + c_{41} * V_5$. The coefficients $c_{11} - c_{41}$ are computed using multivariate linear regression from ECGs in the learning set. Leads V_3, V_4, and V_6 can be reconstructed in a similar way.

Data analysis

Reconstruction accuracy of the missing leads was evaluated on three different levels. First, overall waveform similarity for each ECG was assessed by the average of the correlation coefficients and root mean square errors (RMSE) between the QRS-T complexes of the original and the reconstructed leads.

Second, reconstruction accuracy was determined at the measurement level, focusing on the ST amplitude, 60 ms after the J point for each lead. We determined the average and the maximum of the absolute differences ($|\Delta ST|$) between the original and reconstructed ST amplitudes. Furthermore, the sum of the absolute ST deviations (SUMST) was also computed for the original and reconstructed ECGs.

Third, reconstruction accuracy was assessed at the diagnostic level. For each original and derived 12-lead ECG, we applied seven decision rules and calculated the sensitivity, specificity, and accuracy (percentage agreement) between the original and the reconstructed 12-lead ECG. Cohen's κ was computed to correct for chance agreement.

The first decision rule, named REPAIR1988, was the originally developed decision rule (Bouten *et al.*, 1990) for initiation of thrombolytic therapy. The ECG criteria were: $\geq$ 300 μV ST elevation in two or more leads of V_1-V_6 or $\geq$ 200 μV in two or more leads in II, III, and aVF. A total ST deviation of at least 1000 μV was also required. The exclusion criteria were: left or right bundle branch block, intraventricular conduction delays, a Wolf-Parkinson-White pattern, and pacemaker rhythms.

The REPAIR protocol was optimized in 1996 (REPAIR1996) (Boersma *et al.*, 2001) and included additional criteria for ST elevation and depression in the inferior and anterior leads. In 2001, REPAIR was extended with recommendations for primary PCI for patients with a total ST deviation of $\geq$ 1500 μV (REPAIR2001) (Boersma *et al.*, 2001).

The fourth decision rule, AMI_1, is a classical decision rule for determining in-hospital acute myocardial infarction. AMI_1 holds true if two or more leads of V_1-V_6 show $\geq$ 200 μV ST elevation or if at least one lead of II, III and aVF shows $\geq$ 100 μV of ST elevation.

The fifth decision rule, AMI_2, is a rule recommended by the European Society and American College of Cardiology for the detection of myocardial ischemia and evolving myocardial infarction (Thygesen *et al.*, 2000). The rule holds true when two or more contiguous leads show ST elevation at J point of $\geq$ 200 μV in anterior leads V_1, V_2, or V_3 and $\geq$ 100 μV ST elevation in the other leads.

Lastly, two additional decision rules were included. ST depression was considered if two or more leads showed at least 50 μV ST depression. ST elevation was considered if two or more leads in V_1-V_6 had $\geq$ 200 μV ST elevation or two or more limb leads (I-III, aVL, and aVF) had at least $\geq$ 100 μV ST elevation.

The decision rules have been designed for different purposes. For example, the REPAIR decision rules were designed with a high specificity in order to minimize the number of false-positive cases, because of the elevated risk of complications when using throm-

Table 5.1: Median (inter-quartile range) correlation, average, and maximum absolute ST differences of the test set and subsets according to the discharge diagnosis.

Data set	Correlation	Absolute ST difference (μV)	
		Average	Maximum
Complete set (n=825)	0.985 (0.971 – 0.992)	25 (16 – 45)	49 (29 – 88)
Myocardial infarction (n=235)	0.984 (0.972 – 0.991)	41 (23 – 76)	76 (42 – 247)
Angina pectoris (n=189)	0.984 (0.968 – 0.992)	24 (15 – 38)	43 (28 – 74)
Atypical chest pain (n=278)	0.978 (0.975 – 0.992)	19 (13 – 33)	38 (24 – 62)

Table 5.2: Median (inter-quartile range) summated ST (SUMST) of the original and derived ECGs and differences of the test set.

SUMST	Original (μV)	Derived (μV)	Difference (μV)
Complete test set	671 (423 – 1357)	669 (411 – 1339)	2 (-41 – 55)
Myocardial infarction	1479 (904 – 2493)	1472 (789 – 2261)	18 (-41 – 139)
Angina pectoris	585 (380 – 879)	589 (383 – 874)	3 (-36 – 50)
Atypical chest pain	494 (355 – 748)	507 (343 – 714)	-10 (-45 – 22)

bolytic therapy. For the AMI_1, AMI_2, and the ST-depression and ST-elevation rules, a high sensitivity and low false-negative cases are important.

Results

The median age (inter-quartile range) of patients in the test set was 67 (57–74) years. A total number of 438 (53.1%) patients were male. The final discharge diagnoses were: myocardial infarction (28.6%), angina pectoris (22.9%), atypical chest pain (33.6%), severe cardiac pathologies (2.4%), other or minor cardiac pathologies (3.1%), and a group of other or non-cardiac diagnoses (9.4%).

The reconstruction technique was applied to the test set and to the largest three subgroups (myocardial infarction, angina and atypical chest pain). Performance results are presented in Table 5.1. SUMST for the myocardial infarction group is higher than for the angina pectoris and atypical chest pain groups. In Table 5.2, a similar pattern can be observed for the SUMST differences and average and maximum absolute ST differences in these groups.

Table 5.3 contains the median correlation coefficients, RMSE, and ST differences for each reconstructed lead, respectively. Overall, lead V_3 has the lowest median correlation, highest RMSE and ST difference across the complete test set and subgroups. Reconstructed lead V_6 has the overall highest median performance and lowest ST difference.

For each reconstructed ECG, we determined the lead which had the largest ST-difference. The number of cases was for lead V_1 202 (24%), V_3 444 (53.1%), V_4 115 (13%),

Table 5.3: Median (inter-quartile range) correlation coefficients, root mean square errors, and absolute ST differences (|ΔST|) of each reconstructed lead in the test set.

Correlation Coefficient	V_1	V_3	V_4	V_6
Complete test set (n=825)	0.983 (0.960–0.993)	0.953 (0.877–0.980)	0.980 (0.954–0.991)	0.986 (0.967–0.994)
Myocardial infarction (n=235)	0.979 (0.957–0.992)	0.943 (0.864–0.976)	0.976 (0.948–0.988)	0.986 (0.969–0.994)
Angina pectoris (n=189)	0.986 (0.962–0.994)	0.960 (0.897–0.982)	0.981 (0.965–0.992)	0.980 (0.958–0.993)
Atypical chest pain (n=278)	0.986 (0.966–0.993)	0.958 (0.898–0.984)	0.985 (0.959–0.993)	0.988 (0.969–0.995)
Root Mean Square Error (μV)	V_1	V_3	V_4	V_6
Complete test set	67 (44–102)	134 (87–210)	84 (57–127)	47 (33–64)
Myocardial infarction	73 (47–111)	154 (105–233)	98 (67–143)	48 (35–70)
Angina pectoris	67 (45–106)	118 (77–180)	78 (54–114)	48 (34–68)
Atypical chest pain	63 (42–86)	127 (81–191)	76 (55–117)	43 (29–55)
Absolute ST Difference (μV)	V_1	V_3	V_4	V_6
Complete test set	20 (9–41)	38 (16–78)	23 (11–45)	13 (6–26)
Myocardial infarction	25 (11–57)	63 (29–136)	39 (17–76)	20 (7–38)
Angina pectoris	19 (8–36)	32 (16–59)	21 (12–37)	13 (6–24)
Atypical chest pain	17 (9–34)	30 (14–55)	18 (9–32)	9 (4–17)

Table 5.4: Sensitivity (Sens), specificity (Spec), number of false-negative (FN) and false-positive (FP) cases, accuracy and chance-corrected accuracy (κ) based on a comparison of the original and reconstructed ECGs for seven decision rules on the test set (n=825).

Decision rule	Sens (%)	Spec (%)	FN	FP	Accuracy	κ
REPAIR1988	94.3	99.6	2	3	0.994	0.926
REPAIR1996	82.1	99.6	7	3	0.988	0.859
REPAIR2001	84.3	99.6	8	3	0.987	0.880
AMI_1	98.1	98.3	2	12	0.983	0.931
AMI_2	93.7	99.2	11	5	0.981	0.941
ST elevation	96.2	96.8	16	13	0.965	0.930
ST depression	97.5	98.1	6	11	0.979	0.951

and V_6 64 (7%). Overall, lead V_3 had the largest ST difference in most cases. Similar results were found in the subgroups.

Reconstruction performance results of the myocardial infarction group were slightly lower than the angina pectoris and atypical chest pain groups. However, the myocardial infarction subgroup contains large changes in the ECG, caused by ischemia or ongoing infarction at the time of recording, resulting in high SUMST values and higher ST differences (cf. Table 5.1).

In Table 5.4, performance results are presented for sensitivity, specificity and accuracy between the actual and reconstructed ECGs of the described decision rules. The number of false positive and false negative cases are also reported for each rule. The current REPAIR rules had three false positive cases. Two cases would not receive thrombolytic therapy, but would be directly transported for PCI. These false positive PCI cases were found in several rules (REPAIR1996, REPAIR2001, AMI_1 and ST elevation) and had mediocre overall correlation and high ST differences. In these two cases, a single, large, ST elevation (380 μV) was found in a source lead, which propagated in the reconstructed leads and increased the reconstruction errors. The third false positive case would have received unjustified thrombolytic therapy based solely on these ECG criteria.

The ST-depression rule with a threshold of ≥ 50 μV had the highest number of false-negative and false-positive cases. After setting the depression threshold to ≥ 100 μV, accuracy (agreement: 0.977, kappa: 0.945) increased and the number of false negative cases (13) and false positive cases (6) decreased. These results may indicate that thresholds of ≤ 50 μV are more vulnerable to errors in lead reconstruction (cf. ST differences in Tables 5.1 and 5.3).

Discussion

The findings in this study show that high overall accuracy (≥0.880), waveform similarity (≥0.985), and small ST differences (maximum ≤ 49 μV) were obtained between the recorded 12-lead ECG and the reconstructed 12-lead ECG based on a reduced lead subset of leads I, II, V_2, and V_5.

Overall, the number of misclassifications are low. The accuracy results of REPAIR2001 indicate three false positive cases of which two would be transported directly to a PCI

center, and that a single case would receive unjustified thrombolytic treatment based solely on the ECG data. In practice, the final decision will also be based on other variables.

Leads V_3 and V_4 had the lowest reconstruction performance. A possible explanation is that these leads are often considered as transition leads between the left- and right-precordial areas on the chest. Because this transition is often specific for a patient, a reconstruction technique based on a training population does not need to be best for each individual patient. Lead V_6 had the overall highest reconstruction performance, which does not come as a surprise as V_6 is highly correlated with leads I and V_5.

In a previous study (Nelwan *et al.*, 2004b), we evaluated this reconstruction technique for all lead subset combinations on a group of 234 patients who were monitored for 24 hours in the coronary care unit. The lead subset of I, II, V_2, and V_5 was found best in this study. We also determined the best lead subsets of varying sizes on the present training set (data not shown) and found that the best lead subset also included leads I, II, V_2, and V_5.

Other investigators also evaluated the use of reduced lead sets. Drew *et al.* (2002) considered a lead subset consisting of leads I, II, V_1, and V_5. Lead V_1 was preferred over V_2, because this lead is frequently used for diagnosis of QRS morphology and atrial activity. However, lead V_1 is not most efficacious for detection of myocardial ischemia (Drew *et al.*, 2002; Drew and Krucoff, 1999). For this lead subset, we derived coefficients from the learning set and applied it to our test set. A slight performance loss was observed; the number of false-positive cases increased from three to seven cases for the REPAIR rules. However, further investigation is needed to evaluate both lead set strategies.

Schreck *et al.* (1998) evaluated the use of a lead subset consisting of leads I, aVF, and V_2. This lead subset corroborates with the best lead subset (I, II, and V_2) determined after a separate analysis on our training set (data not shown). However, we found an overall moderate performance loss for this lead subset. For example, the number of false-positive cases for the REPAIR rules increased from three to eight. These findings indicate that inclusion of a left-precordial lead, such as lead V_5, increases overall reconstruction performance.

A study limitation is that we did not evaluate reconstruction accuracy of other ECG abnormalities, such as cardiac arrhythmias. However, a typical lead selected for arrhythmia monitoring is lead II (Drew *et al.*, 2002; Drew and Krucoff, 1999). As this lead is part of the lead subset, arrhythmia monitoring will not be influenced by reconstruction errors.

Conclusion

This study shows that high accuracy, high waveform similarity, and small ST_{60} differences can be obtained from a reconstruction of a 12-lead ECG using reduced lead sets. In emergency care situations, where a 12-lead ECG cannot be recorded because of technical or organizational restrictions, a reduced lead set can be considered.

6

Simultaneous Comparison of Three Derived 12-Lead ECGs with Standard ECG at Rest and During Percutaneous Coronary Occlusion

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Abstract

Background

In recent years, several derived 12-lead ECG systems have been developed, but have never been directly compared for accuracy. The aim of the study was to simultaneously test the EASI lead system and two other derived ECG methods against the standard 12-lead ECG during percutaneous coronary intervention.

Methods

During 44 percutaneous coronary interventions, a simultaneously recorded 12-lead and EASI ECG were marked at the start of the recording (baseline) and at known ischemia caused by balloon inflation (peak). ST deviations were measured 60 ms after the J point at baseline and peak in all leads and were summated (SUMST) to assess overall changes. For regional changes, the lead with the highest ST deviation (PEAKST) was marked.

For each patient, derived 12-lead ECGs were computed from the EASI leads and a lead subset using patient-specific coefficients (PS) and coefficients based on a patient population (GEN). Absolute differences were computed between each derived and routine ECG for SUMST and PEAKST. Accuracy was tested with paired t-tests at a level of $p < 0.05$.

Results

SUMST was at baseline 567 μV (range: 150–1707) and increased at peak to 871 μV (range: 350–2101). SUMST differences at peak were for EASI: 49 μV (CI: 19–220, p=0.02), GEN: 48 μV (CI: -43–154, p=0.26), and PS: 20 μV (CI: -51–32, p=0.65). PEAKST differences were for EASI: 163 μV (CI: 90–236, p<0.001), GEN: 46 μV (CI: 2–91, p=0.40), and PS: 16 μV (CI: 3–30, p=0.15).

Conclusion

Simultaneous direct comparison of three derived ECG methods shows overall and regional differences in accuracy across PS, GEN, and EASI. Median SUMST and PEAKST differences for PS are lower than for GEN and EASI, and show a more accurate reconstruction.

Introduction

In patients with acute coronary syndromes, continuous 12-lead ST-segment monitoring is an important noninvasive diagnostic tool for real-time assessment of evolving myocardial ischemia and infarction (Drew and Krucoff, 1999; Johanson *et al.*, 2003). Online analysis of dynamic ST-segment changes before, during, and after treatment make it possible to quantify the presence, speed, and quality of reperfusion of the infarcted artery and is a class I recommendation of the recently published practice guidelines by the American Heart Association (Drew *et al.*, 2004).

However, 12-lead ST-segment monitoring is underused in clinical practice (Patton and Funk, 2001), even though it is available in modern patient monitoring equipment. An important limitation of the technology is that the ten electrodes used in standard ECG present a nursing burden and are sensitive to artifacts, which may result in false alarms and both of which may actually hinder patient care.

A possible solution to these problems might be to monitor patients with fewer electrodes strategically positioned to support accurate reconstruction of the full 12-lead ECG. In recent years, several methods to derive the 12-lead ECG from fewer leads have been proposed. The EASI lead system (Dower *et al.*, 1988; Feild *et al.*, 2002) uses five electrodes and synthesizes all 12 ECG leads, while another approach uses six electrodes as a subset of the 12-lead ECG, reconstructing the missing leads using coefficients either obtained from the patient's own ECG (PS) (Nelwan *et al.*, 2004b) or from a large archived data set (GEN) (Nelwan *et al.*, 2004b). However, the accuracy with which derived ECGs from reduced lead sets approximate the spatial information of the absent leads could affect key diagnostic features such as ischemic ST changes, and needs to be precisely defined.

The purpose of this study was to directly compare the three (EASI, GEN, and PS) different derivation methods of the 12-lead ECG at rest and at ischemia as a result of balloon inflation during percutaneous coronary intervention (PCI) from simultaneously recorded ECG measurements.

Methods

Patient selection

Patients scheduled for PCI at the Durham VA Medical Center gave informed consent to undergo simultaneous 15-lead ECG monitoring before, during, and after their PCI procedure. The PCI procedures were performed in the usual fashion following the clinical standards of the institution.

ECG monitoring

A total of 14 radiolucent electrodes were attached to the patient to allow simultaneous registration of the 12-lead and EASI ECG. Of the ten electrodes required for 12-lead ECG registration, four electrodes (right arm, etc) were placed on the Mason-Likar landmarks (Mason and Likar, 1966) and six electrodes (V_1-V_6) were positioned on the conventional precordial locations. The remaining four electrodes were placed on the EASI locations (E, A, S, and I) (Dower *et al.*, 1988). The EASI reference electrode was shared with the electrode RL of the 12-lead system.

All lead wires were connected to a modified dual pod (Siemens/Dräger Medical Systems) to allow simultaneous registration of all signals by two Delta patient monitors (Siemens/Dräger Medical Systems) which facilitated basic arrhythmia and continuous ST-segment monitoring. Monitoring was started at least 30 minutes before the first contrast injection and continued at least 30 minutes after the final contrast injection. A computer program on a laptop acquired high fidelity 500-Hz ECG data from both patient monitors simultaneously. The system stored averaged beats every 15 seconds for all leads during the entire recording period.

ECG analysis

ECGs were analyzed with the Modular ECG Analysis System (MEANS) (van Bemmel *et al.*, 1990). MEANS computes representative averaged beats of all leads from which ECG measurements are derived. The waveform recognition and diagnostic interpretation of MEANS has been extensively evaluated (van Bemmel *et al.*, 1990; Willems *et al.*, 1991).

A 10-second, 12-lead and EASI ECG were marked at the start of the recording (baseline) and at balloon inflation (peak). In case of multiple balloon inflations, the first balloon inflation was selected. ST-segment amplitudes were measured at J point and at J+60 ms (ST_{60}) for each lead. ST deviations were summated over all leads (SUMST) at baseline and peak.

The lead with the highest ST deviation (PEAKST) at balloon inflation relative to the initial baseline ECG (≥ 100 μV) (Krucoff *et al.*, 1988) was defined. We identified the region (anteroseptal: V_1-V_4, lateral: I, AVL, V_5-V_6, and inferior: II, III, aVF) affected by balloon inflation. ECG changes indicative of acute ischemia were assessed at baseline and peak when at least two or more contiguous leads showed ST elevations at J point of ≥ 200 μV in the anterior leads V_1, V_2, or V_3 or ≥ 100 μV in other leads (Thygesen *et al.*, 2000). Secondly, ST depression was defined as ≥ 50 μV below the iso-electric level in one or more leads.

ECG derivation

For each patient, 12-lead ECGs were derived over the complete recording period from the EASI leads and from lead subsets of the 12-lead ECG using coefficients based on a archived data set of patients and using patient-specific coefficients.

The first derived 12-lead method (EASI) is based on the EASI lead system. EASI uses a modified Frank configuration with three leads (A–S, E–S, and A–I). Each lead of the 12-lead ECG can be derived from EASI using a linear combination of these three EASI leads and transformation coefficients. Because the 12-lead ECG was recorded on Mason-Likar positions, we applied the modified EASI coefficients described by Feild *et al.* (2002).

The second method (GEN) uses a lead subset (I, II, V_2, and V_5) of the 12-lead ECG and reconstructs the remaining precordial leads using coefficients obtained from a large study population consisting of patients with acute myocardial infarction, unstable angina pectoris and normal ECGs (Nelwan *et al.*, 2004b). The extremity leads III, aVR, aVL, and aVF are computed from leads I and II in the standard way with no loss of information.

The third method (PS) is similar to GEN, but uses the patient's own baseline 12-lead ECG to select the two precordial leads with the highest morphological correlation. In addition, patient-specific coefficients are determined from this baseline 12-lead ECG for derivations of the other four precordial leads.

Quantitative analysis

The derived ECGs from EASI, GEN, and PS were compared with the corresponding simultaneously recorded 12-lead ECG at baseline and peak. For each recording, absolute ST_{60} differences were calculated between the original and derived ECG for each lead separately, for the summated value of all 12 leads (SUMST) and for the peak ST lead (PEAKST). Furthermore, the angle differences of the frontal QRS axis in the frontal plane were computed between the original and EASI ECG. Overall waveform similarity for each derived ECG was assessed by root mean square errors (RMSE) between the original and derived waveforms based on all samples in the QRS-T complex.

Statistical analysis

Data was recorded, coded, and archived at the Duke University Medical Center, and all statistical analyses were completed at the Erasmus MC. Baseline characteristics are presented as mean±SD, or median (inter-quartile range), where appropriate. SUMST and PEAKST are presented as median (confidence interval). The Wilcoxon signed rank test was used to statistically compare differences. McNemar's test was used to measure agreement in occurrence of maximum ST deviations and regional changes. Percentage agreement and Cohen's kappa (κ) were computed for evaluation of the detection of acute myocardial ischemia (Thygesen *et al.*, 2000) and ST depression. A p-value of <0.05 was considered significant.

For each reconstruction method, Receiver Operating Characteristic (ROC) curves were constructed to assess the performance of the derived ECGs at varying levels of SUMST on the balloon inflation ECG. Mean sensitivity and specificity of SUMST were determined by the bootstrap method (Horacek *et al.*, 2000) using sampling with replacement on the data set of the peak ECGs. For each ROC curve, the area under the curve (AUC) and 95% confidence intervals were calculated. Differences in AUC were statistically compared using Hanley's method (Hanley and McNeil, 1982) (MedCalc, Mariakerke, Belgium).

Results

Recordings were acquired from 44 patients during PCI with balloon inflations in 45 coronary arteries LAD: 11 (24.4%), LCX: 17 (37.8%), RCA: 9 (20%), and graft segments: 8 (17.8%). Patients were all male with an average weight of 88±15 kg, height of 178±6 cm, and body surface area of 2.07±0.18 m^2. The average recording time was 113±45 minutes (range: 22–238 minutes), with an average time to peak of 79±13 minutes. Average duration of coronary occlusion by balloon inflation was 67 seconds (range: 10–175).

A total of 33 recordings showed ST deviations ≥ 100 μV at peak relative to baseline. The most frequent leads with peak ST deviations were observed in V_2: 11 (33.3%), followed by III: 8 (24.2%), and V_4: 4 (12.1%). Regional changes were spatially distributed over the sites: anteroseptal 18 (54.5%), inferior 10 (30.3%), and lateral 5 (15.2%). SUMST for all 12 leads was 518 μV (range: 150–1707) at baseline and increased to 730 μV (range: 171–2079) at peak.

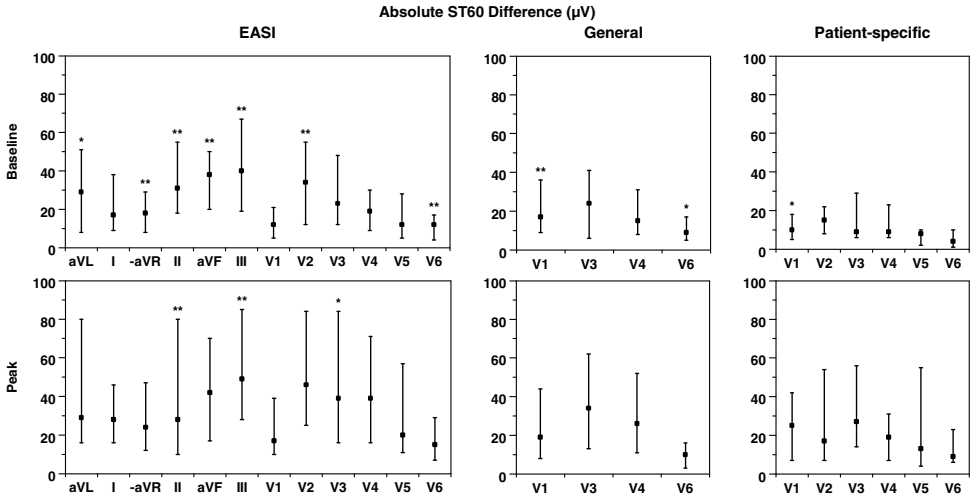

Figure 6.1: Median (inter-quartile range) ST differences between the 12-lead ECG and the derived ECGs from the EASI, general, and patient-specific methods at baseline and at balloon inflation (peak); $p<0.05$; $p<0.01$ in Wilcoxon rank test.

ST measurements

Median absolute ST differences for EASI, GEN and PS are presented in Figure 6.1 for all leads at baseline and peak. For EASI, the highest median absolute ST_{60} differences were observed in the inferior leads II, aVF, and III. Median absolute ST differences in the limb leads for EASI were overall higher than in the precordial leads, but were less pronounced at peak.

For GEN, the highest absolute ST_{60} differences were found in the anteroseptal leads V_1-V_3 at baseline and at peak. Compared with EASI, the maximum absolute ST_{60} difference of 21 μV in V_3 at baseline was twice as low as the maximum difference of 43 μV in lead III observed in EASI. At peak, median differences were overall larger.

The highest median ST_{60} differences for PS were found in anterior leads V_2 and V_3. Overall, absolute median ST_{60} differences were twice as low as GEN. At peak, median absolute ST differences in leads V_2-V_4 for PS remained lower than EASI and GEN, but the differences and inter-quartile ranges in leads V_1, V_5, and V_6 for PS were similar to GEN and EASI.

Accuracy of regional and overall ST changes

Overall, regional ST changes were also found in the derived ECGs of EASI (p=0.639), GEN (p=0.311), and PS (p=0.261). Absolute ST differences between the original and derived peak leads were for EASI: 163 μV (CI: 90–236, $p<0.001$), GEN: 46 μV (CI: 2–91, p=0.40), and PS: 16 μV (CI: 3–30, p=0.15).

SUMST difference was for EASI: 49 μV (CI: 19–220, p=0.02), GEN: 48 μV (CI: -43–154, p=0.26), and PS: 20 μV (CI: -51–32, p=0.65). SUMST ROC curves for EASI, GEN, and PS are presented in Figure 6.2. AUC was for EASI: 88.6% (CI: 82.5–94.7, p=0.02), for GEN:

Table 6.1: Agreement (confidence interval), accuracy (κ), and missed cases (false positive and negative cases) for detection of acute myocardial ischemia/infarction and ST depression based on the original and derived 12-lead ECGs from EASI, general and patient-specific methods at baseline and at balloon inflation (peak).

Decision Rule	Baseline			Peak		
	Agreement	κ	Missed Cases	Agreement	κ	Missed Cases
Acute myocardial ischemia/infarction						
EASI	1.0	1.0	0	0.78 (0.65 – 0.93)	0.45 (0.10 – 0.80)	7
General	1.0	1.0	0	0.91 (0.82 – 1.0)	0.78 (0.54 – 1.0)	3
Patient-specific	1.0	1.0	0	1.0	1.0	0
ST depression						
EASI	0.88 (0.79 – 0.97)	0.60 (0.28 – 0.93)	5	0.69 (0.54 – 0.85)	0.29 (0.0 – 0.66)	12
General	1.0	1.0	0	0.87 (0.77 – 0.98)	0.64 (0.31 – 0.97)	4
Patient-specific	1.0	1.0	0	0.94 (0.86 – 1.0)	0.82 (0.57 – 1.0)	2

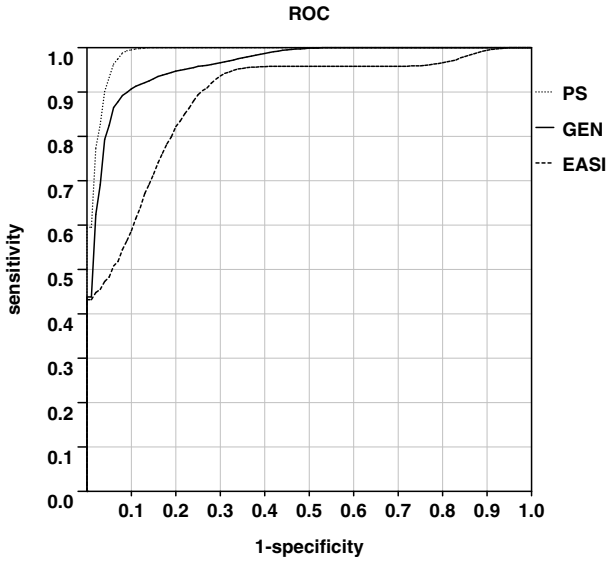

Figure 6.2: Receiver operator characteristic curves for EASI, general, and patient-specific reconstruction methods at varying levels of summated ST (SUMST).

96.1% (CI: 93.1–99.1, p=0.45), and for PS: 98.6% (CI: 97.4–99.8, p=0.61). Of these three reconstruction methods, the AUC of EASI was statistically significant.

Table 6.1 contains the results of the detection of ischemia and evolving infarction (Thygesen *et al.*, 2000) and ST depression of the ECGs at baseline and peak for EASI, GEN, and PS. While PS had an almost perfect agreement and kappa for both decision rules, GEN and EASI missed several cases.

Waveform morphology

Figure 6.3 contains the median and inter-quartile RMSE between the original and derived ECGs for the three methods at baseline and at peak. At baseline, EASI, GEN and PS had the largest RMSE in lead V_3. Overall, EASI had the largest RMSE across all leads, while PS had the lowest RMSE. At peak, median RMSE for EASI, GEN, and PS were overall higher than at baseline. The leads with the highest RMSE were for EASI and GEN lead V_3 and for PS lead V_2.

For EASI, frontal QRS axis angle differences were calculated at baseline and peak between the original and derived ECG. Differences were statistically significant at baseline: 37° (CI: 26–47, p<0.001), and at peak: 36° (CI: 24–47, p<0.001), but the angle difference from baseline to peak did not change significantly.

Figure 6.4 shows the derived 12-lead ECGs from EASI, GEN, and PS at baseline. The original 12-lead ECG is presented in row A. Row B contains all 12 ECG leads that were reconstructed from the EASI leads. In rows C and D, leads V_1, V_3, V_4, and V_6 were reconstructed using GEN and PS, respectively. Visual reconstruction differences are present for EASI in the inferior leads, for GEN in precordial lead V_1, and for PS in lead V_3. However, ST differences were small. Figure 6.5 presents the reconstructed ECGs at peak balloon inflation. Overall, reconstruction performance was lower for all three derived ECGs. The

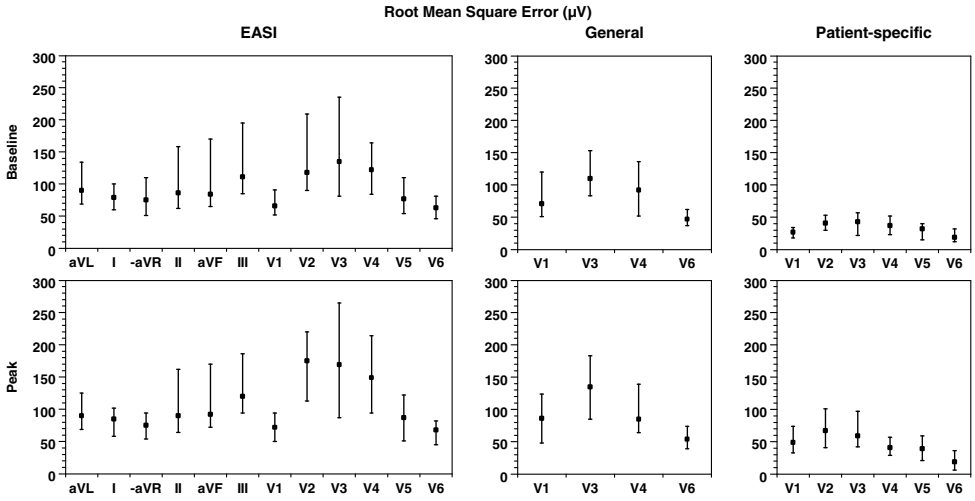

Figure 6.3: Median (inter-quartile range) root mean square errors between the 12-lead ECG and the derived ECGs from EASI, general, and patient-specific methods at baseline and at balloon inflation (peak).

highest ST differences were found for EASI in the inferior leads, and the highest ST difference for GEN and PS was observed in lead V_3.

Discussion

The findings in this study show that several measurable differences were found between the standard 12-lead ECG and the derived ECGs produced by the three methods tested. The PS method had the best performance with the lowest absolute differences for lead-specific peak ST deviations, overall SUMST and RMSE values. PS coefficients are tailored for each individual, while GEN and EASI provide coefficients mathematically based on large data sets that may be more applicable to some patients than to others. However, PS requires the availability of a previously recorded 12-lead ECG for derivation of the individualized reconstruction coefficients. Thus, based on our findings, in clinical settings where an initial resting ECG can be acquired, the PS method would support ongoing monitoring using only 6 electrodes with very good accuracy. In clinical settings where an initial ECG could not be acquired, 5- or 6-electrode monitoring would be more feasible but with less accurate waveforms compared to standard 12-lead ECG.

GEN differences were overall higher than PS, but were smaller than EASI. In this study, we applied a fixed lead subset of I, II, V_2, and V_5, but GEN performance depends on placement of electrodes (Nelwan *et al.*, 2004b; Horacek *et al.*, 2002). Lower lead-specific differences might be obtained if a different combination is selected based on other clinical information, such as the infarct location. Drew *et al.* (2002) also used lead subset technology, but used V_1 instead of V_2 to increase accuracy in atrial QRS morphology.

In this study, EASI showed the highest differences for both overall SUMST and lead-specific ST measurements, and RMSE. EASI has been investigated in various settings including ambulatory monitoring (Denes, 1992), in-hospital patient monitoring settings

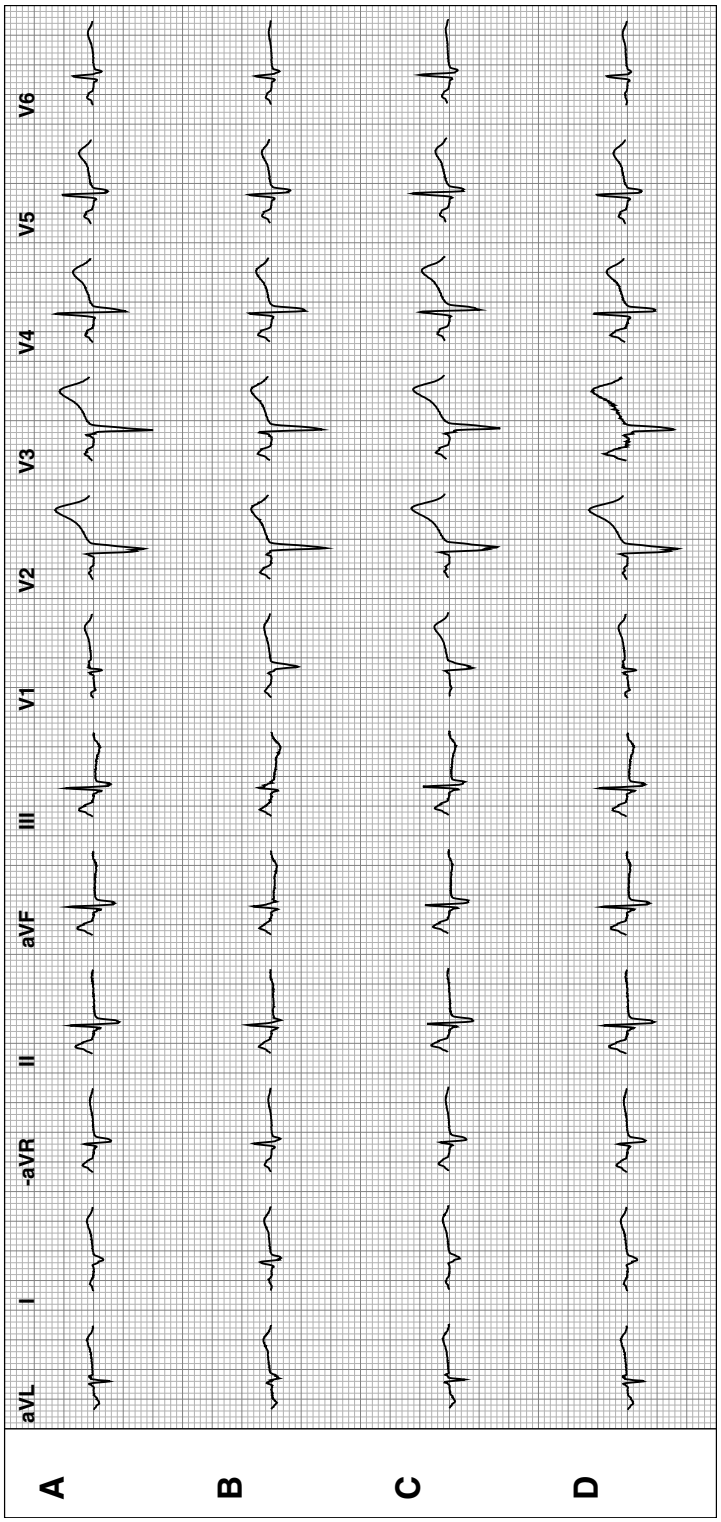

Figure 6.4: Example of the conventional 12-lead ECG (A) and the three reconstructed ECGs prior to a percutaneous coronary intervention. Row B contains all 12 ECG leads reconstructed from the EASI leads. Rows C and D present the reconstructed leads V_1, V_3, V_4, and V_6 from a reduced lead set of I, II, V_2, and V_5 using general and patient-specific reconstruction, respectively.

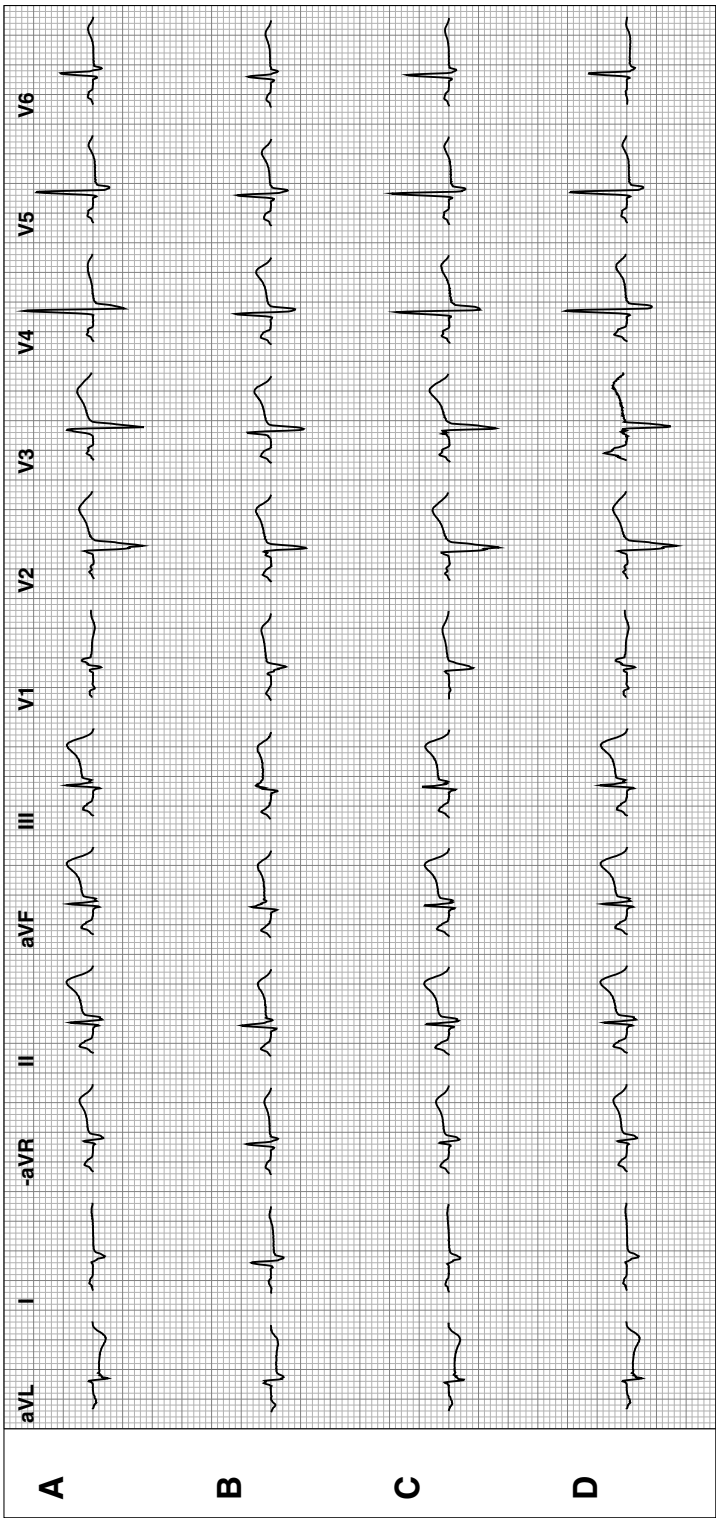

Figure 6.5: Example of the conventional 12-lead ECG (A) and the three reconstructed ECGs during balloon inflation as part of a percutaneous coronary intervention procedure. Row B contains all 12 ECG leads reconstructed from the EASI leads. Rows C and D present the reconstructed leads V_1, V_3, V_4, and V_6 from a reduced lead set of I, II, V_2, and V_5 using general and patient-specific reconstruction, respectively. Note the ECG differences with the standard ECG (A) in the inferior leads (EASI) and lead V_3 (general and patient-specific).

(Drew *et al.*, 1996), and has been commercially available for several years. EASI requires five electrodes placed on well-defined ECG locations, which may reduce artifacts and noise. However, an important disadvantage of EASI is that all 12 leads, including the extremity leads, are derived. For EASI, the highest absolute ST differences and RMSE were found in the inferior region, while both GEN and PS always contain the directly recorded leads in this area.

Clinical implications

Statistically significant differences in AUC, SUMST, and PEAKST observed in comparing digital waveforms in this study may not always be clinically significant per se. In general, less than 30 μV differences are about the width of the ink line in paper ECGs, and are considered of little meaning in routine clinical use. However, for automated ischemia detection algorithms in digital instruments, a 30 μV variation in borderline conditions might have an important impact — for instance, if new ST deviation of 90 μV is recorded, over-estimation by 30 μV would trigger an alarm if the threshold was set for new 100 μV deviations. Thus, in addition to the direct measurement differences documented in this study, derived ECG technologies will require careful integration into clinical monitoring systems.

Another important clinical aspect of using derived ECGs for continuous monitoring is reduction of noise artifacts resulting in uninterpretable ECG signals. The derived ECGs showed overall less noise than the actual 12-lead ECG recording, but certain artifacts can be introduced. In three recordings, the EASI derived ECG was for a certain period completely unavailable as a result of a lead failure condition of electrode A. For GEN and PS, monitoring still continues if one or two precordial leads have problems.

Study limitations

This study has several limitations. First, the total number of patients is relatively small. However, the study was set up as a prospective, comparative, within-subjects study in which patients served as their own controls. Furthermore, this study uses Mason-Likar electrode positions instead of the standard extremity locations at the wrists and ankles. Thus, this study did not directly compare the derived 12-lead ECGs with standard 12-lead ECG. However, Mason-Likar monitoring is preferred in clinical settings over the standard extremity positions because of reduced interference of muscle artifacts and patient comfort.

Conclusion

Simultaneous direct comparison of the original 12-lead and derived ECGs from the EASI, GEN and PS methods show significant differences across these methods. Median root mean square errors, ST_{60} and SUMST differences were overall lower for the GEN and PS methods than for EASI at baseline and during balloon inflation. PS has the lowest measurement differences and the highest overall accuracy, and is preferred over GEN and EASI.

Part III

Patient Monitoring

7

Detection and Correction of Body Position Changes

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Abstract

Background

Electrocardiogram (ECG) variations due to changes in body position are a common problem during continuous ECG and ST monitoring. Body position changes (BPC) may cause QRS and ST-T changes, trigger false alarms, and may complicate diagnostic interpretation. The purpose of this study was to assess the effects of these changes and to develop a detection and correction strategy.

Methods

Continuous 12-lead ECG recordings were obtained from 114 patients admitted to the coronary care unit. Each patient underwent a body position test (supine, left, right, and upright position). A body position change detector was developed using the EXPLORE automated rule induction algorithm. To distinguish positional from ischemic changes, a separate set of 71 PCI recordings was included with ECGs at rest and during balloon inflation. ECG variations were corrected using a patient-specific mapping technique based on a combination of leads. Performance of the correction method was assessed by Pearson's correlation coefficient and by similarity coefficient ($SC = 1 - RMS_{residual}/RMS_{signal}$).

Results

ST changes ≥ 100 μV in ≥ 1 lead caused by a body position change were observed in 50 (43%) patients. Most pronounced changes were found in the left-lateral position. With a fixed specificity at 95%, sensitivity of the detection rules was for left: 97.4%, right: 69.9%, upright: 64.3% and combined: 66.1%. False alarm rate per hour in the PCI set was 2.22 at rest and 4.31 during balloon inflation. Performance of the patient-specific correction yielded an overall correlation coefficient of 0.970 and similarity coefficient of 0.889.

Conclusion

ECG changes due to BPC are most pronounced for the left-lateral position. BPC detection rules showed high but varying levels of sensitivity for each position. Accurate reconstruction of any position to the supine position is possible.

Introduction

A well-known problem during continuous ECG monitoring is that body position changes (BPCs) may alter the surface 12-lead ECG. ECG variations may occur, such as changes in R and S waves in the limb and lateral leads, sudden ST-segment shifts and/or T-wave inversions, which may trigger false alarms during continuous ECG and ST monitoring (Adams and Drew, 1997; Jernberg *et al.*, 1997; Norgaard *et al.*, 2000; Pharand *et al.*, 2003).

Detection of body position changes is important to avoid misclassification of ischemic episodes. Recently, methods to detect these body position changes have been proposed on ECG parameters only (Shinar *et al.*, 1999; Astrom *et al.*, 2003; Garcia *et al.*, 2003), while other investigations (Adams and Drew, 2002; Ng *et al.*, 2003) proposed detection with auxiliary devices such as small accelerometers which detect gravitational changes. Although these detection methods show promising results, detected episodes would leave a gap in the ST trends, making retrospective ST-segment analysis difficult.

The aim of this study was to investigate the effects of body position changes on the ECG, and to develop methods to detect and correct for these changes.

Methods

Data sets

Two different data sets were used. The first data set consisted of patients who were admitted to the coronary intensive care unit due to chest pain or suspicion of acute myocardial infarction and who were able to undergo a body position test. A total of 114 patients participated in the study. The patients were predominantly male (n=93, 83%) with an average age of 60 years (range 20–85) . Of these patients, 59 (51.8%) were admitted with (unstable) angina pectoris, 44 (38.6%) were diagnosed with acute myocardial infarction and the remaining 11 (9.6%) patients were admitted for other cardiac reasons. Patients were prospectively monitored using a patient monitoring device with continuous 12-lead ST monitoring capabilities (SC7000, Siemens Medical Systems, Danvers, USA). Electrodes were placed on monitoring compatible locations according to Mason and Likar (1966). All ECGs were recorded at a sample rate of 500 Hz with a least significant bit of 2.5 μV.

A body position test was performed as soon as the patient was haemodynamically stable and free of chest pain and ongoing ischemia. During the body position test, the patient was asked to move into the positions: *supine*, *left-lateral*, *supine*, *right*, *supine*, and in a *60 degrees upright* position. Each position was maintained for five minutes. A 10-second, 12-lead ECG was recorded in the middle of this period in order to minimize possible ST artifacts and heart rate changes as a result of turning. The time of the body position change was marked on the patient monitor. All body position tests were performed by the same investigator, who was informed of the purpose of this study.

A second data set consisted of 71 patients (all males, 63 ± 12 years) undergoing percutaneous coronary intervention procedures (PCI data set). For each patient, continuous 12-lead ECG data was recorded 30 minutes prior to and after the PCI procedure with the same type of Siemens patient monitoring equipment as was used for the body position data set. At the start of the procedure, a 5-minute 12-lead baseline ECG (*baseline*) was marked. ST changes indicative of ischemia during the baseline recordings were considered unlikely. Another ECG (*inflation*) was marked at balloon inflation. The inflation

ECG was started one minute prior to the marked first balloon inflation and continued for four minutes. An inflation ECG may contain multiple balloon inflations and one or more ST changes. The study group and protocols have been described previously (Nelwan *et al.*, 2004a).

Data analysis

ECG measurements, including QRS and T-wave amplitudes, frontal QRS axis and ST_{60} values for each lead were processed with the Modular ECG Analysis System (MEANS). MEANS computes representative averaged complexes for each of the 12 leads from which ECG measurements are derived. MEANS is also capable of reconstructing the vectorcardiographic X, Y, and Z leads on the basis of the standard ECG leads. MEANS has been extensively evaluated and validated in several clinical and preclinical settings (van Bemmel *et al.*, 1990; Willems *et al.*, 1991). Average complexes were computed every 10 seconds over the entire observation period for the recordings in both data sets. MEANS also computed the spatial angle between the QRS and T loops, spatial J amplitude, and maximum spatial T amplitude.

Body position detection

The detection method is based on the assumption that a body position change shifts the chest electrodes relative to the heart. As a result, the dominant R and T peaks may shift spatially, but the change should not alter global measurements, such as the angle between the QRS and T wave or the spatial vector magnitude.

Parameter differences between the supine and the left, right, or upright position were computed and each position ECG was labelled. To distinguish position changes from ischemic changes, we included the PCI data set (Nelwan *et al.*, 2004a). Parameter differences were computed between the baseline and the first marked balloon inflation ECG.

Using both data sets, classification rules were automatically generated using the EXPLORE rule induction algorithm (Rijnbeek *et al.*, 2000, 2001). EXPLORE exhaustively searches the rule space for optimal decision rules with respect to user-selected performance measures, such as sensitivity and specificity. Rule induction was performed using 10-fold cross validation with separate learning and test sets.

The body position change detector was designed to separate the different positions from ischemic changes given an ECG with ST-T changes. EXPLORE was set up to maximize sensitivity with a minimum level specificity of 95% for the detection of each position change separately and for any position (combined) versus ischemic change. Secondly, we set up EXPLORE to search for a combined decision rule based on spatial parameters only in order to reduce dependency of single ECG leads in which noise or lead failure might cause false positives.

The intended use of the body position detector would be in a clinical situation with an ST alarming functionality. In patient monitoring, ST alarms are set to detect an ST change of a certain threshold ($\geq$ 100 μV) in one or more leads lasting $\geq$ 1 minute (Klootwijk, 1998). In order to rule out ST alarms caused by patient movement, a positive body position detection can be used to suppress or advise the clinician to ignore the ST alarm. For the purpose of assessing the number of false positive body position detections during patient monitoring, we applied the decision rules on the 5-minute baseline and balloon inflation ECGs and computed the number of false alarms per hour. In this study, the

latency time of the ST-change detector was reduced to 30 seconds, because the balloon inflations in the PCI data set were ≤ 1 minute.

Body position correction

The body position correction method is based on the recorded body position test. Each known position can be mapped to the supine position for each of the 12 leads by stepwise multiple linear regression (Galassi *et al.*, 2000). With this approach, all available information is used to reconstruct each lead, but variables with little contribution are discarded from the fit.

Because the reconstruction technique is patient-specific, a second body position test was performed and was used for the test set. Overall reconstruction performance was assessed for each lead using Pearson's correlation coefficient and the average of these 12 correlation coefficients was taken. Reconstruction performance per lead was also assessed using the similarity coefficient ($SC = 1 - RMS_{error}/RMS_{source}$) (Kornreich and Rautaharju, 1981), and then averaged over the 12 leads.

Statistical analysis

Differences are presented as mean ± standard deviation or median (inter-quartile range), where appropriate. Differences in baseline characteristics were evaluated by t-test or by χ^2-test. Paired t-tests were employed for within-patient ECG differences caused by body position changes. Classificator performances were evaluated with sensitivity, specificity, and accuracy. A p-value of <0.05 was considered significant.

Results

Initial ECG characteristics

Compared to the reference ECG in supine position, 50 of 114 (43%) patients showed marked ST changes ($|\Delta ST| \geq 100$ μV in ≥ 1 lead) in one or more positions. A comparison of the characteristics of patients with or without ST changes is presented in Table 7.1. Patients with or without position change had a similar age, gender and BMI composition. In the group of patients with ST changes, initial summated ST_{60}, spatial J amplitude, and spatial QRS-T angle were larger.

ECG changes

An example of a patient with a frontal QRS axis change of 30 degrees caused by body position is shown in Figure 7.1. Local T-wave inversion is present in lead V_5 of the supine position (row A) and disappears in the left position (row B). Other ECG changes caused by turning to the left-sided position are the decrease in R_{V_4} and elevation of ST_{V_4}. Figure 7.2 presents the frontal QRS axis and ST_{60} trends in leads V_3-V_6 during the night and morning of the same patient. During the night, the patient moved into several positions and sudden shifts in the lateral leads can be observed.

Table 7.2 presents the average ST_{60} differences and the number of occasions in which the differences were ≥ 100 μV for each position change. The largest differences were found for the left-sided position in anterolateral leads V_3-V_6. The maximum absolute ST

Table 7.1: Characteristics of patients with or without ST changes ≥ 100 µV in ≥1 lead caused by body position changes (n=114).

Characteristic	No ST Change (n=64)	ST Change (n=50)	*p*-value
Demographics			
Men (n,%)	54 (84)	39 (78)	0.068
Age (years, range)	58 (32 – 79)	60 (20 – 85)	0.361
BMI (kg/m^2)	26.8 ± 3.68	25.6 ± 3.79	0.083
Discharge Diagnosis			0.068
Myocardial infarction (%)	19 (30)	25 (50)	
Angina pectoris (%)	39 (60)	20 (40)	
Other (%)	6 (10)	5 (10)	
ECG			
HR (bpm)	67 ± 15	77 ± 19	0.004
LVH (%)	4 (6.3)	9 (18)	0.05
Summated ST_{60} (µV)	536 ± 244	872 ± 468	<0.001
Frontal QRS Axis (°)	28 ± 51	21 ± 63	0.195
Frontal T Axis (°)	26 ± 82	16 ± 101	0.237
Spatial QRS-T angle (°)	65 ± 49	83 ± 61	<0.001
Spatial J amplitude (µV)	70 ± 48	88 ± 62	<0.001
Spatial T_{max} (µV)	321 ± 137	320 ± 139	0.984

Table 7.2: ST differences (µV) caused by a position change and number of leads ≥ 100 µV for all patients (n=114).

	Supine → Left		Supine → Right		Supine → Upright	
	ΔST (µV)	≥ 100 µV	ΔST (µV)	≥ 100 µV	ΔST (µV)	≥ 100 µV
I	4 ± 21	–	4 ± 17	–	6 ± 25	–
II	-4 ± 18	–	-3 ± 33	–	0 ± 16	–
III	-9 ± 17	–	-6 ± 36	–	0 ± 14	–
aVR	1 ± 14	–	0 ± 20	–	0 ± 18	–
aVL	6 ± 21	–	5 ± 23	–	0 ± 13	–
aVF	-7 ± 18	–	-5 ± 33	–	0 ± 15	–
V_1	-3 ± 22	2	11 ± 34	–	5 ± 21	–
V_2	-15 ± 39	3	-8 ± 52	4	0 ± 29	1
V_3	12 ± 40	5	12 ± 81	2	-6 ± 24	–
V_4	30 ± 50	11	16 ± 79	4	-2 ± 26	–
V_5	3 ± 60	9	2 ± 55	1	2 ± 16	–
V_6	-18 ± 47	9	-3 ± 26	2	0 ± 16	–

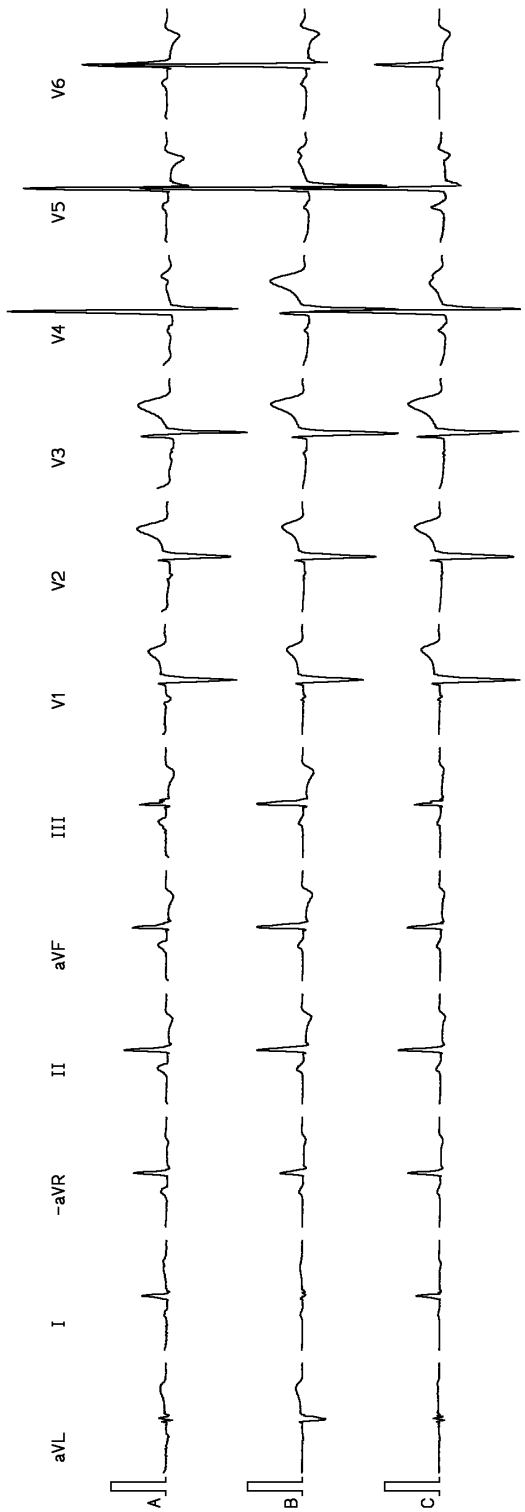

Figure 7.1: Example of ECG changes caused by a body position change to the left side. Row A contains the reference supine position ECG complexes and row B contains the ECG complexes with the patient in left-lateral position. An example of a body position correction is shown in row C, where the complexes of row B have been mapped back to the supine position.

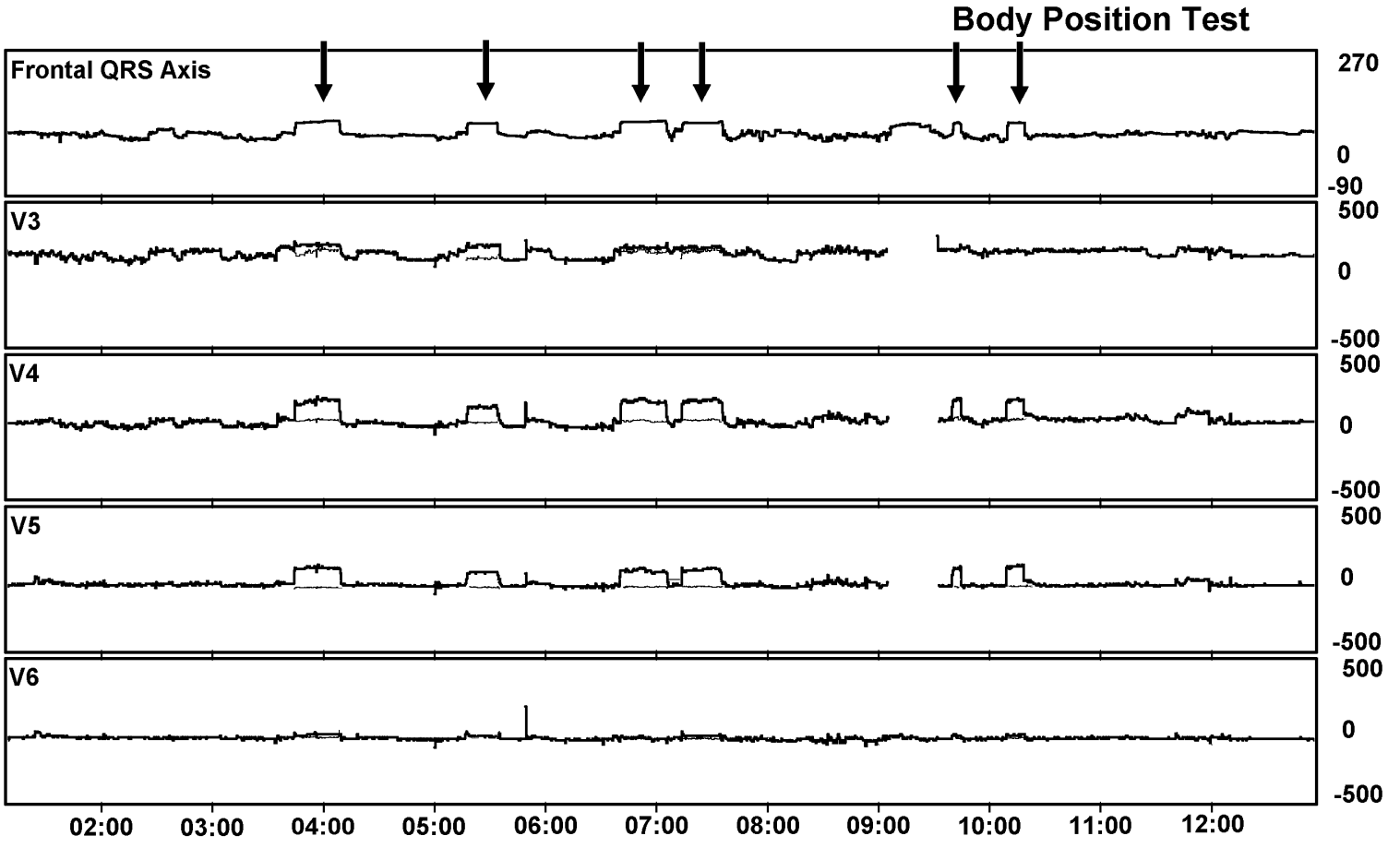

Figure 7.2: Example of a body position correction in leads V_3-V_6 of the patient in Figure 7.1. The arrows indicate a left-lateral position of the patient during the night and subsequent body position test. The corrected trend (thin lines) for the left-lateral position is superimposed on the original trend (fat lines).

difference was 233 μV in lead V_4. For the right-sided position, differences were smaller and were located in the anterior leads V_2-V_4. Changes in the upright position were generally small and were overall 0 in the limb leads. For all positions, ST changes ≥ 100 μV were not found in the limb leads.

Spatial ECG changes are reported in Table 7.3 for all patients. The smallest and largest frontal QRS axis differences were observed for the respective changes to upright and left position. Compared with the frontal QRS axis, the frontal T axis difference was higher for the left and right position change, but also showed a larger variation. Overall, the largest differences for the spatial parameters were found for the left position change and the lowest for the upright position.

Table 7.3: Spatial ECG differences for each body position change (n = 114).

Measurement	Supine → Left	Supine → Right	Supine → Upright
Δ Frontal QRS Axis (°)	15.0 ± 17.5	12.7 ± 14.6	6.1 ± 5.1
Δ Frontal T Axis (°)	22.3 ± 41.2	24.6 ± 55.5	8.9 ± 10.8
Δ Spatial QRS-T Angle (°)	17.5 ± 15.5	16.0 ± 18.7	12.4 ± 9.7
Δ Spatial J Amplitude (μV)	11.3 ± 20.1	7.5 ± 23.0	-3.1 ± 15.1
Δ Spatial T_{max} (μV)	49.2 ± 62.6	13 ± 71.3	-12.7 ± 42.1

Body position detection

Table 7.4 presents the detection rules for each position and the detector performance with a fixed specificity of at least 95% in discriminating between any position versus balloon inflation. The upper part of Table 7.4 contains detection rules for use on any ECG. The lower part of the table contains detection rules which require an ST-change detector (|ΔST| ≥ 100 μV in ≥ 1 lead).

Sensitivity of the detection rule for the left-lateral position was higher than other rules. Sensitivity of the rule with spatial measurements only was low. Sensitivity of the combined detection rule for all body positions was higher. If specificity was lowered from 95.7% to 91.3%, sensitivity of the combined detection rule would increase to 92.1%. Optimal detection rules contain R and S amplitudes of the limb and lateral (I, V_5, and V_6) leads.

The detection rules optimized for use after detection of a marked ST change (|ΔST| ≥ 100 μV in ≥ 1 lead) show increased sensitivity and specificity of up to 100% for the left-lateral detection rule. Because of the low number of cases with ST changes in the upright position (cf. Table 7.4), detection rules were computed using the left or right position only.

Table 7.5 presents the false alarm rate per hour of the body position detection rules applied on the 5-minute baseline and balloon inflation recordings. The total available recording time was 10 hours and 45 minutes. A total of 17 ST events were detected at baseline and 59 during balloon inflation. Multiple balloon inflations may have occurred in a single patient and ST changes may not have reached the threshold of 100 μV in others.

Table 7.4: Sensitivity, specificity, and accuracy of the body position detection rules between the left, right, and upright position versus balloon inflation ECGs with or without the presence of |ΔST| ≥ 100 μV in ≥ 1 lead

	Best detection rule	Sensitivity (%)	Specificity (%)	Accuracy (%)
Position				
Left	$\Delta R_I < -152$ *or* $\Delta R_{V_6} > 245.5$ *or* $\Delta S_{V_6} \leq -56.5$	97.4	95.7	96.7
Right	$\Delta R_{II} > 0.5$ *and* $\Delta S_{V_5} \leq 18.5$ *and* $\Delta QRST \leq 35.5^o$	69.6	95.7	79.6
Upright	$\Delta ST_I > -1.5$ *and* $\Delta S_{V_2} > -88$ *and* $\Delta SPJAMPL^* \leq 12.5$	64.3	95.7	83
Combined				
Spatial only	$\Delta QRST \leq 22.5^o$ *and* $\Delta SPJAMPL^* \leq -0.5$	31.7	95.7	44.8
All parameters	$ST_{aVF} \leq 37.5$ *and* $R_I \leq -70.5$ *or* $R_{V_6} > 276$	66.1	95.7	72.1
Detection rules for use with |ΔST| ≥100 μV in ≥ 1 lead				
Position				
Left	$\Delta R_{V_6} > 280$ *or* $\Delta S_{V_6} \leq -55$	100	100	100
Right	$\Delta R_{aVR} > 64.5$ *or* $\Delta S_{V_6} \leq -126$ *or* $\Delta SPJAMPL^* \leq -4.5$	80	97.4	93.9
Combined				
Spatial only	$\Delta QRST > 3.5^o$ *and* $\Delta QRST \leq 52.5^o$ *and* $\Delta MAXSPAMPLT^{***} > -1$	75	100	87.5
All parameters	$\Delta R_{V_6} > 280$ *or* $\Delta S_{V_6} \leq -55$ *or* $\Delta SPJAMPL^* \leq -4.5$	100	97.4	98.7

* *SPJAMPL: spatial J amplitude*

** *Upright position not investigated due to insufficient number of cases with* |ΔST| ≥ *100 μV)*

*** *MAXSPAMPLT: maximum spatial T amplitude*

Table 7.5: False alarm rate per hour of the body position detection rules applied on baseline and balloon inflation recordings (total recording time 10 hours and 45 minutes).

Detection rule		Baseline	Balloon inflation
	Left	2.03	3.56
	Right	1.11	5.81
	Upright	0	0.56
Combined	Spatial parameters only	3.14	5.95
	All parameters	2.22	4.31
$\|\Delta ST\| \geq 100$ μV in ≥ 1 lead			
	Left	0	0.75
	Right	0	0
Combined	Spatial parameters only	0	0.93
	All parameters	0	0.75

The highest false alarm rate of the body detection rules was found for the rules using spatial parameters only at baseline and at balloon inflation. The lowest false alarm rate was observed for the upright position. In combination with an ST-change detector, the false alarm rate of all detection rules dropped to 0.75 at balloon inflation.

Body position correction

Table 7.6 presents median correlation and similarity coefficients for the correction of the left, right, and upright to the supine position. Overall, high median correlation and similarity coefficients were observed. The highest overall correlation and similarity were found for the correction of the upright position, but differences with the other two corrections were small.

Table 7.6: Median (inter-quartile range) correlation and similarity coefficients of the body position correction method between the left, right, and upright position.

Position	Correlation	Similarity Coefficient	QRS Axis Difference (°)
Left	0.964 (0.921 – 0.985)	0.883 (0.802 – 0.921)	2 (1 – 4)
Right	0.967 (0.946 – 0.973)	0.901 (0.830 – 0.933)	2 (-1 – 6)
Upright	0.975 (0.937 – 0.991)	0.911 (0.880 – 0.941)	1 (0 – 3)

Figure 7.2 shows a retrospective patient-specific correction of the left-lateral body position change during the night based on the body position test that was performed between 9:00 and 10:00 the following morning.

Discussion

In this study, ECG changes caused by body position changes were investigated. Detection rules and a patient-specific correction method were developed and evaluated.

Body position change

ST changes of ≥ 100 μV as a result of body position changes occurred in 50 of the 114 (43%) patients and could be identified as a clinically significant ST change. Body position changes were most pronounced in the left-lateral position and least pronounced in the upright position. Body position changes caused ST changes of ≥ 100 μV in the precordial leads only.

Body position detection

In this study, body position detection rules were developed for two strategies. First, rules were developed for the detection of body position changes versus ischemic changes. Second, detection rules were optimized for use with a standard ST-change detector as commonly used in clinical practice. High to very high sensitivities at a fixed sensitivity of 95% were observed for both strategies.

Automated detection of body position changes can also be performed using scalar and spatial techniques described in another study by Garcia *et al.* (2003). These investigators developed an ECG-based body position detector and report sensitivity between 89% to 95% with a specificity rate up to 97 ± 5% in a group of 20 volunteers performing several body position tests. The body position detector in our study had a lower sensitivity, but a direct comparison cannot be made because our detector was designed to separate body positions from ischemia. Garcia *et al.* (2003) have also tested their method in a group of 83 angioplasty recordings. A false alarm per hour rate was reported of 2–4 at baseline and 7–11 during balloon inflation. In this study, lower false alarm rates were found for the detection rules with or without the use of an ST-change detector.

Use of external devices, such as motion detectors or accelerometers might be a more direct way of measuring the position change and prior studies by Adams and Drew (2002) and Ng *et al.* (2003) show promising results. An auxiliary device requires additional training and can be a source of errors as a result of artifacts. A more advanced approach might be video recording and computer image recognition of the patient's position. However, the presented body detection rules in this study do not require additional devices and can easily be applied with the available ECG equipment.

Body position correction

The body position correction method shows very high reconstruction performance results, but it requires a previously recorded body position test from each patient. If the body position is known (either from a body position detector or from other observations), the ECG can be corrected to supine position. An advantage of this method is that it is possible to lessen the effect of body position changes during an ischemic event, so that only ST changes caused by ischemia may be present. Unfortunately, we did not observe such events in our data sets.

Study limitations

Several study limitations can be identified. First, we did not prospectively analyze body position changes during a long-term stay of the patient at the intensive care. Furthermore, to represent ischemic episodes on the ECG, we used PCI database recordings with ST changes caused by balloon inflation. In intensive care settings, ischemic events may appear more gradual over time and the magnitude of changes may be less. Further investigation on a data set of long-term recordings and verifiable body position is advisable.

Conclusion

In conclusion, this study confirms that ECG changes as a result of body position changes are frequent and can be identified as clinically significant ST changes. Furthermore, the body position detection rules in this study show high sensitivity and can be applied by clinicians or by a computer. Lastly, the body position correction method can be applied to remove body position changes in the waveforms.

Appendix

The presented optimal body position detection rules require measurements from the 12-lead ECG and VCG. These measurements can be difficult to compute by patient monitoring devices with limited processing power and memory resources. The following rules were determined by EXPLORE and only require 12-lead ECG measurements. Minimum sensitivity was set at 95%.

Position	Best detection rule	Sensitivity (%)
Left	$\Delta R_I < -152 \; or \; \Delta R_{V_6} > 245.5 \; or \; \Delta S_{V_6} \leq -56.5$	97.4
Right	$ST_{aVF} \leq 37.5 \; and \; R_{AVF} > 25.5 \; and \; R_{V2} \leq 191$	68.8
Combined	$ST_{aVF} \leq 37.5 \; and \; R_I \leq -70.5 \; or \; R_{V_6} > 276$	66.1
Detection rules for use with $\lvert\Delta ST\rvert \geq 100$ µV in ≥1 lead		
Left [1]	$\Delta RV_6 \geq 280 \; or \; SV_6 \leq -55$	100
Right [1]	$\Delta SV_2 > -33 \; and \; SV_5 \leq -127.5 \; or \; RaVR > 64.5$	80
Combined [2]	$\Delta RV_6 > 280 \; or \; SV_2 \leq -615 \; or \; SV_6 \leq -42.5$	91.2

[1] specificity: 100%, [2] specificity: 97.4%

8

Correction of ECG Variations due to Non-Standard Electrode Positions

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Abstract

Introduction

Electrode positions for continuous 12-lead ECG monitoring are different from those for recording a standard 12-lead ECG. To reduce noise and to minimize false alarms, proximal placement of the limb leads is preferred over the standard location at the wrists and ankles. Differences are often associated with frontal QRS-axis shifts, disappearing Q waves, and marked changes of R amplitudes in the extremity leads. This study presents general and patient-specific reconstruction methods to correct for these changes.

Methods

A simultaneously acquired 9-lead ECG in standard and monitoring positions was recorded in 88 patients. Data was split into a learning (n=30) and test set (n=58). General reconstruction coefficients were computed from the learning set and applied to the test set. Patient-specific coefficients were also computed and applied. Performance was evaluated using a similarity coefficient ($SC = 1 - RMS_{residual}/RMS_{signal}$) and frontal QRS axis angle difference ($\Delta\angle$QRS, monitoring – standard). Accuracy was tested with paired t-tests (p<0.05).

Results

Median (inter-quartile range) SC between standard and monitoring ECGs was for lead I 0.737 (0.595–0.777) and lead II 0.687 (0.613–0.778), and $\Delta\angle$QRS was 13 (4–25)°($p < 0.001$). For general reconstruction, SC was for lead I 0.770 (0.672–0.815) and lead II 0.866 (0.783–0.918), and $\Delta\angle$QRS was 2 (-3–12)°(p = N.S.). For patient-specific reconstruction, the respective SC were 0.891 (0.828–0.933) and 0.927 (0.865–0.950), and $\Delta\angle$QRS 0 (-1–3)°(p = N.S.).

Conclusions

Reconstruction of ECG leads from monitoring positions to standard positions is possible using general and patient-specific coefficients. Patient-specific reconstruction performance is overall higher than general reconstruction, but requires the recording of an additional ECG.

Introduction

During continuous ECG monitoring, proximal placement of the extremity electrodes (LA, RA, LL, and RL) on the torso is often preferred over the positions of the standard resting ECG at the wrists and ankles. In these situations, the torso positions proposed by Mason and Likar (1966) reduce noise and minimize false alarms as a result of motion artifacts.

However, previous investigations (Sevilla *et al.*, 1989; Pahlm *et al.*, 1992; Krucoff *et al.*, 1994; Bartosik *et al.*, 1995; Jowett *et al.*, 2005) have indicated that the change to proximal electrode positions may produce a different 12-lead ECG. Changes between the standard and monitoring ECG may vary from sudden frontal QRS-axis shifts, changes in Q waves in the inferior leads, to marked changes in R amplitudes in the extremity leads (I, II, III, aVR, aVL, and aVF). The influence of the proximal placements on the precordial leads and on the ST-T segment during percutaneous coronary interventions was found minimal (Krucoff *et al.*, 1994).

The primary purpose of this study was to investigate the effect of the lead placement on the ECG in a routine practice and to investigate methods to correct for these changes using general and patient-specific reconstruction methods.

Methods

Study population

The study population consisted of 93 subjects who were admitted to the coronary intensive care unit of the Erasmus MC due to chest pain or suspicion of acute myocardial infarction. The patients were randomly selected over a period of 18 months (January 2000 to June 2001). The study group was predominantly male (71 of 93) with an average age of 62 years (range 32–86). At the start of each recording, all patients were haemodynamically stable and free of chest pain, ongoing ischemia or infarction.

ECG recording

For each patient, two 9-lead ECGs were simultaneously recorded using a standard 12-lead ECG patient monitor (SC7000, Siemens Medical Systems, Danvers, USA). This configuration was described by Pahlm *et al.* (1992) and allows simultaneous recording of the limb leads in standard and in monitoring positions. In this modified 12-lead configuration, the electrodes V_2, V_3, and V_5 remain on the standard chest positions, while the V_1, V_4, and V_6 electrodes are moved to the Mason-Likar (Mason and Likar, 1966) monitoring positions of RA, LA, and LL. Figure 8.1 contains the positions on the chest. With these electrode measurements, the limb leads can be computed off-line for the monitoring positions.

The ECGs were recorded at a sampling rate of 500 Hz with a resolution of 2.5 μV, for 10 seconds and were processed with the Modular ECG Analysis System (van Bemmel *et al.*, 1990). For both 9-lead recordings, average representative beats and measurements were computed. All recordings were inspected visually. A total of five recordings were excluded because of excessive noise.

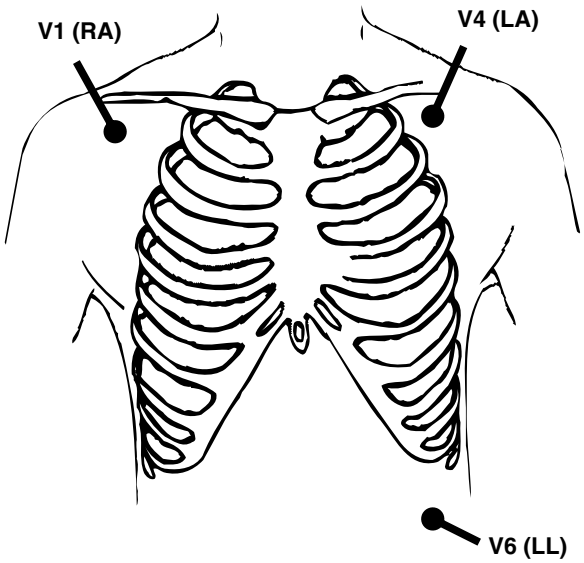


Figure 8.1: Alternative placements of the electrodes V_1, V_4, and V_6 on the monitoring locations RA, LA, and LL. Illustration © Siemens/Dräger Medical Systems, Inc., used with permission.

ECG reconstruction

The study group was split into a learning set consisting of the first 30 patients and a test set of the remaining 58 patients. General reconstruction coefficients for leads I and II were computed by linear regression from the monitoring to the standard leads of the learning set and were applied to each recording.

The following equations were used for reconstruction of a standard ECG from the recorded signals on the monitoring positions:

$$\begin{aligned} I_r &= c_1 I_m + c_2 II_m \\ II_r &= c_3 I_m + c_4 II_m \end{aligned} \tag{8.1}$$

I_m and II_m denote the limb leads in monitoring position and, I_r and II_r the reconstructed ECGs representing the standard position. Patient-specific reconstruction coefficients for each ECG were also computed in a similar way.

Overall waveform similarity was assessed by a similarity coefficient (SC) (Kornreich and Rautaharju, 1981) between the complexes of the original and reconstructed leads I and II over the samples of the QRS-T interval. SC is defined as:

$$SC = 1.0 - \frac{RMS_{residual}}{RMS_{signal}} \tag{8.2}$$

In addition, we compared the R amplitudes, ST-segment levels 60 ms after the J point for leads I and II, the difference of the Wilson central terminal and the angle difference of QRS axis in the frontal plane between the original and reconstructed ECGs. Correlation coefficients (CC) were also calculated, as these measurements are widely used to compare similar data. However, a CC is nonlinear and it is only reported next to the SC.

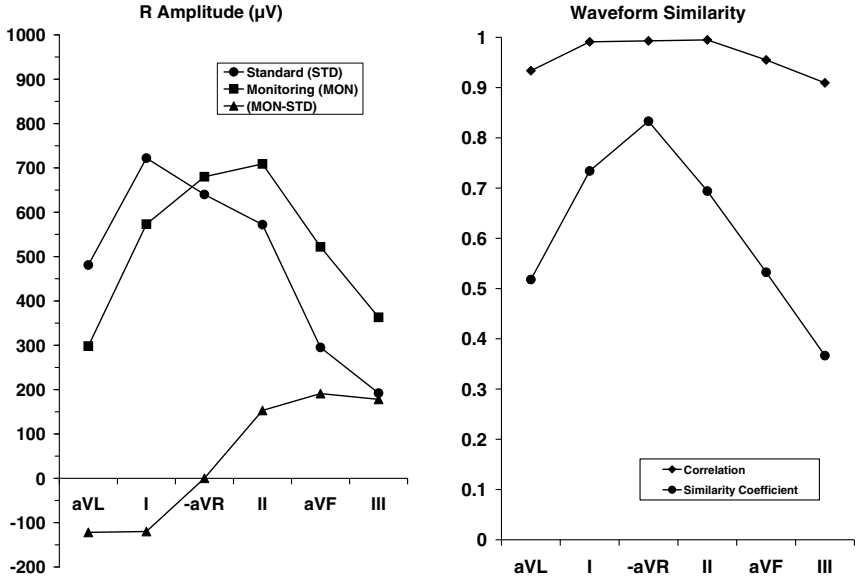


Figure 8.2: Median R amplitudes and differences, similarity and correlation coefficients of the standard and monitoring positions for the extremity leads (n=88). p<0.01 for all extremity leads, except for -aVR (p<0.22).

Results are presented as median (inter-quartile range) or mean±SD, as required. Paired t-tests were used to compare differences between continuous variables. A value of p<0.05 was considered significant.

Results

ECG differences

Figure 8.2 contains the R amplitudes and differences, correlation coefficients, and similarity coefficients over the complete data set (n=88). Overall, substantial differences were found between the ECGs in standard and monitoring positions. R amplitudes of leads aVL and I were lower in monitoring position (p<0.001), but were higher in the leads -aVR to III (p<0.001). Differences between the central Wilson terminals were small (2±11 µV) and remained in the order of the quantization level. Q waves diminished in six recordings with the electrodes in monitoring position.

The median (inter-quartile range) frontal QRS axis was for the standard positions 8 (-25–43) degrees and for the monitoring positions 37 (-21–66) degrees. The mean difference of the frontal QRS axis was 16 (4–25) degrees (p<0.001). Rightward frontal QRS-axis shifts were observed between the standard and monitoring limb leads. QRS-axis angle differences > 30 degrees were found in 21 cases (23.8%). In 6 (7%) cases, an abnormal left-axis deviation in the frontal QRS axis (-90 to -30 degrees) was observed in the stan-

Table 8.1: Similarity results between leads derived from electrodes in monitoring and standard position for general and patient-specific reconstruction methods in the test set (n=58).

	No reconstruction	General	Patient-specific
Similarity Coefficient			
I	0.737 (0.595 – 0.777)	0.770 (0.672 – 0.815)	0.891 (0.828 – 0.933)
II	0.687 (0.613 – 0.778)	0.866 (0.783 – 0.918)	0.927 (0.865 – 0.950)
ΔR *amplitude* (μV)			
I	-141 (-236 – -51)[a]	-74 (-156 – 20)[b]	-9 (-24 – 6)
II	163 (80 – 288)[a]	7 (-30 – 56)	1 (-11 – 10)
ΔST_{60} (μV)			
I	3 (-10 – 18)	8 (-9 – 20)	1 (-9 – 11)
II	-5 (-19 – 9)[c]	-4 (-16 – 9)[b]	-3 (-15 – 4)[c]
Frontal QRS Axis (°)	41 (-17 – 68)	22 (-24 – 53)	17 (-24 – 53)
Angle difference (°)	13 (4 – 25)[a]	2 (-3 – 12)	0 (-1 – 3)

[a] $p<0.001$, [b] $p<0.01$, [c] $p<0.05$

dard ECG and was shifted into the normal range (-30 to 90 degrees) in the monitoring ECG. In 4 (5%) cases, a normal QRS axis resulted in a right-axis deviation (> 90 degrees).

ECG reconstruction

Similarity results of the standard and monitoring ECGs, before and after general and patient-specific reconstruction, are presented in Table 8.1. Results are presented for the independent limb leads I and II only. Lead III and the augmented leads can be calculated from leads I and II without error.

Median SCs between the standard and monitoring leads were moderately high (≥ 0.687) for leads I and II and increased after reconstruction. Patient-specific reconstruction had higher SCs than general reconstruction. Median SCs of lead II were overall higher than those computed for lead I. Correlation coefficients (data not shown) showed a similar performance increase from general to patient-specific reconstruction.

Median R-amplitude difference in lead I decreased by 50% for general reconstruction, and were very small for patient-specific reconstruction. For general and patient-specific reconstruction, median R amplitude difference was small in lead II. However, the interquartile range for general reconstruction was wider than for patient-specific.

ST_{60} measurements were small in the standard and monitoring ECGs. Median ST_{60} of the standard positions were for lead I -13 (-50–13) μV and lead II 11 (-21–53) μV, respectively. Median ST_{60} differences were overall small in the uncorrected situation. General and patient-specific reconstruction did not reduce these differences.

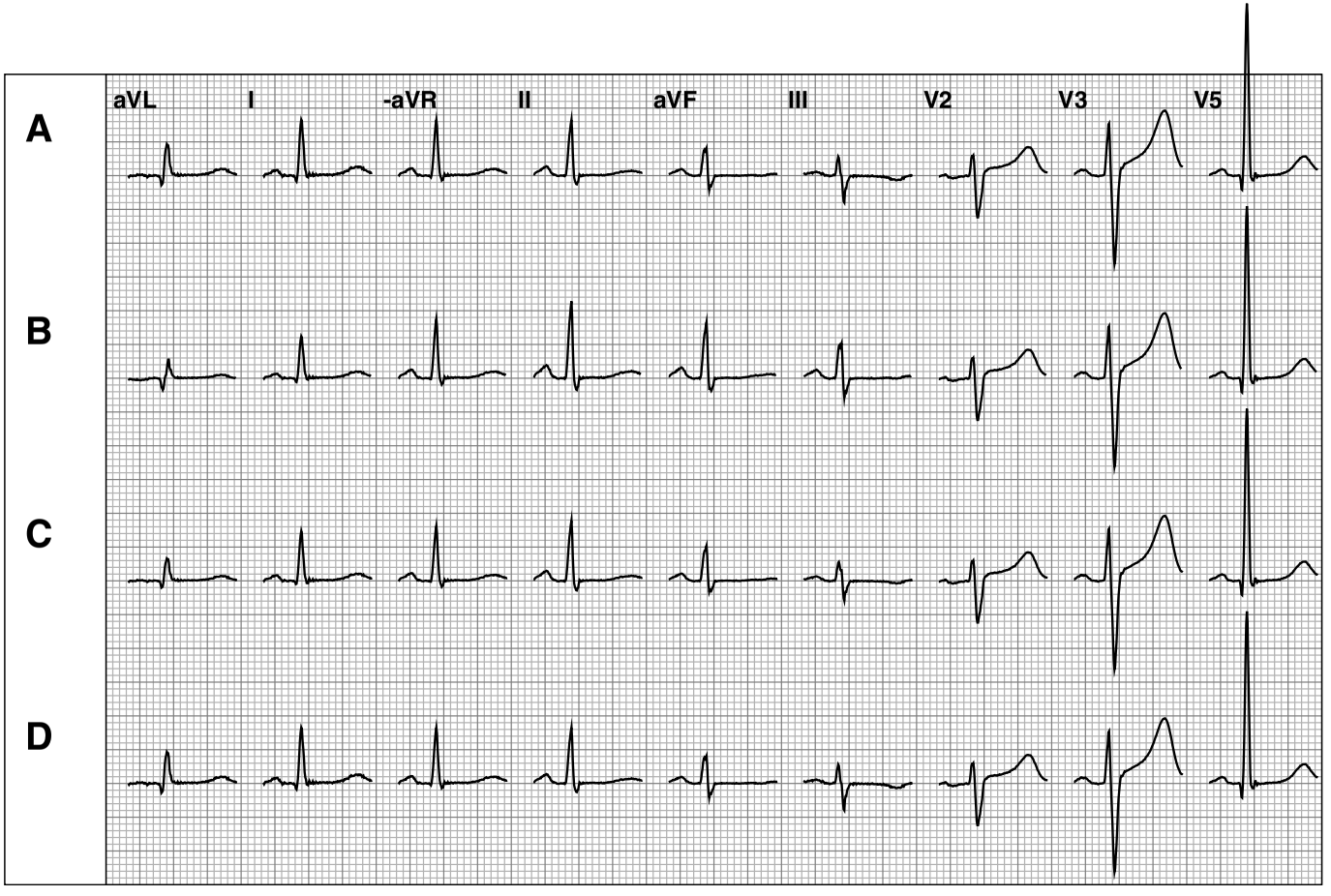


Figure 8.3: Example of ECG reconstruction from monitoring to standard locations: (A) Standard ECG with the extremity electrodes placed on the ankles and wrists; (B) ECG with the extremity electrodes on the monitoring locations; (C) Reconstructed ECG using general coefficients; (D) Reconstructed ECG using patient-specific coefficients.

The median QRS axis angle difference after general and patient-specific reconstruction was reduced to 1 and 0 degrees, respectively. However, general reconstruction had a wider inter-quartile range than patient-specific reconstruction.

Patient-specific performances were overall higher than general. However, the reconstructed waveforms of general reconstruction were visually similar to the standard waveforms in most patients. Figure 8.3 shows an example of a corrected recording using general and patient-specific coefficients.

The general reconstruction coefficients are based on a relatively small subset of 30 patients. To present general purpose coefficients for use in clinical practice, we also computed generalized reconstruction coefficients from our complete data set. Table 8.2 contains the general coefficients based on the complete data set for the conversion to and from the standard and monitoring leads. While we could not compute performance results, the presented coefficients were very similar to those from the learning set of 30 patients. However, a separate performance analysis should be carried out on an independent data set.

Table 8.2: Coefficients calculated over the learning set for reconstruction of a monitoring to a standard ECG and coefficients calculated over the complete set (n=88).

Coefficient	Monitoring to standard	Standard to monitoring
C_1	0.9897	0.863
C_2	0.1091	-0.057
C_3	-0.0699	0.116
C_4	0.8229	1.121

Discussion

This study shows that extremity electrode positions from standard to monitoring produce significant changes in morphology and in QRS and ST-segment measurements, but changes were small in the central Wilson terminal and in the precordial leads. These results support observations from earlier studies (Pahlm *et al.*, 1992; Krucoff *et al.*, 1994; Jowett *et al.*, 2005).

Practical application

In this study, methods were developed that allow reconstruction of the standard ECG from monitoring positions using general and patient-specific coefficients and vice versa. General reconstruction performs worse than patient-specific. A practical application of these methods is that ECGs recorded with a patient monitor can be corrected to allow serial comparison with previously recorded standard ECGs. The presented reconstruction techniques can also be applied to online ECG monitoring and full disclosure waveform storage. Review and analysis of recorded data with previously recorded standard 12-lead ECGs is possible. The reconstruction coefficients are well-suited for implementation in

ECG monitoring equipment. General and patient-specific reconstruction require a limited amount of extra computer processing time (four multiplications) and a minimal user input for selection of the appropriate electrode configuration. For patient-specific reconstruction, an additional 9-lead ECG is required, but this increases the accuracy.

In a previous investigation by Bartosik *et al.* (1995), general coefficients were also computed from a set of 30 patients. The limb leads in this study were mapped from positions introduced by Krucoff *et al.* (1990) to standard positions. The extremity electrode positions of Krucoff are closely positioned to the Mason-Likar positions. Therefore, we also applied the coefficients published by Bartosik *et al.* (1995) to our data set. Median (inter-quartile) SC for leads I and II were 0.650 (0.389–0.800) and 0.687 (0.613–0.777), respectively. The median angle difference of the frontal QRS axis was 2 (-6–7) degrees. These results were slightly worse than the results based on our general reconstruction. General reconstruction coefficients can only be used on the intended electrode positions. Patient-specific does not have this restriction, provided that the electrode positions do not change during monitoring.

Study limitations

There are several study limitations. The study population is of a modest size, which may restrict the generalizability of the presented results. To address the variability of the reconstruction coefficients, we determined coefficients from the test set and applied those on the learning set. Overall, reconstruction performance was comparable with the data in Table 8.1. Differences between the coefficients of Table 8.2 and those from the learning set and test set were also small.

Furthermore, general reconstruction performance depends on the correct placement of the extremity electrodes. The Bartosik coefficients perform worse on the monitoring location we used. We do not know of any standardized electrode placement for ECG monitoring. For this reason and for additional accuracy, we recommend using the patient-specific technique, which is not influenced by the exact electrode positions.

Conclusion

Reconstruction of ECG leads from monitoring positions to standard positions is possible using general and patient-specific coefficients. Patient-specific reconstruction performance is overall higher than general reconstruction, but requires the recording of an additional ECG.

9

Discussion

Introduction

Over the years, the goals of continuous ECG monitoring have expanded from single-lead rhythm monitoring to the detection and classification of cardiac arrhythmias and dynamic assessment of ST-segment changes (Krucoff *et al.*, 1988; Veldkamp, 1996; Klootwijk, 1998). Present day patient monitoring systems are equipped with full 12-lead ECG acquisition modules, are integrated in a monitoring network, and are able to store all ECG leads (full disclosure) for retrospective analysis. Despite these technological advancements, it is often difficult in clinical practice to manage a good quality, long-term, continuous registration of the ECG for several reasons:

- **Technical limitations**
  Aside from proper recording procedures with appropriate electrodes and careful skin preparation (Schijvenaars, 2000), slight electrode misplacements are not uncommon in standard and precordial leads. Multiple electrode changes, such as a change from the standard 12-lead ECG to the Mason-Likar system (Mason and Likar, 1966), remain difficult to detect without additional user annotation.
  Patient monitoring devices are often different from regular 12-lead electrocardiographs in various aspects. For correct interpretation of ECG waveforms, patient monitors should be set to the correct diagnostic frequency (0.05–150 Hz) (Bailey *et al.*, 1990) even though these frequencies may fail to remove muscle artifacts or respiration induced baseline wander. Furthermore, ECG monitoring devices may not support all ten standard ECG wires, because of technical limitations or as a result of size and price tradeoffs. In particular, telemetry transmitters often only support configurations with five electrodes (seven leads).

- **Patient variations**
  Patient variations, such as increased perspiration, may have a detrimental effect on the quality of the recording. These variations may cause low frequency noise, or baseline wander or high frequency distortions of the ECG. Dynamic changes during the recording period, such as body position changes, may also produce changes in the ECG and may generate false alarms (Adams and Drew, 1997; Jernberg *et al.*, 1997; Norgaard *et al.*, 2000).

- **Patient management**
  Patient monitoring systems are designed to process signals and to alarm when certain thresholds are exceeded. The presence of low signal amplitudes or artifacts results in false alarms, which may burden the medical staff. With an increasing number of lead wires to manage next to other cables such as infusion lines and instruments, false alarms may also increase. Systems requiring fewer electrodes may alleviate parts of these patient management problems.

An essential part of patient monitoring is the ability to detect changes in a patient's condition. For derived 12-lead ECG systems, accurate detection of those changes is more important than the precise reproduction of the reconstructed waveforms.

The aims of the thesis were to investigate, develop, and clinically validate solutions to address the problems listed above. In the introduction, several research questions were formulated and provisional answers are discussed below.

Part I: ECG reconstruction

The 12-lead ECG reconstruction methods presented in parts I and II of this thesis have been based on the recording of reduced lead sets and the subsequent reconstruction of the absent leads. Before the first research question of how many leads and which leads are required for a reconstruction is addressed, a definition of accuracy measures is required.

Accuracy measures

In Chapters 1–6, leads were reconstructed in various settings and a common question was how to compare these derived leads with the actual leads. In our investigations several quantitative and qualitative assessments were done. Quantitative assessment was performed on three different levels: overall waveform similarity, reconstruction accuracy of single measurements, and accuracy of diagnostic decision rules.

First, several methods to compare the original with derived waveforms in an overall fashion have been used: Pearson's correlation coefficient, root mean square error (RMSE), and Similarity Coefficient (SC) (Horan and Flowers, 1968; Kornreich and Rautaharju, 1981). Although the correlation coefficient is highly non-linear, it is a widely used and reported measure of shape similarity and has a convenient and easy to interpret scale of -1 to 1. The RMSE is the root mean square of the error signal and is reported in the units of the source signal. The SC is sensitive to amplitude differences, but it is not a widely reported measure. As such, there is no single waveform similarity measure to report. So in our investigations we decided to report several similarity measures.

Second, clinical ECG interpretation is based on global and local measurements. In our studies, the computer program MEANS was used to determine measurements from the original and derived leads. The amplitude of the ST segment at 60 milliseconds after the J point (ST_{60}) for each lead was selected as a clinically important measurement. Average and maximum absolute differences ($|\Delta ST_{60}|$) between the original and derived amplitudes were calculated. Where appropriate, differences of other local measurements, such as R and S wave differences, and global measurements, such as the frontal QRS and T axis, were computed.

Third, quantitative accuracy was assessed at the diagnostic level. We applied several decision rules that are used in clinical practice. Overall, the ESC/ACC criteria for acute myocardial ischemia and evolving infarction have simple, sensitive decision rules (Thygesen *et al.*, 2000) which can also be implemented in ECG analysis systems. Accuracy between the original and reconstructed ECGs was measured with Cohen's kappa.

Comparisons on a qualitative level were performed using visual comparisons of static ECGs and continuous ECG recordings. Software and printouts facilitated superimposition of original and derived leads and error signal plots, or a blinded review by several investigators in Chapters 4 and 6.

Question 1: How many leads are required and which lead subset can be used for reconstruction of the 12-lead ECG?

In Chapters 2 and 3, the reconstruction methods were developed and tested on a large data set of 10-second, 12-lead ECGs obtained from patients diagnosed with acute myocardial infarction, angina pectoris, or atypical chest pain. The data set was split in

equally-sized learning and test sets. By systematically removing one and up to six precordial leads, a total of 62 lead subsets were considered. For each lead subset, general coefficients to reconstruct the remaining leads were computed on the learning set and were tested on each ECG of the test set. Reconstruction performance was assessed by correlation and root mean square errors between the original and reconstructed leads.

Overall, any one or two absent precordial leads can be reconstructed (average correlation ≥ 0.988) very well from the remaining leads using general coefficients. In clinical practice, where leads may fall off or may cause excessive noise, a potential application might be automatic reconstruction of an absent lead.

When three or four precordial leads were removed, we found that some lead subset combinations performed better in reconstructing the missing leads than others of the same size. For example, in lead subsets with four precordial leads removed, the best lead subsets included a left and right precordial lead. A possible explanation is that these subsets form a quasi-orthogonal set of leads, representing the vectorcardiographic X, Y, and Z leads that describe the heart vector.

The rationale for examining 4-lead subsets in more detail was based on two reasons. First, it was found in Chapters 2 and 3 that a minimal lead subset for general and patient-specific reconstruction should contain two or three precordial leads in addition to two limb leads. Secondly, the use of a reduced lead set was considered by Dräger Medical Systems for inclusion into their telemetry transmitter system, which was limited to only seven leads (limb leads and one precordial lead). An additional precordial lead would increase complexity and result in hardware modifications to the acquisition and transmitter boards.

Question 2: General versus patient-specific reconstruction

In addition to general reconstruction, patient-specific reconstruction coefficients were computed for each of the lead subsets on the ECGs in the test set. Overall, patient-specific reconstruction was superior over general reconstruction. Correlation coefficients were higher. RMSE and absolute ST differences were twice as low.

The availability of a previously recorded 12-lead ECG remains an important limitation of the application of the patient-specific method in the clinical workflow. Integration of a monitoring system with an ECG management system should be investigated further. While ECGs in such a system are recorded on the standard electrode positions at the wrists and ankles, the ECGs could be transformed to the monitoring compatible locations with the methods described in Chapter 9. For testing purposes, a separate handheld 12-lead ECG recorder was introduced in one of the telemetry wards at the Erasmus MC to easily obtain a 12-lead ECG and to upload this ECG for analysis at the nurse desk. With the introduction of wireless communications, it may even be possible to upload these data on the spot.

For ease of use in clinical situations, a computer algorithm to select the optimal patient-specific lead subset was developed. The algorithm was designed to only require a 10-second, 12-lead ECG. No further user intervention is needed, except for final confirmation of the selected lead set. The algorithm selects the lead subsets and matrices based on the highest similarity measure (SC, RMSE, or correlation), but does not evaluate lead subsets with adjacent precordial leads or matrices containing large coefficients. During visual assessment, we found that matrices with large coefficients perform well in

the learning phase, but that during the monitoring period noise in the measured leads can be amplified in the reconstructed leads.

The best patient-specific lead subsets were in concordance with the best lead subsets found for general reconstruction. For example, the most frequently found optimal patient-specific lead subset with two precordial leads (I, II, V_2, and V_5) in Chapters 4 and 6 was also found with general lead subset reconstruction (cf. Table 2.1 on page 13).

Question 3: How accurate are derived lead systems over time?

While the ECG reconstruction methods performed well on a set of 10-second, 12-lead ECGs, it was not known how well the reconstruction methods would perform over time. For this purpose, the methods were applied on a data set of 24-hour, continuous 12-lead ECG recordings of patients with acute coronary syndromes without persistent ST-segment elevation. General and patient-specific reconstruction methods were applied using correlation and average and maximum absolute ST differences to assess reconstruction performance.

Accurate reconstruction of the 12-lead ECG over a 24-hour period appeared to be possible. General reconstruction performance remained at a similar performance level. Patient-specific performance initially slightly decreased and then stabilized over time, but remained much better than general reconstruction. It is not known how well the patient-specific coefficients would perform after days or weeks. It could be hypothesized that the patient-specific coefficients remain valid as long as there are no significant alterations to the electrical conduction of the heart and electrode placement.

The validity of general and patient-specific coefficients over a time period is a problem that should be addressed in further research. It is likely that in the busy clinical practice, a 12-lead ECG for patient-specific coefficients will not be made every day and that reconstruction performance may become lower. A possibility that could be used to notify the user of a suboptimal patient-specific matrix might be a quality index of the reduced lead set. This index can be calculated for each original lead in the reduced lead set from the remaining leads. For example, in a reduced lead set of I, II, V_2 and V_5, the matrices I, II, V_2 and I, II, V_5 are also calculated. Of these two 3-lead matrices, reconstruction performance is calculated periodically and if one of the performances becomes lower, the system may warn the user to acquire and recompute the patient-specific coefficients.

Part II: Clinical evaluation

Question 4: How accurate is the method in a clinical setting?

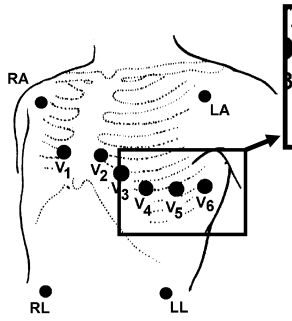
The general and patient-specific methods were tested in a clinical setting at the VA Medical Center, Durham, NC, USA. Chapter 4 presents a study of 39 ECG recordings that were made prior, during, and after percutaneous coronary intervention (PCI) executed according to the clinical standards of the medical center. The aim of this study was to prospectively assess the reconstruction accuracy in patients with possible ST changes caused by balloon inflations. The study protocol was designed to blind the Rotterdam group from the procedure in order to minimize potential bias. In order to perform and calculate the best patient-specific lead set, the Rotterdam group only had access to the recording prior to the PCI recording. During each intervention, 12-lead ECG reconstruction was evaluated at baseline and during ST changes caused by balloon inflation.

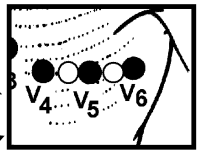
The main results of the study show that a reduced lead set may accurately reconstruct the ST-segment changes caused by balloon inflation. The 4-lead subset with two limb leads and precordial leads V_2 and V_5 using general reconstruction coefficients performed very well. The patient-specific optimal lead subset and coefficients showed even better results, corroborating the results reported in Chapters 2 and 3.

Question 5: Application of a reduced lead set for pre-hospital triage

In Chapter 5, the general lead reconstruction method with a reduced lead set consisting of the limb leads and precordial leads V_2 and V_5 was evaluated for use in a pre-hospital situation. In these emergency care situations, diagnosis and risk stratification by the ambulance service on the spot with a protocol and computerized ECG systems may result in early initiation of reperfusion therapy. Reperfusion has shown to dissolve or remove the occluding coronary thrombus, thus recovering blood flow, left ventricular function, and oxygen delivery to the jeopardised myocardium (Boersma *et al.*, 2001). A reduced lead set method may save time and can be implemented with existing devices, such as defibrillators which are not equipped with 12 leads. The reduced lead set of I, II, V_2 and V_5 was applied on a data set of 12-lead ECGs obtained from the ambulance service in Rotterdam. This data set was used to develop the REPAIR thrombolytic triage algorithm (Boersma *et al.*, 1996) and consisted of a learning (n=1435) and test set (n=825). Reconstruction performance was assessed on the accuracy of the REPAIR (2001) decision rule.

High to very high sensitivity and specificity was observed in the test set (n=825). As a result of reconstruction differences, three cases would have been referred to a PCI center instead of receiving thrombolytic treatment. Three false negative cases would not have received therapy, but would have been referred to the emergency room for further evaluation.





Misplacement of V5?
V4½ or V5½

Decision Rule: REPAIR (2001, n=825)

Lead subset	Sens (%)	Spec (%)	FN	FP	Agreement	Kappa
I, II, V2, V4½	93.2	99.5	4	5	0.989	0.905
I, II, V2, V5	84.3	99.6	8	3	0.987	0.880
I, II, V2, V5½	82.4	99.6	9	3	0.985	0.867

Figure 9.1: Example of small electrode misplacements in lead V_5 and the effects on the accuracy of the pre-hospital decision algorithm.

Accurate placement of the electrodes is important for reduced lead set methods, because misplacements may not only alter the recorded lead, but may also have an effect on the reconstructed leads. In the best 4-lead subset (I, II, V_2, and V_5) used in our investigations, the sites of the extremity electrodes (Mason-Likar placement) and lead V_2 (fourth intercostal space, left sternal border) are easier to locate than lead V_5 (anterior

axillary line, horizontal to V_4). Therefore, the effect of an incorrectly placed V_5 electrode was evaluated by introducing small changes to lead V_5. Leads $V_{4\frac{1}{2}}$ (midway V4 and V5) and $V_{5\frac{1}{2}}$ (midway V5 and V6) were approximated by cubic spline interpolation (Schijvenaars *et al.*, 1995) and served as input for the REPAIR decision rules. Figure 9.1 depicts the effects of simulated changes of V_5 on sensitivity and specificity. Overall, changes were small; the number of misclassified cases decreased by two with lead $V_{4\frac{1}{2}}$ and increased by one with lead $V_{5\frac{1}{2}}$. A possible explanation for the overall low number of misclassified cases might be that REPAIR was designed with robust decision rules which are not sensitive to small changes in particular leads.

Question 6: Comparison of several derived 12-lead methods

Reconstruction of the 12-lead ECG from a subset of leads for patient monitoring has received a lot of attention in the last two decades. In the area of continuous online ST analysis, vectorcardiographic monitoring systems, such as Ortivus' MIDA system, are based on the recording of three orthogonal leads and contain a transformation by Dower *et al.* (1980) for presenting a 12-lead ECG. In the mid-nineties, the 5-electrode system, EASI, was also clinically evaluated (Drew *et al.*, 1996) and has become a widely used lead system.

In Chapter 6, a study was carried out at the VA Medical Center to evaluate EASI and the general and patient-specific reconstruction methods with the 12-lead ECG during PCI. A total of 44 recordings were acquired and it was observed that the performances of EASI, general, and patient-specific reconstruction differ substantially. In this setting, EASI had the lowest reconstruction performance.

In addition to the EASI lead system, a number of other methods have been developed and have become commercially available. The general and patient-specific method presented in Chapters 1-2 and Appendix A have been implemented by Dräger Medical Systems for use in their patient monitoring equipment under the respective names TRUST GEN and TRUST PS. A brief overview of those methods, manufacturers, and required lead systems is presented in Table 9.1. Drew *et al.* (2002), Wei *et al.* (2004), and TRUST are similar methods which use lead subsets and reconstruct the remaining leads of the 12-lead ECG using coefficients determined on a patient-specific ECG or on a learning set.

Table 9.1: Overview of reduced lead set strategies and their commercial availability.

Method	Vendor	Lead system
Drew *et al.* (2002)	General Electric (GE)	I, II, V_1, V_5
Dower *et al.* (1980)	Ortivus, Danica	Frank lead system
EASI, Dower *et al.* (1988)	Philips Medical Systems	E, A, S, I
Scherer *et al.* (1989)	-	I, II, V_2
TRUST GEN	Dräger Medical Systems	I, II, V_2, V_5
TRUST PS	Dräger Medical Systems	I, II, 2 precordial leads
Wei *et al.* (2004)	Nihon Kohden	I, II, V_1, V_6

To our knowledge, no studies have been carried out which compare the performances of the different reconstruction methods. For this purpose, the PCI recordings in Chapter 6 were used to simultaneously compare six different methods: EASI, Wei, Drew, Scherer, TRUST GEN, and TRUST PS. It was not possible with the existing data set to include a VCG-based lead system, because not all Frank electrodes were acquired in this data set. Furthermore, the coefficients and exact algorithm implementation of the other methods have not been made publicly available. Therefore, we used the coefficients determined from our learning sets (Nelwan *et al.*, 2000). Coefficients are presented on page 106.

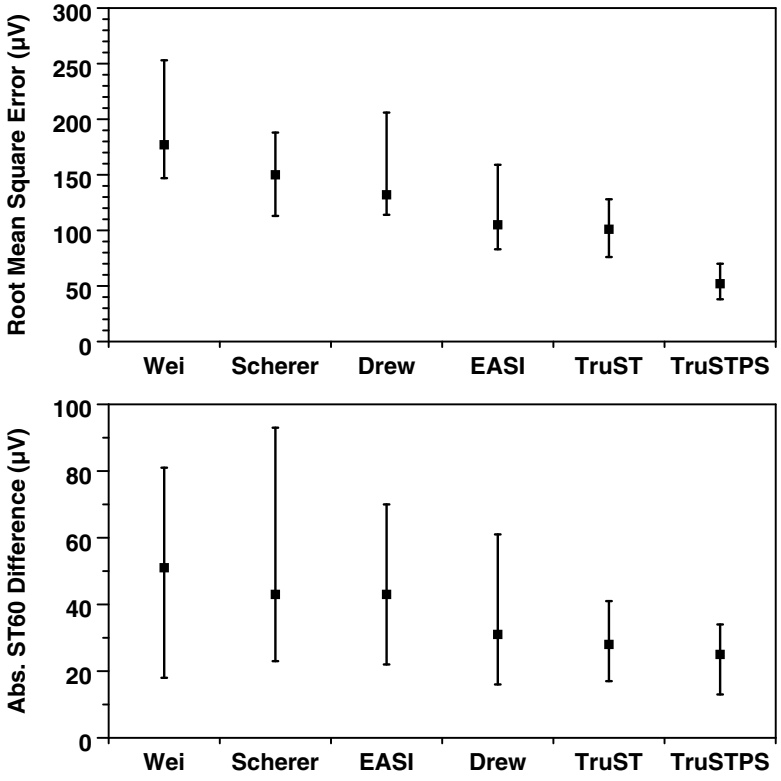


Figure 9.2: Median (inter-quartile range) of the root mean square errors and absolute ST_{60} differences at balloon inflation of different lead reconstruction strategies (n=33).

Table 9.2 contains median (inter-quartile range) RMSE and $|\Delta ST_{60}|$ of the reconstruction methods at balloon inflation for each precordial lead. Mean RMSE and $|\Delta ST_{60}|$ are summarized in Figure 9.2. Overall, TRUST PS had the lowest RMSE and $|\Delta ST_{60}|$. The highest RMSE and $|\Delta ST_{60}|$ were observed in the Wei method, followed by Scherer. EASI, Drew, and TRUST GEN have similar median $|\Delta ST_{60}|$, but the inter-quartile ranges differ. Based on these results, we conclude that the reconstruction methods greatly differ in performance.

Table 9.2: Median (inter-quartile range) root mean square errors (μV) and absolute ST_{60} differences (μV) of the precordial leads during balloon inflation of several different lead reconstruction strategies (n=33).

Method	V_1	V_2	V_3	V_4	V_5	V_6
Root Mean Square Error (μV)						
Drew *et al.* (2002)	–	213 (129 – 289)	184 (116 – 286)	87 (64 – 122)	–	46 (36 – 64)
EASI[1]	72 (50 – 94)	175 (113 – 220)	169 (87 – 265)	149 (94 – 214)	87 (51 – 122)	68 (45 – 82)
Scherer *et al.* (1989)	93 (62 – 142)	–	152 (108 – 198)	191 (133 – 282)	156 (116 – 223)	111 (98 – 149)
TRUST GEN	86 (48 – 124)	–	135 (85 – 183)	85 (64 – 139)	–	54 (39 – 74)
TRUST PS	49 (33 – 74)	67 (41 – 101)	59 (42 – 97)	41 (29 – 57)	39 (21 – 59)	36 (19 – 63)
Wei *et al.* (2004)	–	209 (148 – 301)	231 (175 – 333)	156 (108 – 265)	77 (43 – 106)	–
Absolute ST_{60} Difference (μV)						
Drew *et al.* (2002)	–	39 (15 – 81)	35 (15 – 94)	25 (16 – 40)	–	16 (9 – 29)
EASI[1]	17 (10 – 39)	46 (25 – 84)	39 (16 – 84)	39 (16 – 71)	20 (11 – 57)	15 (7 – 29)
Scherer *et al.* (1989)	19 (12 – 39)	–	47 (22 – 87)	39 (19 – 143)	42 (14 – 105)	40 (21 – 73)
TRUST GEN	19 (8 – 44)	–	34 (13 – 62)	26 (11 – 52)	–	16 (10 – 31)
TRUST PS	25 (7 – 42)	17 (7 – 54)	27 (14 – 56)	19 (7 – 31)	13 (4 – 55)	23 (9 – 61)
Wei *et al.* (2004)	–	50 (22 – 104)	69 (12 – 103)	42 (24 – 88)	21 (10 – 47)	–

[1] *limb lead results available in Chapter 6*

Reconstruct or fabricate?

Over the years, methods to reconstruct the 12-lead ECG from a subset of leads or from alternate lead systems have been scrutinized by different research groups, industry, and governmental agencies, such as the United States Food and Drug Administration (FDA). When the EASI lead system was introduced, several research groups (Drew *et al.*, 1996; Horacek *et al.*, 2000; Rautaharju *et al.*, 2002) investigated the accuracy of EASI in clinical settings. Based on these investigations, Zymed, at present Philips Medical Systems, was able to market and sell this product for the purpose of ST-segment monitoring. However, in 2003, the British Medicines and Healthcare products Regulatory Agency (MHRA), issued a medical device alert to all medical personnel concerning the reproducibility of the EASI lead system *:

> *Problem:* The EASI 12-lead ECG derived from five electrodes is inappropriate for diagnosis of acute ischaemic heart disease. (...)
> The MHRA has received reports where a patient was suspected of having ischaemic heart disease or rapidly changing ST segments and the EASI 12-lead ECG did not correlate with the conventional ECG. Users employing only the EASI 12-lead ECG may therefore misdiagnose certain conditions particularly myocardial infarction, leading to inappropriate use of thrombolytic therapy. (...)
> *Action:* Diagnosis of acute ischaemic heart disease should not be based on the EASI 12-lead ECG. Users should instead use the conventional 10-electrode, 12-lead diagnostic ECG configuration.

In this alert, the MHRA warns about the differences between a conventional and 12-lead ECG synthesized from EASI. This may have implications for other ECG reconstruction methods, such as the VCG to 12-lead ECG transformation and the lead subset methods including TRUST. While EASI and the TRUST algorithms differ substantially (cf. Chapter 6), both methods reconstruct unavailable leads with a degree of uncertainty. EASI, a model-based system, employs a transformation from an orthogonal lead set to the 12-lead ECG system. This model may not fit all patients, so outliers are inevitable. TRUST reconstruction uses four out of the eight measured leads to reconstruct the remaining four leads, such that the limb leads and two precordial leads remain identical to the conventional ECG. However, the accuracy of the four reconstructed leads depends for a great deal on size and composition of the learning set used for computation of the coefficients. The learning set for the TRUST coefficients contained a large variation of patients with or without acute coronary syndromes (Nelwan *et al.*, 2000). For both EASI and TRUST, it is impossible to predict which patients will have large deviations in the reconstructed leads.

In addition to uncertainties in waveforms of reconstructed leads, the reconstruction methods also may affect noise and baseline drift in the reconstructed signals. Figure 9.3 demonstrates a noise reduction effect of lead reconstruction. In the top panel, lead V_6 contains baseline wander and high frequency noise, but the reconstructed dV_6 is not affected. This is a double edged sword, because if lead V_5 would have been constructed from V_6, noise would be propagated into dV_5. The lead reconstruction method also depends on other monitoring modules which detect lead-off conditions of the measured

* Full report available at `http://www.rcoa.ac.uk/docs/mda-2003-024.pdf`

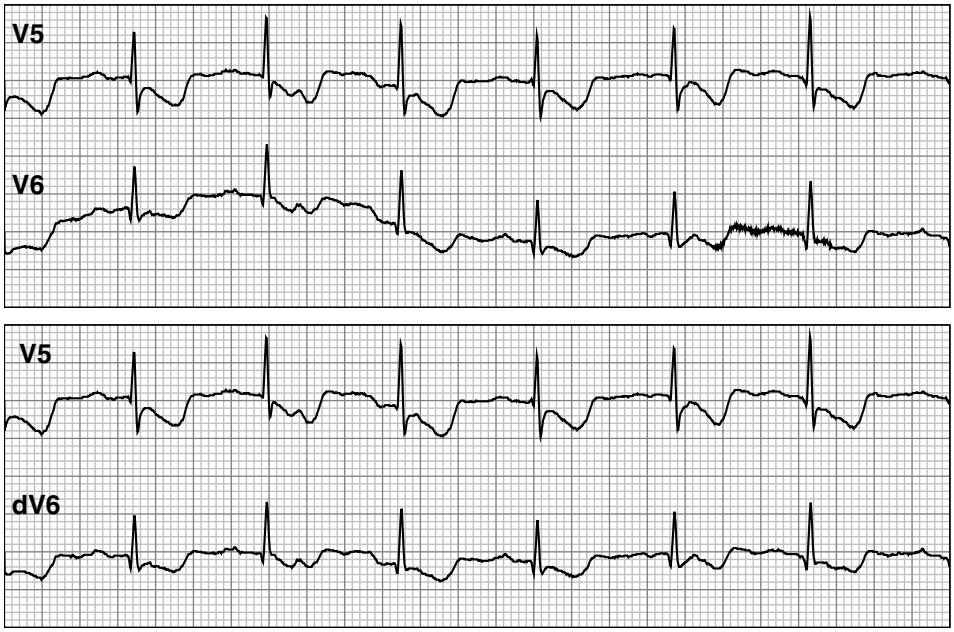


Figure 9.3: Example of noise reduction after lead reconstruction. The top panel contains the actual V_5 and V_6. The bottom panel shows a reconstructed V_6 lead with the low frequency noise removed.

leads. In case of a lead-off condition or asystole alarm, the reconstructed leads should switch into a lead-off condition.

Limitations

A few study limitations can be noted. First, we have not evaluated the reconstruction of ECGs containing arrhythmias, such as atrial fibrillation, premature ventricular complexes, or bundle branch blocks. While it may not be expected that these arrhythmias would not be properly represented in the reconstructed leads, we have not extensively verified how arrhythmias are visualized in the reconstructed leads. Since the extremity leads always remain identical, there will be no reconstruction differences if the typically used lead II is selected for arrhythmia interpretation (Drew and Krucoff, 1999). Furthermore, in a subanalysis of a lead subset consisting of I, II, V_1, and V_5 (Drew *et al.*, 2002), high to perfect agreement was found between the original and reconstructed ECGs. The only difference with the presented best lead set of I, II, V_2, and V_5 is the change from lead V_2 to V_1, because lead V_1 is an efficacious lead for atrial rhythm monitoring.

Second, no prospective studies were performed on the actual day-to-day clinical use by various users (nurses, physicians, and technicians). In particular, we have not quantified reconstruction accuracy in the presence of small changes in repositioning electrodes. Lastly, the logistics of recording a 12-lead ECG for patient-specific reconstruction should be investigated.

Part III: Patient monitoring

During long-term continuous ECG monitoring, body position changes may alter the surface ECG and the electrode positions of the limb leads are often different from standard positions at the wrists and ankles. Questions 7 and 8 address these interpretation problems and present detection and correction methods.

Question 7: ECG variations caused by body position changes

Body position changes (BPC) are known to alter the surface 12-lead ECG, resulting in changes in QRS amplitude, ST-segment shifts, and T-wave inversions. Some of these changes can be interpreted as ischemia and may trigger false positive alarms by the patient monitor. While previous studies (Shinar *et al.*, 1999; Astrom *et al.*, 2003; Garcia *et al.*, 2003) have quantified and described detection algorithms in small groups of volunteers and cardiac patients, we have attempted to quantify these body position changes, to provide an ECG-based detector and a patient-specific correction method. Continuous 12-lead ECG recordings were obtained from 114 patients admitted to the coronary care unit and each patient underwent a body position test (supine, left, right, and upright position). A body position detector was developed using the EXPLORE automated rule induction algorithm. To distinguish positional from ischemic changes, a separate set of 71 PCI recordings was used including ECGs at rest and during balloon inflation. The ECG variations were corrected using a patient-specific mapping technique based on a combination of leads. Performance of the correction method was assessed by Pearson's correlation coefficient and by similarity coefficient. ST changes of ≥ 100 μV in ≥ 1 lead caused by BPC were observed in 50 (43%) patients and the most pronounced changes were found in the left-lateral position. With a fixed specificity at 95%, sensitivity of the detection rules was for left 97.4%, right 69.9%, upright 64.3% and combined 66.1%. False alarm rate per hour in the PCI data set was 2.22 at rest and 4.31 during balloon inflation. Performance of the patient-specific correction method yielded an overall correlation coefficient of 0.970 and similarity coefficient of 0.889.

Question 8: Correction of ECG variations due to non-standard electrode positions

Electrode positions for continuous monitoring are different from those for recording of a standard 12-lead ECG, because the standard electrode positions at the wrists and ankles may introduce noise and artifacts. Therefore, most institutions move the limb electrodes to the chest and lower abdomen, the so-called monitoring positions, according to Mason and Likar. However, this position change may alter the ECG significantly: QRS shifts, (dis)appearing Q waves and changes in R waves may appear. A study was set up to develop a method to correct for these changes. Using a data set of 93 subjects with a simultaneously recorded 9-lead ECG in standard and monitoring positions, patient-specific and generalized methods were developed and evaluated. The main results show that the generalized reconstruction coefficients can be used to map the monitoring leads to the standard leads with high accuracy.

Future directions

In order to facilitate an independent evaluation and reproduction of our results, the TRUST reconstruction methods and the coefficients are given in Appendix A. To evaluate TRUST in clinical settings, the algorithms have been made available in patient monitoring equipment, such as telemetry transmitters and bedside patient monitors. The data sets used in Chapters 7 and 8 will be made available in the PHYSIONET databank (Goldberger *et al.*, 2000).

The methods for body position detection and correction (cf. Chapter 7) and for the correction of standard to monitoring ECGs (cf. Chapter 8) have not been implemented and validated in clinical practice. While the standard to monitoring ECG reconstruction method can be readily applied in a patient monitoring system, because of the limited amount of required computations, the practical implementation might be difficult. Automatic export and data exchange standards, such as DICOM for medical imaging systems, are presently not widely available for ECG data management systems, despite standardization efforts such as SCP (Willems *et al.*, 1992) and by the FDA (Kligfield, 2003).

ECG lead systems with reduced lead sets can be applied in locations outside of the hospital. A possible application in a pre-hospital setting is described in Chapter 5. Telemedicine (Klootwijk *et al.*, 2004; Rubel *et al.*, 2004) is another possible application area. For example, a reduced lead set is easier to apply, and is less cumbersome for patients in home monitoring settings. However, small changes in precordial and limb electrodes due to improper electrode placement may result in a performance decrease in the reconstructed leads.

Furthermore, the coefficients used in our investigations were derived from a specific learning set of patients who were evaluated for a possible myocardial infarction. These coefficients may not be appropriate for other groups of patients. Therefore, future work should focus on evaluating these coefficients on other patient groups.

Finally, it is still unknown how stable patient-specific coefficients will remain over a long period of time, despite the stabilizing pattern observed in Chapter 2. A prospective study of ECGs taken over a longer period (week, month, or year) may provide additional information.

Conclusions

In conclusion, the methods developed and clinically validated in this thesis may alleviate problems during ECG monitoring. The following remarks can be made:

- Accurate reconstruction of up to four precordial leads is feasible with general or patient-specific reconstruction coefficients.
- Patient-specific reconstruction is more accurate than general reconstruction.
- Accurate general and patient-specific reconstruction is possible over time.
- A reconstructed 12-lead ECG based on a reduced lead set containing leads I, II, V_2, and V_5 can be used to facilitate pre-hospital decision making on patients with acute coronary syndromes.

- ST changes caused by body position changes can be distinguished from ischemic changes and patient-specific methods have been developed to correct these ST changes.
- Proximal placement of the extremity leads may result in ECG variations, but these changes can be corrected by general and patient-specific reconstruction methods with high reconstruction performance.

Appendix: Methodology

Based on:

US Patent No. 6,690,967 (S. H. Meij and S. P. Nelwan)
US Patent No. 6,643,539 (S. H. Meij and S. P. Nelwan)
US Patent Application. 2004/0030257 (B. Tabbara, S. H. Meij, and S. P. Nelwan)

Introduction

In chapters 1-3, the reconstruction methods were described in a concise manner. This appendix contains a more detailed description of the calculations and techniques for synthesizing electrocardiographic leads. In light of the work of Cady (1969); Smith *et al.* (1975); Dower *et al.* (1988); Scherer *et al.* (1989); Nelwan *et al.* (2000); Drew *et al.* (2002), and the various similar patented techniques (Nicklas and Scherer, 1993; Dower, 1989; Wang, 2000; Meij and Nelwan, 2003; Brodnick, 2003; Meij and Nelwan, 2004; Wei *et al.*, 2004; Tabbara *et al.*, 2004), our reconstruction methods are presented.

Lead reconstruction

As presented in Equation 9.1, the basic algorithm for synthesis of ECG leads (D) is a multiplication of the available source lead vector(S) and a coefficient matrix (M). The reconstruction coefficient matrix M can be obtained from a large data set (general) or from the patient's own ECG (patient-specific). D contains a combination of one or more precordial leads, while S contains the extremity leads and at least one precordial lead. The precordial lead sets in D and S are disjunct.

$$D = MS \tag{9.1}$$

The linear regression algorithm in our reconstruction method uses singular value decomposition (SVD) (Press *et al.*, 1993) without a zero-intercept vector. Although SVD requires more computations than ordinary multiple linear regression, SVD properly handles the selection of two or more possible fits with similar reconstruction performance. In short, the variance-covariance matrix is estimated from the scatter of the observations around the best fit. An optimized SVD algorithm is used (Galassi *et al.*, 2000) with column scaling to improve the accuracy of the singular values. Components with zero singular value are discarded from the fit.

Ranking techniques

The synthesis techniques can be applied in situations where patients are monitored with a reduced number of ECG leads. For example, a patient can be moved from full 12-lead monitoring to 7-lead or 8-lead (telemetry) monitoring. Another situation where this technique can be applied is for ECG monitoring with right-sided chest leads (e.g. V_4R, V_5). In this situation, the end-user needs to be assisted in the choice of which and how many chest electrodes can be moved to the right side while maintaining adequate synthesis of the conventional chest electrodes. For these purposes, the patient-specific matrices that have been derived for all possible lead sets can be ranked so that the end-user may decide which electrode(s) to select.

Two methods can be used to rank lead sets:

1. *Pearson's correlation coefficient*
   The Pearson correlation coefficient is widely used to correlate data. The coefficient ranges from -1 to 1, where -1 indicates a perfect negative correlation, 0 no corre-

lation at all and 1 indicates a perfect correlation. Pearson's correlation coefficient captures shape rather than absolute differences.

$$\text{corr}(x,y) = \frac{\sum_i (x_i - \mu_x)(y_i - \mu_y)}{\sqrt{\sum (x_i - \mu_x)^2}\sqrt{\sum (y_i - \mu_y)^2}} \tag{9.2}$$

2. *Similarity coefficient*
A second coefficient is modified for the end-user to have the same range as the Pearson's correlation coefficient. The similarity coefficient is calculated as follows:

$$\text{SC} = 1.0 - \frac{\text{RMS}_{error}}{\text{RMS}_{source}} \tag{9.3}$$

The RMS (root mean square) is defined as:

$$\text{RMS} = \sqrt{\frac{1}{n}\sum_{i=1}^{n} {x_i}^2} \tag{9.4}$$

Technical implementation considerations

Details about technical and practical considerations of the reconstruction methods were left out for conciseness in the previous chapters. The lead subset reconstruction methods have been implemented in research and commercial systems (Siemens/Dräger Medical Systems TRUST Telemetry). The following remarks can be made:

- **Investigation of 4-lead subsets**
Telemetry devices are often technically limited to a reduced number of ECG channels. The TRUST telemetry devices transmit leads I, II, and two generic unipolar leads (V and V+). In Chapters 2 and 3, it was found that the best 4-lead subsets performed well if one precordial lead is selected from V_1-V_3 and the other from V_4-V_6. The best five 4-lead subsets and their coefficients are presented in Table 9.3. Performance was based on the average correlation coefficient over the four reconstructed leads. Lead sets with adjacent precordial leads had overall lower correlation values. Users were not allowed to select these combinations in the user interface.

- **Quality of the extremity leads**
It is not uncommon for patients to have a small or near iso-electric ECG complex in limb lead I. For those patients, lead I should not be used as a source lead for reconstruction. The reconstruction methods used in previous chapters detect this situation and switch to a new matrix in which lead I is not used.

- **User interface**
The user interface program (signals and trends) marks a reconstructed lead with a unique label and code. For example, a reconstructed precordial lead V_1 is labelled as dV_1. Patient-specific matrices should always be marked with the date and time of the ECG from which the coefficients were computed.

- **Computer-based recommendation of the best lead set**
  The selection process of the best lead set for patient-specific reconstruction was also implemented in a computer program. The program selects the matrix with the highest similarity measure (correlation coefficient or similarity coefficient), but does not select a matrix containing unstable reconstruction coefficients (i.e. over-learning) or lead subsets with adjacent precordial leads.

Table 9.3: Reconstruction performance and coefficients of the five best lead subsets based on average correlation coefficients.

	Correlation Coefficient		Lead subset configuration			
			I	II	V_2	V_5
1	0.956	dV_1	-0.463	-0.069	0.527	-0.097
		dV_3	0.170	0.256	0.742	0.518
		dV_4	0.162	-0.032	0.289	1.139
		dV_6	-0.083	0.161	-0.115	0.599
2	0.953		I	II	V_2	V_6
		dV_1	-0.478	-0.072	0.514	-0.133
		dV_3	0.313	0.651	0.750	0.984
		dV_4	0.400	0.393	0.390	0.840
		dV_5	0.181	0.086	0.138	1.145
3	0.953		I	II	V_1	V_5
		dV_2	0.692	0.080	1.494	0.054
		dV_3	0.682	0.420	1.073	0.475
		dV_4	0.356	0.066	0.444	1.125
		dV_6	-0.175	0.112	-0.214	0.595
4	0.952		I	II	V_3	V_5
		dV_1	-0.551	-0.290	0.430	-0.352
		dV_2	-0.168	-0.396	0.857	-0.512
		dV_4	0.071	-0.111	0.435	0.924
		dV_6	-0.046	0.187	-0.160	0.683
5	0.950		I	II	V_1	V_6
		dV_2	0.698	0.229	1.429	-0.201
		dV_3	0.791	0.840	0.970	-0.143
		dV_4	0.649	0.491	0.505	0.714
		dV_5	0.276	0.119	0.194	1.114

US006643539B2

(12) **United States Patent**
Meij et al.

(10) **Patent No.: US 6,643,539 B2**
(45) **Date of Patent: Nov. 4, 2003**

(54) **ELECTROCARDIOGRAM SYSTEM FOR SYNTHESIZING LEADS AND PROVIDING AN ACCURACY MEASURE**

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(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 261 days.

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(65) **Prior Publication Data**

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Related U.S. Application Data

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(51) **Int. Cl.**[7] **A61B 5/0402**

(52) **U.S. Cl.** **600/509**; 600/521

(58) **Field of Search** 607/509, 512, 607/521

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(57) **ABSTRACT**

An electrocardiogram (ECG) system provides a set of ECG lead signals. The system includes a source of a subset of ECG lead signals. A synthesizer, coupled to the ECG lead signal source, generates a set of synthesized ECG lead signals from the subset of ECG lead signals. Data is also generated representing the accuracy of the set of synthesized ECG lead signals.

23 Claims, 3 Drawing Sheets

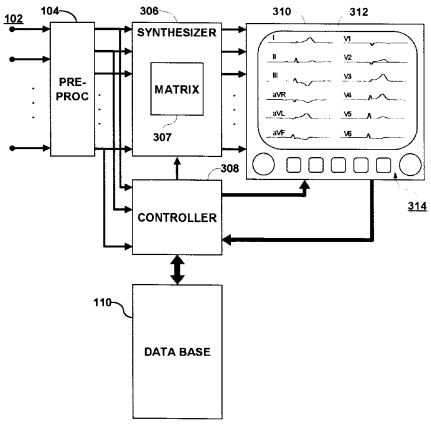

Figure 9.4: Front Page of US Patent Number 6,643,539.

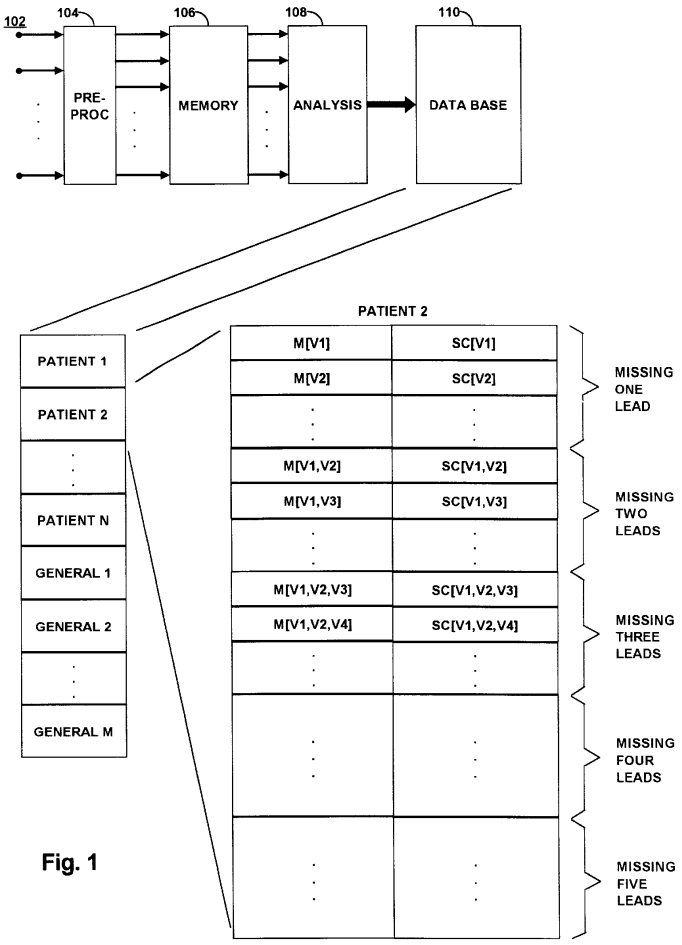

Fig. 1

Figure 9.5: Analysis (Figure 1).

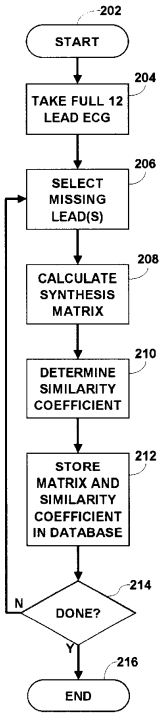

Fig. 2

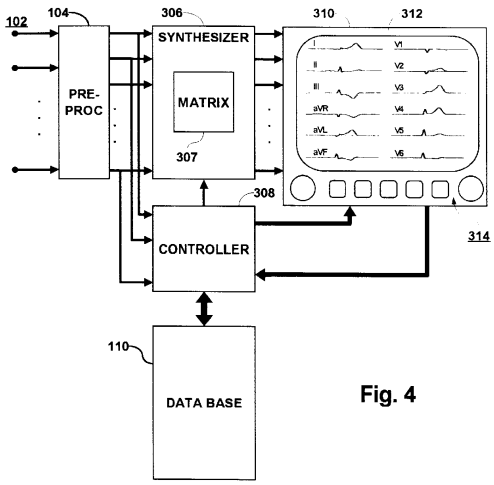

Fig. 4

Figure 9.6: Analysis flowchart (Figure 2) and synthesis (Figure 4).

a)

S		M[V1]								I
SI		1	0	0	0	0	0	0	0	I
SII		0	1	0	0	0	0	0	0	II
SV1		CI(V1)	CII(V1)	0	CV2(V1)	CV3(V1)	CV4(V1)	CV5(V1)	CV6(V1)	V1
SV2		0	0	0	1	0	0	0	0	V2
SV3	=	0	0	0	0	1	0	0	0	V3
SV4		0	0	0	0	0	1	0	0	V4
SV5		0	0	0	0	0	0	1	0	V5
SV6		0	0	0	0	0	0	0	1	V6

b)

S		M[V1,V3]								I
SI		1	0	0	0	0	0	0	0	I
SII		0	1	0	0	0	0	0	0	II
SV1		CI(V1)	CII(V1)	0	CV2(V1)	0	CV4(V1)	CV5(V1)	CV6(V1)	V1
SV2		0	0	0	1	0	0	0	0	V2
SV3	=	CI(V3)	CII(V3)	0	CV2(V3)	0	CV4(V3)	CV5(V3)	CV6(V3)	V3
SV4		0	0	0	0	0	1	0	0	V4
SV5		0	0	0	0	0	0	1	0	V5
SV6		0	0	0	0	0	0	0	1	V6

Fig. 3

Figure 9.7: Matrix Calculations (Figure 3).

Patent Description

Method and Apparatus, Monitoring Method, User Interface, and Analysis System for Synthesizing and Electrocardiogram

Abstract of the Disclosure

An electrocardiogram (ECG) system provides a set of ECG lead signals. The system includes a source of a subset of ECG lead signals. A synthesizer, coupled to the ECG lead signal source, generates a set of synthesized ECG lead signals from the subset of ECG lead signals. Data is also generated representing the accuracy of the set of synthesized ECG lead signals.

Field of the invention

The present invention relates to electrocardiogram (ECG) systems, and in particular to ECG systems which can provide synthesized signals corresponding to signals generated from electrodes which provide the actual ECG signals.

Background of the invention

ECG systems are well known, and provide information about the physiological status of a patient's heart to a physician. More specifically, so called 12-lead ECG systems exist which provide twelve waveforms, called leads, to the physician. To provide such a 12-lead ECG, ten electrodes are placed on the patient's body, and the signals from these electrodes are processed to provide the twelve leads, all in a known manner. These ten electrodes include four electrodes which provide signals processed to generate six of what are known as limb leads, and six electrodes which provide signals processed to provide six of what are known as precordial or chest leads.

However, such a system does not always operate in the ideal manner. Sometimes, electrodes slip on, or work loose from, a patient's body and produce a null signal, or produce signals which are otherwise degraded to the point of being unusable. Furthermore, the location on the patient's body at which one or more of the electrodes should be placed may be unavailable due to injury or surgery. In addition, under some circumstances it may be desirable to place an electrode at a location on the body different from the normally used locations. It is desirable under these conditions to still provide the signals needed to generate the 12-lead ECG.

It is known that the signals representing the respective lead signals contain mutually redundant information. It is also known that, should one electrode be missing or malfunctioning, an appropriate combination of signals from the other electrodes and/or the other leads, which are available and functional, can be used to generate a synthesized signal which closely approximates the lead signal derived from the missing or malfunctioning electrode. To apply this technique, at least some portion of a full 12-lead ECG is recorded, during an analysis phase. The recorded signals are then processed to generate a function, which may be applied to the lead signals which are available, to synthesize a lead signal which approximates the lead signal which is missing or distorted beyond use. During a synthesis phase, this function is then applied to the available ECG lead signals. Using this technique, a missing lead may be synthesized.

In U.S. Patent No. 5,058,598, issued Oct. 22, 1991 to Nicklas *et al.,* a system is disclosed for synthesizing a desired precordial lead from what is termed a set of base leads. First, in an analysis phase, a set of ECG lead signals, including at least the

set of base leads (in Nicklas et al, the base leads are leads I, II, and V_2), and the precordial lead signal (other than V_2) which is desired to be synthesized, is processed to generate coefficients for a linear equation. Then, in a synthesis phase, signals representing only the base leads are received, and the values of those base leads are substituted into the linear equation to derive values which represent the desired synthesized precordial lead signal. Nicklas *et al.* also discloses partitioning the ECG complex into segments (e.g. QRS, ST, etc.), and processing each segment separately to generate respective sets of coefficients for a separate linear equation corresponding to each segment. In this case, during the synthesis phase, values for each segment from the base leads are substituted into the appropriate linear equation, to derive values which represent the desired synthesized precordial lead signal in that segment.

In U.S. Patent No. 5,490,515, issued Feb. 13, 1996 to Mortara, a system is disclosed for synthesizing a single specified lead from a set of eight lead signals. In the analysis phase, the set of eight lead signals, derived from respective electrodes, is received by the system and a coefficient table, having entries representing coefficients of a set of linear equations, is generated. In the synthesis phase, the coefficient table is then used to synthesize a selected one of the eight lead signals, based on the values of the other seven lead signals. Mortara also discloses simultaneously synthesizing more than one missing lead.

In neither of these systems is any indication of the accuracy of the synthesized signal provided to the operator. In addition, in neither of these systems is any information provided to the operator to assist in preparation for the ECG, nor in interpreting the displayed 12 ECG lead waveforms.

It is desirable to determine the accuracy of the synthesized signal relative to other potential synthesized signals, and to provide that information to the operator. It is further desirable to provide information to the operator to assist in the preparation for the ECG and the interpretation of the results. In some cases, such as telemetered ECGs, it is further desirable to monitor patients with a minimum number of electrodes, while producing a full 12-lead ECG and maintaining a desired level of accuracy.

Brief summary of the invention

In accordance with principles of the present invention, an electrocardiogram (ECG) system provides a set of ECG lead signals. The system includes a source of a subset of ECG lead signals. A synthesizer, coupled to the ECG lead signal source, generates a set of synthesized ECG lead signals from the subset of ECG lead signals. Data is also generated representing the accuracy of the set of synthesized ECG lead signals.

Brief description of the drawings

In the drawing:

1. Figure 1 (cf. Figure 9.5) is a diagram in block form with the database block also shown in memory layout form, illustrating a portion of an ECG system according to principles of the present invention;

2. Figure 2 (cf. Figure 9.6) is a flowchart useful in understanding the operation of the system illustrated in Figure 1;

3. Figure 3 (cf. Figure 9.7) is a diagram illustrating matrix calculations which are useful in understanding the operation of the present invention; and

4. Figure 4 (cf. Figure 9.6) is a block diagram illustrating a different portion of a system according to principles of the present invention.

Detailed description of the invention

Figure 1 is a diagram in block form with the database block also shown in memory layout form, illustrating a portion of an ECG system according to principles of the present invention. In Figure 1, a plurality 102 of electrodes are intended to be attached to respective locations on a patient's body. The plurality 102 of electrodes are coupled to respective input terminals of a preprocessor 104. Respective output terminals of the preprocessor 104 are coupled to corresponding input terminals of a memory 106. Respective output terminals of the memory 106 are coupled to corresponding input terminals of an analysis circuit 108. An output terminal of the analysis circuit 108 is coupled to an input terminal of a database 110.

In operation, the plurality 102 of electrodes are ECG electrodes which are intended to be attached to predetermined locations on a patient. In the illustrated embodiment, 10 electrodes are provided. The preprocessor 104 processes the signals from the 10 electrodes to generate signals representing a 12-lead ECG at respective output terminals. More specifically, signals from the four limb lead electrodes are processed to provide limb lead signals I and II. From limb lead signals I and II, the remaining limb lead signals III, aVR, aVL and aVF, may be mathematically derived. In the illustrated embodiment, the derivation of those other limb lead signals is not germane to the present invention and they are not discussed in the remainder of this application. The other six electrodes are processed separately to provide corresponding precordial lead signals (V_1, V_2, V_3, V_4, V_5, V_6). Thus, signals representing eight lead signals (I, II, V_1, V_2, V_3, V_4, V_5, V_6) are generated by the preprocessor 104 in a known manner and are further processed in the manner described below.

In the illustrated embodiment this preprocessing further includes analog-to-digital conversion. The eight lead signals, therefore, are in multibit digital form. The preprocessor 104 may further provide processing to identify characteristics of each ECG complex and to time align and aggregate (e.g. average, median filter, etc.) some number of successive ECG complexes for each lead, all in a known manner. Digital data representing the eight, possibly averaged, ECG lead complexes is stored, in a known manner, in respective locations in the memory 106.

Figure 2 is a flowchart useful in understanding the analysis phase operation of the analysis system illustrated in Figure 1. The operation starts in block 202. In block 204 a full 12-lead ECG is taken and the result, as described above, is multibit digital data representing eight respective ECG lead complexes (I, II, V_1, V_2, V_3, V_4, V_5, V_6), possibly aggregated. The data representing these eight lead complexes are stored in respective locations in the memory 106, all in a known manner.

The analysis circuit 108 retrieves data, in a known manner, from the locations in the memory 106 corresponding to the eight lead complexes. The analysis circuit 108 then analyzes the retrieved data. In general, every possible combination of one or more of the leads is treated as if it were missing or otherwise unusable. Then, for each such combination, the other remaining lead complexes, treated as if they remain available, are compared to the missing lead complex or complexes, and a function of the available lead complexes is calculated which will most accurately synthesize the one or more missing leads from the available leads. A measure of the accuracy of the synthesis is also determined

and both the calculated function and the determined accuracy measure are stored in the database 110. The processing applied to each such combination is illustrated in Figure 2 and described in more detail below.

In block 206 a subset of leads, consisting in the first place of one of the eight leads, is selected as the missing lead. For the purposes of the following description, the selected lead is the precordial lead V_1. In block 208, the stored lead complex data representing the selected lead V_1 is compared to the stored lead data representing the other seven lead complexes (I, II, V_2, V_3, V_4, V_5 and V_6) to calculate a function of those other seven lead complexes (I, II, V_2, V_3, V_4, V_5 and V_6) which will most closely approximate the selected lead complex (V_1).

In the illustrated embodiment, a lead complex SV_1, approximating the selected lead complex V_1, is synthesized by a linear combination of the other seven lead complexes (I, II, V_2, V_3, V_4, V_5 and V_6). That synthesis is represented by a set of coefficients $CI(V_1)$, $CII(V_1)$, $CV_2(V_1)$, $CV_3(V_1)$, $CV_4(V_1)$, $CV_5(V_1)$ and $CV_6(V_1)$. The notation Cx(y) is intended to represent the coefficient C to be applied to the x^{th} available lead complex to synthesize the missing y^{th} lead complex. That is, this set of coefficients represents the proportion of the other seven lead complexes (I, II, V_2, V_3, V_4, V_5 and V_6), respectively, in the linear combination representing the synthesized lead complex SV_1 most closely approximating the missing lead complex V_1. In the illustrated embodiment, the coefficients are calculated using a least squares linear regression with a zero intercept vector, in a known manner. One skilled in the art will understand that any form of combination, such as polynomial or trigonometric, could also be used.

The calculation in block 208 produces a synthesis matrix M. Figure 3 is a diagram illustrating matrix calculations which are useful in understanding the operation of the present invention. In Figure 3a, a matrix $M[V_1]$ illustrates a matrix which is produced when the selected lead is lead V_1. The notation M[z] is intended to represent the synthesis matrix M for synthesizing the synthesized vector S from an input vector I missing the set z of ECG lead complexes. An input vector I contains elements representing data points from the eight lead complexes (I, II, V_1, V_2, V_3, V_4, V_5, V_6). The matrix $M[V_1]$ has as its basis an identity matrix. However, the row corresponding to the synthesized lead complex SV_1 (e.g. the third row from the top) is replaced by the set of coefficients $CI(V_1)$, $CII(V_1)$, 0, $CV_2(V_1)$, $CV_3(V_1)$, $CV_4(V_1)$, $CV_5(V_1)$ and $CV_6(V_1)$ calculated in block 208 by the analysis circuit 108. The column corresponding to the selected lead complex V_1 (e.g. the third column from the left) is set to zero, so that the selected lead complex V_1 makes no contribution to the combination forming the synthesized selected lead complex SV_1.

One skilled in the art will understand that when the synthesis matrix $M[V_1]$ is multiplied by the input vector I, the result is a synthesized vector S. The synthesized vector S contains elements representing synthesized data points for the eight synthesized lead complexes (SI, SII, SV_1, SV_2, SV_3, SV_4, SV_5, SV_6), in which the synthesized lead complex SV_1 for the selected lead is synthesized from the other seven leads (I, II, V_2, V_3, V_4, V_5, V_6) while the remaining leads (SI, SII, SV_2, SV_3, SV_4, SV_5, SV_6) are equal to the corresponding elements in the input vector I.

In block 210 a similarity coefficient SC is determined in the following manner. When the matrix $M[V_1]$ has been calculated in block 208, it is used to generate eight synthesized lead complexes (SI, SII, SV_1, SV_2, SV_3, SV_4, SV_5, SV_6). Then the synthesized lead complexes (SI, SII, SV_1, SV_2,

SV_3, SV_4, SV_5, SV_6) are compared to the actual leads complexes (I, II, V_1, V_2, V_3, V_4, V_5, V_6) stored in the memory 106 to calculate a similarity coefficient SC. This is designated in Figure 2 as SC(V_1) to indicate that it is the similarity coefficient SC for the selected lead V_1. In the illustrated embodiment, this coefficient SC[V_1] is calculated from the differences between the root mean square (RMS) values of the synthesized lead complex data (SI, SII, SV_1, SV_2, SV_3, SV_4, SV_5, SV_6) and the stored actual lead complex data (I, II, V_1, V_2, V_3, V_4, V_5, V_6). More specifically, the synthesis coefficient is calculated as $SC = (RMS_{source} - RMS_{error})/RMS_{source})$.

Alternatively, the known Pearson's correlation technique may be used to generate a similarity coefficient SC. One skilled in the art will understand, however, that any technique of rating the similarity of the synthesized lead complexes to the actual lead complexes may be used.

In step 212, the calculated matrix M[V_1] and the corresponding similarity coefficient SC[V_1] are stored in the database 110 in a known manner. The database 110 is maintained on a non-volatile storage device. For example, the database may be located on a disk drive system in a central location accessible by a hospital network, in a known manner. The specific configuration of the storage device and database 110 is not germane to the invention, provided it is accessible by the ECG system.

One skilled in the art will understand from Figure 1 that the database 110 contains a plurality of entries respectively corresponding to different patients and to different general populations. This will be described in more detail below. Each patient and general population entry contains a sequence of synthesis entries corresponding to different sets of selected (missing) lead complexes, derived as described above. In Figure 1, the entry for patient 2 is illustrated. The patient 2 entry in turn contains a first synthesis entry into which the matrix M[V_1] and the similarity coefficient SC[V_1] is stored. Other data not germane to the present invention may also be stored in the patient entry and/or the patient entry's synthesis entries.

In block 214, if all the synthesis entries have been filled, then the process ends in block 216. Otherwise processing returns to block 206 where another subset of leads is selected and treated as missing. In the illustrated embodiment, all subsets consisting of a single missing lead are processed, followed by all subsets consisting of two missing leads, all subsets consisting of three missing leads, and so forth. One skilled in the art will understand that the order in which the subsets are determined and processed is not germane to the present invention.

More specifically, in the illustrated embodiment, the precordial lead V_2 is selected next and the processing described above performed again. In this case, referring again to Figure 1, the results of this processing, M[V_2] and SC[V_2], are stored in the second synthesis entry in the patient 2 entry. This continues for all of the remaining subsets of a single missing lead. Then all sets of two simultaneously missing leads are processed. For example, leads V_1 and V_2 are simultaneously selected and treated as missing and the same processing described above performed and the results, synthesis matrix M[V_1,V_2] and similarity coefficient SC[V_1,V_2], are stored in the appropriate patient 2 synthesis entry. Then the next set of two missing leads, V_1 and V_3 are simultaneously selected and treated as missing and the same processing performed.

Figure 3b illustrates a matrix M[V_1,V_3] which is calculated in response to the simultaneous selection of leads V_1 and V_3 as missing. As before, the matrix M[V_1,V_3] has as its basis the identity matrix. But in this case the row corresponding to the synthe-

sized lead SV_1 is replaced with coefficients $CI(V_1)$, $CII(V_1)$, 0, $CV_2(V_1)$, 0, $CV_4(V_1)$ $CV_5(V_1)$ and $CV_6(V_1)$ and the row corresponding to the synthesized lead SV_3 is replaced with coefficients $CI(V_3)$, $CII(V_3)$, 0, $CV_2(V_3)$, 0, $CV_4(V_3)$, $CV_5(V_3)$ and $CV_6(V_3)$. At the same time, the columns corresponding to the selected lead complexes V_1 and V_3 are replaced with zeroes to ensure that input signals from those lead complexes do not contribute to the synthesized lead signals. Again, a similarity coefficient $SC[V_1,V_3]$ is determined and both the matrix $M[V_1, V_3]$ and the similarity coefficient $SC[V_1,V_3]$ are stored in the appropriate synthesis entry in the patient 2 entry. This continues for all sets of two missing leads, followed by all combinations of three missing leads and so forth until the patient 2 entry is completed and the process ends in block 216 (of Figure 2).

As was disclosed in Nicklas *et al.* it is possible to partition each of the eight lead complexes stored in the memory 108 into segments, and perform the calculations described above on each segment independently. In the present invention, this would result in a plurality of matrices, one for each segment, stored in each synthesis entry in the patient 2 entry. When the missing lead(s) is synthesized from the available leads, the appropriate matrix is used depending on which segment is currently being synthesized, all as disclosed in Nicklas *et al.*

Figure 4 is a block diagram illustrating a synthesis portion of a system according to principles of the present invention. In Figure 4, those elements which are the same as those illustrated in Figure 1 are designated by the same reference number and are not described in detail below. In Figure 4, the respective output terminals of the preprocessor 104 are coupled to corresponding input terminals of a synthesizer 306 and a controller 308. Respective output terminals of the synthesizer 306 are coupled to corresponding data input terminals of a display device 310. A synthesizer control output terminal of the controller 308 is coupled to a control input terminal of the synthesizer 306, and a display device control output terminal of the controller 308 is coupled to a control input terminal of the display device 310. The display device includes a display screen 312 and a set of user controls 314. These user controls 314 may include, among other controls, knobs, illustrated as circles, and buttons, illustrated as rounded squares. A user control output terminal of the display device 310 is coupled to a user control input terminal of the controller 308. A bidirectional terminal of the controller 308 is coupled to a corresponding terminal of the database 110.

As illustrated in Figure 4, the display device 310 can display the 12-lead ECG waveforms from the synthesizer 306 on the display screen 312 in the usual manner for ECG waveforms. In addition, the controller 308 can respond to user input from the user controls 314 on the display device 310, and can condition the display device 310 to display information on the display screen 312. The controller 308 can also control the operation of the synthesizer 306 in response to the lead signals from the preprocessor 104, in a manner to be described in detail below. The synthesizer 306 in turn performs the matrix multiplication illustrated in Figure 3 on the lead signals received from the preprocessor 104 to generate the lead signals, possibly including synthesized lead signals, for the display device 310.

In general operation, the plurality of electrodes 102 are attached to predetermined locations on a patient by an operator. The operator then manipulates the user controls 314 to enter information concerning the monitoring desired, including, e.g. the identification of the patient. The controller 308 then conditions the synthesizer 306 to operate in a normal mode. The

preprocessor 104 provides the eight lead signals to the synthesizer 306. In the normal mode, all of the plurality 102 of electrodes are operational, and all lead signals from the preprocessor 104 are accurate. The controller 308 conditions the synthesizer 306 to pass the input lead signals through to the output without change. This may be done by placing an identity matrix in the matrix 307 of the synthesizer 306. The synthesizer 306 performs the matrix multiplication illustrated in Figure 3 using the identity matrix to transfer the received 12 lead signals to the display device 310. The display device 310, in turn, displays the 12-lead ECG waveforms from the synthesizer 306 on the display screen 312 all in a normal manner. In this mode of operation, the similarity coefficient has its maximum value.

As described above, however, it is possible for one or more electrodes to detach from the patient. This may be detected automatically by the controller 308 by any of a number of known techniques. For example, if no pulse component is detected in a lead signal, then that lead signal may be identified as inoperative. In this case, the controller 308 retrieves the entry from the database 110 for the current patient, e.g. patient 2 (of Figure 1), and from that entry retrieves the matrix M appropriate for synthesizing the lead or leads which have been identified as inoperative. The controller 308 then inserts that matrix M into the matrix 307 in the synthesizer 306. The synthesizer 306 performs the matrix multiplication described above with reference to Figure 3, to provide a synthesized signal for the lead or leads which are inoperative. The display device 310 continues to display the 12 lead waveforms received from the synthesizer 306, including the synthesized lead waveform or waveforms.

The controller 308 may further condition the display device 310 to display an indication on the display screen 312 to alert the operator that one or more of the displayed leads are being synthesized. This indication may include highlighting the synthesized lead waveform(s), or the background of the synthesized lead waveform(s), in some fashion, such as varying the intensity or color of the synthesized lead waveform(s) relative to the other lead waveforms; or placing an indicative symbol in the vicinity of the synthesized waveform(s); or displaying a textual identification of the synthesized waveform(s) on the display screen 312. In addition, the controller 308 may retrieve the corresponding similarity coefficient SC from the database 110 and display that on the display screen 312 as an indication of the expected accuracy of the displayed waveforms.

Also as described above, all the desired locations on the body of the patient may not be available due to surgery or injury. In this case, the operator can manipulate the user controls 314 to provide an indication of the sites which are unavailable to the controller 308. The controller 308 will then generate a list of electrode configurations for the available locations, and access the data in the database 110 entry associated with this patient to retrieve the similarity coefficients SC associated with each of the electrode configurations. The configuration with the highest similarity configuration SC, i.e. generating the most accurate 12 lead ECG waveform synthesis, is then displayed on the display screen 312 of the display device 310. The controller 308 retrieves the matrix M associated with that configuration and places it in the matrix 307 in the synthesizer 306. In accordance with the displayed information, the operator then applies the electrodes in this desired configuration. Then the display of the 12 lead ECG waveforms can proceed as described above, optionally including specially highlighting the synthesized lead waveforms and displaying the similarity coefficient.

Alternatively, the complete list of available electrode configurations along with their similarity coefficients may be displayed on the display screen 312 of the display device 310. The operator can then select one of the available configurations based not only on the similarity coefficients but possibly also on other clinical considerations. The operator then manipulates the user controls 314 to indicate which of the configurations has been selected, and applies the electrodes in that configuration. The controller 308 retrieves the appropriate matrix M from the database 110 and supplies it to the matrix 307 in the synthesizer 306. The controller 308 then conditions the synthesizer 306 to synthesize the 12 lead ECG waveforms for that configuration, as described above.

By either automatically specifying the electrode configuration with the highest similarity coefficient, or by providing a list of electrode configurations with an associated similarity coefficient to the operator for selection, it is assured that an electrode configuration producing 12 lead ECG waveforms with the maximum accuracy, or the maximum accuracy given the existing clinical considerations, will be displayed.

It is sometimes desired to use a nonstandard electrode configuration. For example, a physician may desire data related to the right side of the heart, or further around the left side of the heart. The former requires one or more electrodes placed at locations to the right of the heart, and the latter at locations further to the left of the heart. There are predetermined such locations known as V_1R, V_2R, V_3R, V_4R, V_5R and V_6R on the right side of the chest and V7, V8 and V9 around the left side of the patient. Prior systems required either extra electrodes and circuitry to process signals and display the waveforms from them, or that electrode(s) be removed from the standard locations V_1, V_2, V_3, V_4, V_5 and V_6 to be placed at the other location(s) V7, V8, V9, V_1R, V_2R, V_3R, V_4R, V_5R and V_6R. Moving a lead from a standard location meant losing the lead signal generated by that electrode.

In the system illustrated in Figure 4, the operator manipulates the user controls 314 on the display device 310 to indicate that it is desired to move one or more of the electrodes from their standard locations to another location. In response, the controller 308 retrieves the entry in the database 110 corresponding to the patient, and retrieves all of the similarity coefficients SC for the configurations missing the number of leads desired to be moved. That is, if two leads are desired to be moved, then the controller 308 retrieves the similarity coefficients SC for all of the configurations missing two leads. The controller 308 then automatically selects the configuration having the highest similarity coefficient SC from among those retrieved, and displays information on the display screen 312 of the display device 310 specifying the electrode configuration corresponding to that similarity coefficient SC. The operator places the appropriate electrodes at the specified locations on the patient, and then places the remaining leads at the other desired locations.

The controller 308 then retrieves the matrix M corresponding to the specified electrode configuration from the database 110 and supplies it to the matrix 307 in the synthesizer 308. The synthesizer 306 then synthesizes the standard 12 lead ECG waveforms from the available leads in the standard locations in the manner described above. The controller 308 may further condition the display device 310 to simultaneously display the 12 lead ECG waveforms and the lead waveforms from the other locations (e.g. from the right side of the chest) on the display screen 312, in a known manner. As before, the synthesized waveforms may be specially identified on

the display screen and/or the similarity coefficient displayed.

As before, alternatively, a list of possible electrode configurations with their respective similarity coefficients, may be displayed on the display screen 312 of the display device 310, from which the operator selects one based on the similarity coefficients and other clinical considerations. The operator manipulates the user controls to select one of the configurations and the controller 308 conditions the system to operate in that configuration as described above. Again, as before, use of the similarity coefficients permits synthesis of the standard 12 lead ECG waveforms having the maximum accuracy, or the maximum accuracy based on existing clinical considerations.

In some situations, the use of the full set of 10 electrodes to produce the full 12 lead ECG is not desirable, for example, if a patient is being transported from one location to another, or if the ECG is being monitored by telemetry. In these situations, it is desired to use the minimum number of electrodes for patient comfort, while still maintaining a desired level of accuracy in the ECG.

Under these situations, the controller 308 retrieves the patient entry from the database 110. The similarity coefficients SC for all the synthesis entries corresponding to one missing lead are compared, and the entry with the largest similarity coefficient is selected. Similarly the similarity coefficients for all the synthesis entries corresponding to two missing leads are compared and the entry with the largest similarity coefficient is selected. This is repeated for each possible number (three, four, etc.) of missing leads. Then the list of selected entries, including the electrode configuration and the similarity coefficient, is displayed on the display screen 312 of the display device 310. The operator then selects the entry which satisfies the minimum accuracy desired using the user controls 314, and attaches the electrodes to the patient according to the configuration represented by that entry. The controller 308 conditions the system to synthesize the 12 lead ECG from the selected electrode configuration. In this manner, the highest accuracy for the number of electrodes selected is guaranteed, while minimizing to the extent possible the number of electrodes necessary, thus, minimizing patient discomfort.

In the preceding description, it was assumed that a full 12 lead ECG for the patient was previously available to be analyzed. This may not always be the case. In those cases, of course, there can be no entry in the database 110 for that patient. Referring again to Figure 1, 12 lead ECG data from a large population may be analyzed by the analysis circuit 108 as a group, in the manner illustrated in Figure 2. In this case, the eight lead complexes assembled in the memory 106 by block 204 will be generated as the aggregation of all the available eight lead ECG complexes for all the people in the population. These general-population lead complexes will be analyzed in the manner illustrated in Figure 2 above to produce a set of general-population matrices M and corresponding similarity coefficients SC. This set of matrices M and similarity coefficients SC will be stored in a general population entry in the database 110, illustrated in Figure 1 as an entry labeled GENERAL 1. The entry GENERAL 1 has exactly the same data structure as that illustrated for Patient 2. The data in the GENERAL 1 entry is based on the aggregated 12 lead complexes for the entire population, however.

If a patient does not have an entry in the database 110, then the general population entry GENERAL 1 is retrieved, and the data in that entry used in exactly the same manner as described above for any of the situations described above: e.g. syn-

thesizing detached electrodes, or synthesizing leads for electrodes whose locations are unavailable or which have been purposely moved to another location. When sufficient complete 12 lead ECG complexes have been accumulated for the patient, then the analysis described above with reference to Figure 1 and Figure 2 is performed on those complexes, a new entry in the database 110 is created for the patient containing the matrices and associated similarity coefficients resulting from that analysis, and the processing continues as described above using the newly created entry in the database 110.

It is also possible to partition the people in the general population discussed above into groups termed categories. For example, groupings may be made by sex, by weight, by age group, by disease and/or by cardiac health (e.g. normal, ischemic/acute myocardial infarction, bundle branch blockage, etc.). The ECG complexes associated with the general population of patients may be partitioned in a corresponding manner and analyzed separately as described above with reference to Figure 1 and Figure 2 to produce further category-specific general-population entries in the database 110, designated as General 2 to General M in Figure 1.

When a patient is being prepared for an ECG, the operator manipulates the user controls 314 on the display device 310 to supply characteristics of the patient (name, sex, age, weight, etc.) to the controller 308. As described above, the controller 308 queries the database 110 for a patient entry for that patient. If a patient does not have a patient entry in the database 110, then the other characteristics related to that patient are processed by the controller 308 to assign the patient to one of the available categories. The controller 308 then retrieves the category-specific general population entry corresponding to the category to which the patient was assigned, and uses the synthesis entries in that entry to provide a 12 lead ECG until that patient is assigned his own entry in the database 11.

Claims

What is claimed is:

1. An electrocardiogram (ECG) system, comprising: a source of a plurality of subsets of data representing ECG lead signals associated with a corresponding plurality of sets of ECG electrode configurations; a synthesizer, coupled to the ECG lead signal source, for generating a plurality of sets of data representing synthesized ECG lead signals from the plurality of subsets of data representing ECG lead signals; a source of data representing a plurality of accuracy values corresponding to the plurality of sets of data representing synthesized ECG lead signals; and a display generator for initiating generation of data representing at least one display image identifying a plurality of accuracy values and identifying the corresponding plurality of sets of ECG electrode configurations and enabling a user to select a configuration based on accuracy values.

2. The system of claim 1 wherein the display image identifies the plurality of sets of ECG electrode configurations enabling a user to select a configuration based on electrode positions.

3. The system of claim 1 wherein the synthesizer comprises circuitry for calculating a function of the subset of ECG lead signals to generate the set of synthesized ECG lead signals and further comprising

   an analyzer, coupled to the synthesizer and the accuracy representative

data source, and responsive to a set of preexisting ECG lead signals, for generating the function of the subset of ECG lead signals and the accuracy representative data.

4. The system of claim 3 wherein the analyzer comprises circuitry, responsive to the set of preexisting ECG lead signals, for calculating respective coefficients of a linear equation representing the function and an individual coefficient is associated with an individual ECG lead signal in the subset of ECG lead signals.

5. The system of claim 1 wherein said synthesizer adaptively generates a set of data representing a selected one of (a) patient specific synthesized ECG lead signals and (b) patient independent synthesized ECG lead signals, in response to user command.

6. The system of claim 1 wherein an accuracy value comprises a similarity coefficient.

7. The system of claim 6 wherein said accuracy value is responsive to the RMS values of the preexisting ECG lead signals and the synthesized ECG lead signals.

8. The system of claim 6 wherein said similarity coefficient SC comprises $SC = (RMS_{source} - RMS_{error})/RMS_{source})$ where represents RMS_{source} the root mean square value of the preexisting ECG lead signals and RMS_{error} represents the RMS value of the difference between the preexisting ECG lead signals and the synthesized ECG lead signals.

9. The system of claim 1 wherein said user is able to select a configuration based on at least one of, (a) accuracy values and (b) clinical considerations, by selecting an image element in said at least one display image.

10. The system of claim 1, wherein the ECG lead signal source comprises: a set of electrodes; and a preprocessor, responsive to respective signals from the electrodes to generate said plurality of subsets of data representing ECG lead signals associated with said corresponding plurality of sets of ECG electrode configurations.

11. The system of claim 1, wherein: the ECG lead signal source generates an input vector representing an individual subset of ECG lead signals; and the synthesizer comprises: a matrix for containing a function of said individual subset of ECG lead signals; and a processor for performing a matrix multiplication of the matrix times said input vector to generate a corresponding output vector comprising a subset of data representing ECG lead signals.

12. The system of claim 1, further comprising a database, containing a plurality of functions respectively corresponding to said plurality of subsets of data representing ECG lead signals associated with a corresponding plurality of sets of ECG electrode configurations; and a controller, coupled between the database and the synthesizer, and comprising: circuitry for retrieving from the database the function corresponding to an individual subset of ECG lead signals; and circuitry for conditioning the synthesizer to apply the retrieved function to said individual subset of ECG lead signals.

13. The system of claim 1, including, a database containing a plurality of matrices respectively representing a plurality of functions; a function retrieving processor for retrieving from the database the matrix corresponding to an individual subset of ECG lead signals; a conditioning processor for supplying the retrieved matrix to the synthesizer; and wherein the ECG lead signal source generates an input vector representing said individual subset of ECG lead signals; and the synthesizer, receives the retrieved matrix corresponding to said individual subset of ECG lead signals; and multiplies said input vector and retrieved matrix to generate a corresponding output vector representing ECG lead signals.

14. The system of claim 1 wherein: said synthesizer adaptively generates a set of data representing a selected one of, (a) patient specific synthesized ECG lead signals and (b) patient independent synthesized ECG lead signals, together with an associated accuracy representative value, in response to user command.

15. The system of claim 14, wherein said synthesizer adaptively generates a set of data representing ECG lead signals in at least one of, (i) standard electrode positions and (ii) non-standard electrode positions.

16. The system of claim 1 further comprising: a memory, responsive to the set of preexisting ECG lead signals, for storing respective ECG complexes respectively corresponding to the ECG lead signals; and a processor, coupled to the memory, for calculating a plurality of functions, and associated accuracy values, in response to the stored ECG complexes.

17. The system of claim 16 wherein said function comprises a matrix.

18. A method supporting operation of an electrocardiogram (ECG) system, comprising the steps of: storing a plurality of subsets of data representing ECG lead signals associated with a corresponding plurality of sets of ECG electrode configurations; generating a plurality of sets of data representing synthesized ECG lead signals from the plurality of subsets of data representing ECG lead signals; storing data representing a plurality of determined accuracy values corresponding to the plurality of sets of data representing synthesized ECG lead signals; and initiating generation of data representing at least one display image identifying a plurality of accuracy values and identifying the corresponding plurality of sets of ECG electrode configurations and enabling a user to select a configuration based on accuracy values.

19. An electrocardiogram (ECG) system, comprising: a source of a plurality of subsets of data representing ECG lead signals associated with a corresponding plurality of sets of ECG electrode configurations; a synthesizer, coupled to the ECG lead signal source, for employing the plurality of subsets of data representing ECG lead signals in adaptively generating a set of synthesized data representing a selected one of, (a) patient specific synthesized ECG lead signals and (b) patient independent synthesized ECG lead signals; and a display generator for initiating generation of data representing at least one display image showing said synthesized data.

20. A system according to claim 19, wherein said synthesizer automati-

cally selects to perform said selected one of, (a) said patient specific ECG lead signal synthesis and (b) said patient independent ECG lead signal synthesis in response to a determination a subset of data representing patient specific ECG lead signals is available.

21. A system according to claim 19, wherein said synthesizer adaptively generates said set of synthesized data in response to user selection, via said at least one display image, of synthesis of said selected one of, (a) patient specific synthesized ECG lead signals and (b) patient independent synthesized ECG lead signals.

22. A system according to claim 19, including, a source of data representing accuracy values corresponding to sets of data representing patient specific synthesized ECG lead signals and patient independent synthesized ECG lead signals and wherein said at least one display image shows accuracy values associated with said patient specific synthesized ECG lead signals and with said patient independent synthesized ECG lead signals.

23. A method supporting operation of an electrocardiogram (ECG) system, comprising the steps of: storing a plurality of subsets of data representing ECG lead signals associated with a corresponding plurality of sets of ECG electrode configurations; adaptively generating a set of synthesized data representing a selected one of, (a) patient specific synthesized ECG lead signals and (b) patient independent synthesized ECG lead signals, in response to user command, said synthesized data being generated using the plurality of subsets of data representing ECG lead signals; and initiating generation of data representing at least one display image showing said synthesized data.

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Brodnick, D. E. (2003). US Patent No. 6,636,761: Method and apparatus for generating a twelve-lead ECG from fewer than ten electrodes. *US Patent Office*.
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Cady, L. D. (1969). Computed relationship of standard electrocardiographic leads. *Med Res Eng*, **8**(3), 37–42.
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Dower, G. E. (1989). US Patent No. 4,850,370: Method and apparatus for sensing and analyzing electrical activity of the human heart. *US Patent Office*.
This document contains the patent description of the EASI lead system. Claims are made on a method of sensing and analyzing electrical activity of the human heart with 4 electrodes located at key positions on the surface of a subject's body. Signal processing means combines and scales the voltage signals to produce xyz vectorcardiographic signals, electrocardiographic signals corresponding to the lead signals of a 12-lead electrocardiograph, or both.

Dower, G. E., Machado, H. B., and Osborne, J. A. (1980). On deriving the electrocardiogram from vectorcardiographic leads. *Clin Cardiol*, **3**(2), 87–95.
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Dower, G. E., Yakush, A., Nazzal, S. B., Jutzy, R. V., and Ruiz, C. E. (1988). Deriving the 12-lead electrocardiogram from four (EASI) electrodes. *J Electrocardiol*, **21 (Suppl)**, 182–187.
This article contains one of the first descriptions of the EASI lead system. EASI uses the E, A, and I electrode positions of the Frank lead system, plus an electrode, S, positioned over the upper end of the sternum and a ground. Its outputs form quasi-xyz signals, x'y'z', that can be approximately transformed into xyz signals by means of a matrix derived from the EASI lead vectors. The result forms a good basis for deriving the 12-lead ECG, using previously published coefficients for the Frank lead system.

Drew, B. J. and Krucoff, M. W. (1999). Multilead ST-segment monitoring in patients with acute coronary syndromes: a consensus statement for healthcare professionals. *Am J Crit Care*, **8**(6), 372–386.
In this document, several practical guidelines are provided for the use of ST-segment monitoring in clinical practice. Consensus was reached on who should and should not have ST monitoring, goals and time frames for ST monitoring in various diagnostic categories, what electrocardiographic leads should be monitored, and what knowledge and skills are required for safe and effective ST monitoring.

Drew, B. J., Adams, M. G., Pelter, M. M., and Wung, S. F. (1996). ST-segment monitoring with a derived 12-lead electrocardiogram is superior to routine cardiac care unit monitoring. *Am J Crit Care*, **5**(3), 198–206.
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Drew, B. J., Adams, M. G., Pelter, M. M., Wung, S. F., and Caldwell, M. A. (1997). Comparison of standard and derived 12-lead electrocardiograms for diagnosis of coronary angioplasty-induced myocardial ischemia. *Am J Cardiol*, **79**(5), 639–644.
The study aim was to determine whether a derived 12-lead ECG would demonstrate typical ST-segment changes of ischemia during percutaneous transluminal coronary angioplasty (PTCA). High to very high accuracy results were found between the standard and derived ECGs.

Drew, B. J., Pelter, M. M., Wung, S. F., Adams, M. G., Taylor, C., Evans, G. T., and Foster, E. (1999). Accuracy of the EASI 12-lead electrocardiogram compared to the standard 12-lead electrocardiogram for diagnosing multiple cardiac abnormalities. *J Electrocardiol*, **32 (Suppl)**, 38–47.
This study was performed to compare a derived 12-lead ECG using a simple 5-electrode lead configuration (EASI 12-lead) with the standard ECG for multiple cardiac diagnoses. It was concluded that EASI and standard 12-lead ECGs are comparable for multiple cardiac diagnoses; however, serial ECG changes (eg, T-wave changes) should be assessed using one consistent 12-lead method.

Drew, B. J., Pelter, M. M., Brodnick, D. E., Yadav, A. V., Dempel, D., and Adams, M. G. (2002). Comparison of a new reduced lead set electrocardiogram with the standard electrocardiogram for diagnosing cardiac arrhythmias and myocardial ischemia. *J Electrocardiol*, **35 (Suppl)**, 13–21.
This investigation presents an interpolated 12-lead ECG method based on a lead sub set of I, II, V_1, and V_5. The method was previously patented by Brodnick. It was concluded that the interpolated 12-lead ECG is comparable to the standard ECG for diagnosing multiple cardiac abnormalities, including wide-QRS-complex tachycardias and acute myocardial ischemia. The advantages of this ECG method are that the standard electrode sites are familiar to clinicians and that eight of the 12 leads are 'true' standard leads. Hence, QRS-axis and morphology criteria for diagnosing wide-QRS-complex tachycardia and bundle branch and fascicular blocks are preserved.

Drew, B. J., Califf, R. M., Funk, M., Kaufman, E. S., Krucoff, M. W., Laks, M. M., Macfarlane, P. W., Sommargren, C., Swiryn, S., and Van Hare, G. F. (2004). Practice standards for electrocardiographic monitoring in hospital settings: an American Heart Association scientific statement from the Councils on Cardiovascular Nursing, Clinical Cardiology, and Cardiovascular Disease in the Young. *Circulation*, **110**(17), 2721–2746.
This article contains the practice standards for ECG monitoring in hospital settings endorsed by AHA counsels and by ISCE. A brief discussion is dedicated to the use of derived 12-lead ECG monitoring.
`http://dx.doi.org/10.1161/01.CIR.0000145144.56673.59`

Edenbrandt, L. and Pahlm, O. (1988). Vectorcardiogram synthesized from a 12-lead ECG: superiority of the inverse Dower matrix. *J Electrocardiol*, **21**(4), 361–367.
In this study, several methods to synthesize the VCG from the 12-lead ECG for diagnostic purposes were investigated. The method of the inverse transformation matrix of Dower (coefficients provided) proved to be the best method of synthesis.

Einthoven, W. (1902). Galvanometrische registratie van het menschelijk electrocardiogram. In *Herinneringsbundel Prof. S.S. Rosenstein*, pages 101–106. Eduard IJdo.

Feild, D. Q., Feldman, C. L., and Horacek, B. M. (2002). Improved EASI coefficients: their derivation, values, and performance. *J Electrocardiol*, **35 (Suppl)**, 23–33.
In this study, new and optimized transformation coefficients are provided to derive the 12-lead ECG from the EASI lead system. The authors also provided coefficients for the Mason-Likar 12-lead ECG, for six other precordial leads and for off-sternum electrodes.

Fye, W. B. (1994). A history of the origin, evolution, and impact of electrocardiography. *Am J Cardiol*, **73**, 1214–1219.
This review article summarizes the origins and development of electrocardiography and addresses its role in defining cardiology as a specialty.

Galassi, M., Davies, J., Theiler, J., Gough, B., Jungman, G., Booth, M., and Rossi, F. (2000). *GNU Scientific Library Reference Manual*. Network Theory Ltd.
This reference book contains a concise usage overview of the GNU Scientific Library (GSL). GSL is a free numerical library for the GNU operating system. http://www.gnu.org/software/gsl

Garcia, J., Astrom, M., Mendive, J., Laguna, P., and Sornmo, L. (2003). ECG-based detection of body position changes in ischemia monitoring. *IEEE Trans Biomed Eng*, **50**(6), 677–685.
The purpose of this paper was to analyze and detect changes in body position (BPC) during recording of the electrocardiogram. Different schemes for feature extraction are used (spatial and scalar), while preprocessing, trend postprocessing and detection are identical. The spatial approach is based on VCG loop rotation angles and the scalar approach is based on the Karhunen-Loeve transform (KLT) coefficients. It is concluded that reliable detection of BPCs may be achieved using the ECG signal and should work in parallel to ischemia detectors.

Goldberger, A. L., Amaral, L. A., Glass, L., Hausdorff, J. M., Ivanov, P. C., Mark, R. G., Mietus, J. E., Moody, G. B., Peng, C. K., and Stanley, H. E. (2000). PhysioBank, PhysioToolkit, and PhysioNet: components of a new research resource for complex physiologic signals. *Circulation*, **101**(23), 215–220.
This article provides a description of PhysioNet, a publicly available toolkit for processing signals, and PhysioBank, a collection of data sets for the development and evaluation of algorithms. More information is available at http://www.physionet.org.

Grijseels, E. W., Deckers, J. W., Hoes, A. W., Boersma, E., Hartman, J. A., van der Does, E., and Simoons, M. L. (1996). Implementation of a pre-hospital decision rule in general practice. Triage of patients with suspected myocardial infarction. *Eur Heart J*, **17**(1), 89–95.
The objective of this study was to improve pre-hospital triage of patients with suspected acute cardiac disease. It was concluded that pre-hospital triage by the general practitioner was facilitated using a standardized questionnaire and pre-hospital electrocardiography, and resulted in a reduction of the number of patients admitted to the Coronary Care Unit, and proved to be safe.

Grijseels, E. W. M. (1996). *Prehospital Triage to Improve Diagnostic and Therapeutic Decisions in Patients with Suspected Myocardial Infarction*. PhD dissertation, Erasmus University.
This PhD thesis contains the background, design, development, and clinical validation of prehospital decision algorithms. In addition to a questionnaire, 12-lead ECG decision rules were developed and presented.

Hanley, J. A. and McNeil, B. J. (1982). The meaning and use of the area under a receiver operating characteristic (ROC) curve. *Radiology*, **143**(1), 29–36.
In this paper, receiver operating characteristic (ROC) curves and statistical tests using the area-under-the-curve are described. Furthermore, the authors developed formulas for standard errors and corrections for pairing, analogous to that used in the paired t-test. Detailed algorithms based on this paper are available online (http://www.anaesthetist.com/mnm/stats/roc).

Horacek, B. M., Warren, J. W., Stovicek, P., and Feldman, C. L. (2000). Diagnostic accuracy of derived versus standard 12-lead electrocardiograms. *J Electrocardiol*, **33 (Suppl)**, 155–160.
The aims of this study were to compare the diagnostic yield of ECGs recorded by 12 standard leads with that of 12-lead ECGs derived from EASI using correlation coefficients and accuracy of a diagnostic classification (Cardiac Infarction Injury Score). It was found that derived 12-lead ECGs correlated well with the recorded ones, and faithfully reproduced the diagnostic features needed for the CIIS.

Horacek, B. M., Warren, J. W., Feild, D. Q., and Feldman, C. L. (2002). Statistical and deterministic approaches to designing transformations of electrocardiographic leads. *J Electrocardiol*, **35 (Suppl)**, 41–52.
The purpose of this study was to compare two approaches to investigate the relationships among electrocardiographic leads: a statistical one, based on the analysis of recorded electrocardiograms (ECGs), and a

deterministic one, based on physical principles that govern the current flow in irregularly shaped volume conductors such as the human body. Results suggest that the lead transformations should be preferably designed by statistical analysis of recorded ECGs. Regression models with a small number of predictors (eg, those based on three ECG leads) are the most reliable.

Horan, L. G. and Flowers, N. C. (1968). The principle of waveform correlation in electrocardiographic research. *J Electrocardiol*, **1**(1), 43–50.
In this study principal factor analysis was performed to determine the minimum number of leads which can contain all of the ECG information on the body surface. To evaluate accuracy of original versus derived, a ratio based on the source and error root mean square errors was presented.

Jernberg, T., Lindahl, B., Hogberg, M., and Wallentin, L. (1997). Effects on QRS waveforms and ST-T-segment by Changes in Body Position during the Continuous 12-lead ECG: a Preliminary Report. In *Computers In Cardiology*, pages 461–463. IEEE Computer Society.
This report contains an overview of changes in the QRS, ST-segment and T waves caused by body positional changes during continuous 12-lead ST monitoring in 36 patients. It was concluded that ST-segment changes due to positional changes are small, but may reach significant levels.

Johanson, P., Rossberg, J., and Dellborg, M. (2001). Continuous ST monitoring: a bedside instrument? A report from the Assessment of the Safety of a New Thrombolytic (ASSENT 2) ST monitoring substudy. *Am Heart J*, **142**(1), 58–62.

Johanson, P., Jernberg, T., Gunnarsson, G., Lindahl, B., Wallentin, L., and Dellborg, M. (2003). Prognostic value of ST-segment resolution-when and what to measure. *Eur Heart J*, **24**(4), 337–345.

Jowett, N. I., Turner, A. M., Cole, A., and Jones, P. A. (2005). Modified electrode placement must be recorded when performing 12-lead electrocardiograms. *Postgrad Med J*, **81**(952), 122–125.
This study compared 12-lead ECGs in 100 patients during routine electrocardiography, one being taken in the approved way and one taken with modified limb electrodes. The use of torso leads produced important waveform changes associated with a more vertical and rightward shift of the QRS frontal axis. It was concluded that ECGs recorded with different limb electrode positions should be marked.

Julian, D. G. (1987). The history of coronary care units. *Br Heart J*, **57**(6), 497–502.

Kligfield, P. (2003). Overview of the ISCE ECG "genome project". *J Electrocardiol*, **36 (Suppl)**, 163–165.
At the ISCE2003 meeting, prof. Kligfield presented an overview of the ISCE genome project, but also introduced the FDA efforts for centralized and standardized storage of ECG information from clinical trials.

Klootwijk, A. P. J. (1998). *Dynamic computer-assisted ST-segment monitoring in patients with acute coronary syndromes*. PhD dissertation, Erasmus University, Thoraxcentrum.
In this thesis the application of computer-assisted continuous vectorcardiographic and multilead ECG monitoring techniques for detection and quantification of myocardial ischemia, prediction of coronary vessel status and for identification of patients at risk of major coronary events is evaluated.

Klootwijk, A. P. J., Meij, S. H., van Es, G. A., Muller, E. J., Umans, V. A., Lenderink, T., and Simoons, M. L. (1997). Comparison of usefulness of computer assisted continuous 48-h 3-lead with 12-lead ECG ischaemia monitoring for detection and quantitation of ischaemia in patients with unstable angina. *Eur Heart J*, **18**(6), 931–940.
The study aim was to test whether the selection of ECG leads used for ST monitoring may influence detection and quantitation of ischemia using 12-lead versus 3-lead ST monitoring in 130 patients. It was concluded that continuous 12-lead ST monitoring increases the detection rate and duration of ST episodes compared to 3-lead ST monitoring. The use of continuous 12-lead ECG monitoring devices on emergency wards and coronary care units is recommended.

Klootwijk, A. P. J., Meij, S., Melkert, R., Lenderink, T., and Simoons, M. L. (1998). Reduction of recurrent ischemia with abciximab during continuous ECG-ischemia monitoring in patients with unstable angina refractory to standard treatment (CAPTURE). *Circulation*, **98**(14), 1358–1364.
In this study, 1265 patients were monitored from start of treatment through six hours post coronary intervention. Ischemic episodes were detected and ischemic burden was calculated as either the total duration of ST episodes per patient or the area under the curve of ST vector magnitude during episodes or the sum of the areas under the curves of 12 leads during episodes.

Klootwijk, A. P. J., Nelwan, S. P., van Dam, T. B., and Meij, S. H. (2004). Remote mobile real-time patient monitoring using a wireless personal digital assistant. *Cardiology Int*, **5**, 7–9.

Kornreich, F. and Rautaharju, P. M. (1981). The missing waveform and diagnostic information in the standard 12 lead electrocardiogram. *J Electrocardiol*, **14**(4), 341–350.
In this study, a similarity coefficient is introduced to quantify the degree of similarity between the recorded and the calculated ECGs.

Kors, J. A. and van Herpen, G. (2002). How many electrodes and where? A "poldermodel" for electrocardiography. *J Electrocardiol*, **35 (Suppl)**, 7–12.
In this study, a practical approach is proposed to increase the diagnostic information content of the standard 12-lead ECG by repositioning selected chest electrodes. Repositioning electrodes V4 and V6 and subsequent reconstruction of the absent leads provided a simple, practical method by which the sampling of diagnostic information from the body surface is improved, while maintaining the full diagnostic content of the standard 12-lead ECG.

Kors, J. A., Talmon, J. L., and van Bemmel, J. H. (1986). Multilead ECG analysis. *Comput Biomed Res*, **19**(1), 28–46.
This paper describes the results of research in computer-assisted ECG and VCG interpretation and to provide on-line analysis of ECGs. The on-line system is based on a modular approach. Changes in the methods and software had to be made mainly because of the simultaneity of all ECG leads and the concurrency of the processing tasks.

Kors, J. A., van Herpen, G., Sittig, A. C., and van Bemmel, J. H. (1990). Reconstruction of the Frank vectorcardiogram from standard electrocardiographic leads: diagnostic comparison of different methods. *Eur Heart J*, **11**(12), 1083–1092.
In this study, three methods for reconstructing the Frank VCG from the standard 12-lead ECG were studied. The first was based on multivariate regression, the second on a model of the cardio-electrical activity, and the third method used a quasi-orthogonal set of ECG leads. The methods were evaluated on a test set of 90 cases by a numerical distance measure and by the agreement in diagnostic classification of the original and reconstructed VCGs. The performance of the regression method and the model-based method was comparable. Both methods were preferable to the quasi-orthogonal method. The kappa values for the preferred methods indicated a good to excellent diagnostic agreement between the original and reconstructed VCGs.

Krucoff, M. W., Parente, A. R., Bottner, R. K., Renzi, R. H., Stark, K. S., Shugoll, R. A., Ahmed, S. W., DeMichele, J., Stroming, S. L., and Green, C. E. (1988). Stability of multilead ST-segment "fingerprints" over time after percutaneous transluminal coronary angioplasty and its usefulness in detecting reocclusion. *Am J Cardiol*, **61**(15), 1232–1237.
Multilead ST-segment recordings taken during percutaneous transluminal coronary angioplasty (PTCA) could function as an individualized noninvasive template or "fingerprint," useful in evaluating transient ischemic episodes after leaving the catheterization laboratory. To evaluate the reproducibility of such patterns over time, these changes were analyzed in patients grouped according to the time between occlusion and reocclusion. ST fingerprints were the same or clearly related with reocclusion in the same patient from less than 1 hour to greater than 1 month after initial occlusion in 87% of patients overall, in 90% in less than 1 hour, in 87% in less than 24 hours and in 84% greater than 1 month later. Thus, multilead pattern ST-segment "fingerprints" may serve as a noninvasive marker for detecting site-specific reocclusion.

Krucoff, M. W., Wagner, N. B., Pope, J. E., Mortara, D. M., Jackson, Y. R., Bottner, R. K., Wagner, G. S., and Kent, K. M. (1990). The portable programmable microprocessor-driven real-time 12-lead electrocardiographic monitor: a preliminary report of a new device for the noninvasive detection of successful reperfusion or silent coronary reocclusion. *Am J Cardiol*, **65**(3), 143–148.
This report presents a continuously updated precise digital recorder of ST-segment activity at the bedside. The recorder may provide valuable information both in monitoring patients during reperfusion therapy to determine the efficacy of such treatment and in the subsequent hours to signal threatened reocclusion. This report describes the salient features of the monitor and presents 4 distinct situations in which the monitor detected timely information regarding coronary patency after reperfusion.

Krucoff, M. W., Green, C. L., Langer, A., Klootwijk, A. P. J., Trollinger, K. M., Sawchak, S. T., Wilderman, N. M., Veldkamp, R. F., Pope, J. E., and Simoons, M. L. (1993). Global utilization of streptokinase and tPA for occluded arteries (GUSTO) ECG-monitoring substudy. Study design and technical considerations. *J Electrocardiol*, **26 (Suppl)**, 249–255.

Krucoff, M. W., Loeffler, K. A., Haisty, W. K., Pope, J. E., Sawchak, S. T., Wagner, G. S., and Pahlm, O. (1994). Simultaneous ST-segment measurements using standard and monitoring-compatible torso limb lead placements at rest and during coronary occlusion. *Am J Cardiol*, **74**(10), 997–1001.

Levkov, C. L. (1987). Orthogonal electrocardiogram derived from the limb and chest electrodes of the conventional 12-lead system. *Med Biol Eng Comput*, **25**(2), 155–164.
This article describes methods of computing orthogonal X,Y, and Z voltages representing the equivalent heart dipole activity. These components were obtained as linear functions of voltages from the limb and chest electrodes of the conventional 12-lead system. The coefficients of these linear functions are given and a close relationship with the Frank lead system is demonstrated. Two methods were used to obtain transformation coefficients – lead vector approach and statistical least-squares fit. ECG data from 92 individuals (healthy and with cardiac disorders) were used to obtain adequate coefficient values.

Lux, R. L., MacLeod, R. S., Fuller, M., Green, L. S., and Kornreich, F. (1995). Estimating ECG distributions from small numbers of leads. *J Electrocardiol*, **28 (Suppl)**, 92–98.
In this study, the authors demonstrate the utility of estimating distributions from small numbers of optimally selected leads, including conventional leads, to reduce uncertainty in the interpretation of electrocardiographic information. This issue is highly relevant when thresholds are used to detect significance of potential levels (exercise testing, detection of myocardial infarction, and continuous monitoring to assess ST-segment changes).

Mason, R. E. and Likar, I. (1966). A new system of multiple-lead exercise electrocardiography. *Am Heart J*, **71**(2), 196–205.
This paper contains a description of the modifications to the standard extremity electrodes for use during stress-ECG exercise tests.

Meij, S. H. and Nelwan, S. P. (2003). US Patent No. 6,690,967: Electrocardiogram system for synthesizing leads and providing an accuracy measure. *US Patent Office*.

Meij, S. H. and Nelwan, S. P. (2004). US Patent No. 6,643,539: Electrocardiogram system for synthesizing leads and providing an accuracy measure . *US Patent Office*.

Nelwan, S. P., Meij, S. H., Lundstrom, L., van Dam, T. B., Gilman, P., and Simoons, M. L. (1996). Continuous 12-lead ST Monitoring. In *Computers In Cardiology*, pages 477–480. IEEE Computer Society.
In this paper, the design and configuration of a continuous 12-lead ST monitoring system is described.

Nelwan, S. P., Kors, J. A., and Meij, S. H. (2000). Minimal lead sets for reconstruction of 12-lead electrocardiograms. *J Electrocardiol*, **33 Suppl**, 163–166.

Nelwan, S. P., Crater, S. W., Green, C. L., Johanson, P., van Dam, T. B., Meij, S. H., Simoons, M. L., and Krucoff, M. W. (2004a). Assessment of derived 12-lead electrocardiograms using general and patient-specific reconstruction strategies at rest and during transient myocardial ischemia. *Am J Cardiol*, **94**(12), 1529–1533.

Nelwan, S. P., Kors, J. A., Meij, S. H., van Bemmel, J. H., and Simoons, M. L. (2004b). Reconstruction of the 12-lead electrocardiogram from reduced lead sets. *J Electrocardiol*, **37**(1), 11–18.

Ng, J., Sahakian, A. V., and Swiryn, S. (2003). Accelerometer-based body-position sensing for ambulatory electrocardiographic monitoring. *Biomed Instrum Technol*, **37**(5), 338–346.
In this study, a method is presented to detect body positional changes using an accelerometer-based device.

Nicklas, J. M. and Scherer, J. A. (1993). US Patent No. 5,058,598: Method and Apparatus for synthesizing leads of an electrocardiogram. *US Patent Office*.
This patent was based on investigations by Dr. Scherer, which were presented at ISCE and Computers In Cardiology and contains a method for synthesizing data for an electrocardiographic lead from a base set of leads using transformation coefficients based on the collected data.

Norgaard, B. L., Rasmussen, B. M., Dellborg, M., and Thygesen, K. (2000). Positional changes of spatial QRS- and ST-segment variables in normal subjects: implications for continuous vectorcardiography monitoring during myocardial ischemia. *J Electrocardiol*, **33**(1), 23–30.
This paper analyzed the influence of changes in body position on continuous vectorcardiography monitoring of QRS-vector difference (QRS-VD) and ST change-vector magnitude (STC-VM) in 21 normal subjects. It was concluded that the clinical use of QRS-VD is limited, but it might be useful for inclusion in a body position detection algorithm.

Pahlm, O., Haisty, W. K., Edenbrandt, L., Wagner, N. B., Sevilla, D. C., Selvester, R. H., and Wagner, G. S. (1992). Evaluation of changes in standard electrocardiographic QRS waveforms recorded from activity-compatible proximal limb lead positions. *Am J Cardiol*, **69**(3), 253–257.
In this investigation, differences between standard ECG and two activity-compatible lead systems (stress ECG) were studied. It was observed that both alternate lead placement systems showed rightward frontal plane axis shift and diminished Q-wave durations in lead aVF compared with those of their simultaneous standard controls.

Patton, J. A. and Funk, M. (2001). Survey of use of ST-segment monitoring in patients with acute coronary syndromes. *Am J Crit Care*, **10**(1), 23–32.
The objectives of this investigation were to determine the proportion of cardiac units in the US that use ST-segment monitoring and how ST-segment monitoring is used. It was concluded that ST-segment monitoring is not routinely used and when it is, research recommendations are often not followed.

Pelter, M. M., Adams, M. G., and Drew, B. J. (2002). Association of transient myocardial ischemia with adverse in-hospital outcomes for angina patients treated in a telemetry unit or a coronary care unit. *Am J Crit Care*, **11**(4), 318–325.
The purpose of this study was to determine whether transient myocardial ischemia (TMI) is predictive of adverse in-hospital outcomes among patients admitted to a telemetry unit with acute coronary syndrome (ACS) using continuous ST-segment monitoring. It was found that continuous 12-lead ECG ST-segment monitoring provides prognostic information for risk stratification of patients admitted to the hospital for treatment of ACS.

Pharand, C., Nasmith, J. B., Rajaonah, J., Dube, B., and LeBlanc, A. R. (2003). Distinction between myocardial ischemia and postural changes in continuous ECG monitoring based on ST-segment amplitude and vector orientation–preliminary results. *Can J Cardiol*, **19**(9), 1023–1029.
The study aim was to present a new method that attempts to distinguish between 'highly probable ischemia' and positional changes. The main finding of the study was that highly probable ischemic events could be

better distinguished from positional changes with objective criteria using ST-segment amplitude and vector orientation.

Press, W. A., Teukolsky, S. A., Vetterling, W. T., and Flannery, B. P. (1993). *Numerical Recipes in C: The Art of Scientific Computing*. Cambridge University Press, Cambridge, UK, 2nd edition.
Numerical Recipes is the standard guide for implementing algorithms into programming languages. The entire book is available online at `http://www.nr.com` (for on screen viewing only).

PURSUIT Trial Investigators (1998). Inhibition of platelet glycoprotein IIb/IIIa with eptifibatide in patient with acute coronary syndromes. *N Engl J Med*, **339**, 436–443.
This paper is one of the primary references for the PURSUIT study. In this thesis, the data set of the ischemia monitoring substudy of PURSUIT was used for performance evaluations.

Rautaharju, P. M., Zhou, S. H., Hancock, E. W., Horacek, B. M., Feild, D. Q., Lindauer, J. M., Wagner, G. S., Pahlm, O., and Feldman, C. L. (2002). Comparability of 12-lead ECGs derived from EASI leads with standard 12-lead ECGs in the classification of acute myocardial ischemia and old myocardial infarction. *J Electrocardiol*, **35 (Suppl)**, 35–39.
In this investigation, a comparison was carried out between 12-lead ECGs derived with an improved transformation matrix from EASI leads and standard 12-lead ECGs in the detection of acute myocardial ischemia and old infarction by manual overreading and by an ECG analysis program. It was concluded that the EASI-derived 12-lead ECG deserves serious consideration as an alternative to the standard 12-lead ECG in emergency situations and for monitoring in acute-care settings.

Rijnbeek, P. R., Witsenburg, M., Hess, J., and Kors, J. A. (2000). Continuous age-dependent normal limits for the pediatric electrocardiogram. *J Electrocardiol*, **33 (Suppl)**, 199–201.

Rijnbeek, P. R., Witsenburg, M., Szatmari, A., Hess, J., and Kors, J. A. (2001). PEDMEANS: a computer program for the interpretation of pediatric electrocardiograms. *J Electrocardiol*, **34 (Suppl)**, 85–91.
The interpretation of pediatric electrocardiograms (ECGs) is complicated because of the strong age-dependency of the diagnostic criteria. The authors wanted to develop and evaluate a computer program for the interpretation of pediatric 12-lead ECGs. Based on the normal limits and the training set, diagnostic rules were formalized in an iterative process by using expert interviews and automatic rule induction. The performance of the program, on their study population, appears to justify its use in a clinical setting.

Rubel, P., Fayn, J., Simon-Chautemps, L., Atoui, H., Ohlsson, M., Telisson, D., Adami, S., Arod, S., Forlini, M., Malossi, C., Placide, J., Ziliani, G., Assanelli, D., and Chevalier, P. (2004). New paradigms in telemedicine: ambient intelligence, wearable, pervasive and personalized. *Stud Health Technol Inform*, **108**, 123–132.

Scherer, J. A., Jenkins, J. M., and Nicklas, J. M. (1989). Synthesis of the 12-lead electrocardiogram from a 3-lead subset using patient-specific transformation vectors. An algorithmic approach to computerized signal synthesis. *J Electrocardiol*, **22 (Suppl)**, 128.
In this investigation, the reduced lead set consisting of I, II, and V2 is presented. Patient-specific coefficients were developed to facilitate reconstruction of the remaining 5 precordial leads. While this reference is available in PubMed, the same authors also produced a full paper for the 'Computers In Cardiology' Proceedings in that same year.

Scherer, J. A., Rubel, P., Fayn, J., and Willems, J. L. (1992). Quantitative assessment of 12-lead ECG synthesis using CAVIAR. *J Electrocardiol*, **25 (Suppl)**, 137–142.
The objective of this study is to assess the performance of patient-specific segment-specific (PSSS) synthesis in QRST complexes using CAVIAR, a new method for the serial comparison of electrocardiograms and vectorcardiograms. Using the mean-quadratic deviation and CAVIAR as methods of performance assessment, this study indicates that the PSSS-synthesis algorithm accurately maintains the signal information within the 12-lead electrocardiogram.

Schijvenaars, B. J. (2000). *Intra-individual Variability of the Electrocardiogram*. PhD dissertation, Erasmus University, Department of Medical Informatics.
This dissertation addresses the topic intra-individual variability of the electrocardiogram. After reviewing the available literature, the author evaluated interpolation techniques on body surface potential maps, assessed the effects of precordial electrode position and simulated electrode displacement on computerized ECG interpretation, and developed a reliability index for electrocardiographic variability.

Schijvenaars, B. J., Kors, J. A., van Herpen, G., Kornreich, F., and van Bemmel, J. H. (1995). Interpolation of body surface potential maps. *J Electrocardiol*, **28 (Suppl)**, 104–109.

Schreck, D. M., Tricarico, V. J., Frank, J. D., Thielen, L. E., Chhibber, P., Brotea, C., and Leber, I. B. (1998). Statistical methodology: VI. Mathematical modeling of the electrocardiogram using factor analysis. *Acad Emerg Med*, **5**(9), 929–934.
The study aim was to identify the minimum number of lead-vectors required to predict the 12-lead ECG using ANOVA and factor analysis. It was found that the 12-lead ECG can be derived from only 3 measured leads. This type of data processing may lead to instantaneous acquisition and may enhance the diagnostic capability of the ECG from routine bedside telemetry equipment.

Sevilla, D. C., Dohrmann, M. L., Somelofski, C. A., Wawrzynski, R. P., Wagner, N. B., and Wagner, G. S. (1989). Invalidation of the resting electrocardiogram obtained via exercise electrode sites as a standard 12-lead recording. *Am J Cardiol*, **63**(1), 35–39.
This study demonstrated that use of body torso positions for limb leads resulted in substantial QRS waveform variations that would disqualify the exercise lead placement ECG as a "standard" recording. Such ECGs should therefore be labeled as "torso positioned" or "nonstandard" to prevent misuse for clinical and investigative purposes.

Shinar, Z., Baharav, A., and Akselrod, S. (1999). R Wave Duration as a Measure of Body Position Changes during Sleep. In *Computers In Cardiology*, pages 49–52. IEEE Computer Society.
In this study, an algorithm is presented to detect body position changes on the ECG using the R-wave amplitudes and duration measurements in the extremity leads.

Simoons, M. L., Boom, H. B., and Smallenburg, E. (1975). On-line processing of orthogonal exercise electrocardiograms. *Comput Biomed Res*, **8**(2), 105–117.

Smith, R. F., Stanton, K., Stoop, D., Brown, D., and King, P. H. (1975). Quantitative electrocardiography during extended space flight. *Acta Astronaut*, **2**(1-2), 89–102.
This study contains a description of the recording of ECGs during space missions. During flight, VCG recordings were continously obtained and transmitted to earth. To reconstruct the 12-lead ECG, a hardware circuit board was used, which was specifically designed for each astronaut (*astronaut-specific*).

Tabbara, B., Meij, S. H., and Nelwan, S. P. (2004). US Patent Appl. 2004/0030257: System for adaptively deriving ECG chest lead signal data. *US Patent Office*.
In this patent application, the coefficients for obtaining a derived 12-lead ECG from each of the fifteen 4-lead subsets, always including two limb leads and any two precordial leads, is described. In addition, a module for selection of the precordial leads is described.

Thygesen, K., Alpert, J. S., Antman, E., and Bassand, J. P. (2000). Myocardial infarction redefined–a consensus document of The Joint European Society of Cardiology/American College of Cardiology Committee for the redefinition of myocardial infarction. *Eur Heart J*, **21**(18), 1502–1513.
In this guideline endorsed by the ACC and ESC, a new definition of myocardial infarction is described. The document also provides decision rules on the ECG for the recognition of an acute infarction.

van Bemmel, J. H., Kors, J. A., and van Herpen, G. (1990). Methodology of the modular ECG analysis system MEANS. *Methods Inf Med*, **29**(4), 346–353.

The methodology used in the Modular ECG Analysis System (MEANS) is described. Overall evaluation of MEANS was done in the CSE study. Evaluation results for modules and for the entire system are presented.

Veldkamp, R. F. (1996). *Continuous digital 12-lead ST-segment monitoring in acute myocardial infarction*. PhD dissertation, Erasmus University, Thoraxcentrum.
This dissertation contains several studies aimed at improving ST-segment monitoring in various settings. Several algorithms were evaluated during Holter ST and catheterization laboratory settings.

Wang, J. (2000). US Patent No. 6,119,035: Method and system for synthesizing the 12-lead electrocardiogram. *US Patent Office*.
This patent describes a method and system for quickly and efficiently producing multiple syntheses of 12-lead electrocardiographs utilizing fewer than the 12 leads provided by a full electrode set. The method and system achieve their objectives as follows. One or more 12-lead electrocardiograph leads are synthesized from a first subset of a patient's physically present 12-lead electrocardiograph leads.

Wei, D., Kojima, T., Nakayama, T., and Sakai, Y. (2004). US Patent No. 6,721,591: Method of deriving standard 12-lead electrocardiogram and electrocardiogram monitoring apparatus. *US Patent Office*.
This patent describes a method and system of deriving the 12-lead ECG from a reduced lead set of I, II, V1, and V6. Coefficients are obtained from a learning set. The patent rights were awarded to the Nihon Kohden cooperation.

Willems, J. L., Abreu-Lima, C., Arnaud, P., van Bemmel, J. H., Brohet, C., Degani, R., Denis, B., Gehring, J., Graham, I., and van Herpen, G. (1991). The diagnostic performance of computer programs for the interpretation of electrocardiograms. *N Engl J Med*, **325**(25), 1767–1773. 01-001.
This article contains the results of a large investigation conducted to compare the performance of nine ECG computer programs and eight cardiologists in interpreting ECGs. It was found that this study shows that some, but not all computer programs perform almost as well as cardiologists.

Willems, J. L., Zywietz, C., Rubel, P., Degani, R., Macfarlane, P. W., and van Bemmel, J. H. (1992). A standard communications protocol for computerized electrocardiography. *J Electrocardiol*, **24 (Suppl)**, 173–178.
In this report, a new communications protocol and file format for electrocardiograms are described.

Wilson, F. N., Macleod, A. G., and Barker, P. S. (1932). Electrocardiographic leads which record potential variations produced by the heart beat at a single point. *Proc Soc Exp Biol Med*, **29**, 1011–1012.
This article contains a description of a central terminal which formed the basis for the definition and recording of the 6 precordial leads.

Summary

The electrocardiogram (ECG) is one of the most widely used diagnostic methods for the evaluation and treatment of patients with (acute) cardiac complaints. Continuous 12-lead ECG patient-monitoring techniques have gained an important place on intensive and medium care units, but have practical and technical considerations. The quality of ECG registration can be distorted by motion artifacts and noise. Electrodes may need to be removed when certain diagnostic tests, such as echocardiograms or X-rays, are required. In addition, 12-lead ECG patient monitoring on telemetry or medium care units is often not practical or technically possible because of the number of electrodes and the decreased patient comfort.

The aims of this thesis were to investigate, develop, and validate ECG reconstruction methods with reduced lead sets of the 12-lead ECG and to address continuous ECG registration problems which may occur as a result of changes in body position and differences in standard versus monitoring lead configurations.

Part I: ECG reconstruction

In Chapter 2, a reconstruction method was developed and assessed on a set of 2484 10-second, 12-lead ECGs obtained from patients diagnosed with acute myocardial infarction, angina pectoris, or atypical chest pain. A total of 62 lead subsets of the 12-lead ECG were considered by systematically removing one or more precordial leads, but always including leads I and II. After splitting the data set in an equally-sized learning and test set, general and patient-specific coefficients were computed. Reconstruction performance was assessed by correlation coefficients and root mean square errors (RMSE) between the original and reconstructed leads. General reconstruction allows synthesis of two to three excluded precordial leads, while for patient-specific reconstruction a minimal set including the limb leads and at least two precordial leads suffices.

Chapter 3 describes an evaluation of reconstruction performance of the general and patient-specific methods over time. For this purpose, the general and patient-specific methods were applied on a data set of 24-hour continuous 12-lead ECG recordings of patients with transient ischemic episodes. General and patient-specific reconstruction methods were applied on the test set. Reconstruction performance was assessed by correlation between the original and reconstructed leads over the QRS and T waves. Average and maximum absolute ST differences ($|\Delta ST|$) were determined between the original and reconstructed leads. Overall, accurate reconstruction of the 12-lead ECG is possible over time. General reconstruction performance remained at a similar performance level. Patient-specific performance initially slightly decreased and then stabilized over time, but remained much better than general reconstruction.

Part II: Clinical evaluation

The second part of the thesis consists of three chapters containing evaluations of the ECG reconstruction methods in clinical settings. Chapters 4 and 6 were set up as prospective studies and were carried out in collaboration with the Duke ECG Ischemia Core Laboratory (Durham, NC, USA).

Chapter 4 presents a validation study of the reconstruction methods in recordings of patients undergoing a percutaneous coronary intervention procedure. The study was set up in the catheterization laboratory of the VA Medical Center (Durham, NC, USA). In 39 recordings, one or more balloon inflations were performed, which caused ischemia and ST-T changes on the ECG. The inflations were marked and were compared to a previously defined baseline ECG recorded prior to the procedure. ECGs were reconstructed using general and patient-specific methods with reduced lead sets including the limb leads and at least two precordial leads. Accuracy on the reproductions of the ST-T changes was assessed in the reconstructed leads. Overall, it was found that the general and patient-specific reconstruction methods, with the limb and two precordial leads, accurately derive the absent leads at baseline and during balloon inflation.

In Chapter 5, the general reconstruction method with a reduced lead set consisting of all limb leads and precordial leads V_2 and V_5, was evaluated for use in a pre-hospital situation. In these emergency care situations, early diagnosis, risk stratification and initiation of treatment on the spot by the ambulance service reduces mortality and final infarct size. Use of a reduced lead set method may save time and can be implemented in devices, such as defibrillators. The general reconstruction method with lead subset I, II, V_2, and V_5 was applied on a data set of 12-lead ECGs obtained from the ambulance service in Rotterdam. This data set, previously used to develop a computer-assisted thrombolytic triage algorithm, consisted of a learning set (n=1435) and test set (n=825). Reconstruction performance was assessed using $|\Delta ST|$ and misclassifications. High to very high sensitivity and specificity was observed. As a result of reconstruction differences, three cases would have been referred to a PCI center instead of receiving thrombolytic treatment. Three false negative cases would not have received therapy, but would have been referred to the emergency room for further evaluation. Overall, the general reconstruction method with the 4-lead subset can be considered in pre-hospital situations.

Chapter 6 presents a comparative assessment of the general and patient-specific reconstruction methods and the well-known EASI lead system. EASI uses five electrodes on conveniently defined electrode sites from which all 12 leads are derived. The three reconstruction methods were evaluated on a set of 44 recordings of patients undergoing a percutaneous coronary intervention procedure. Derivation performance was measured with $|\Delta ST|$, RMSE, and several clinical decision rules. The overall highest differences ($|\Delta ST|$, RMSE, and incorrectly classified cases) were found in EASI. General reconstruction performed better than EASI and patient-specific reconstruction had the overall best performance.

Part III: Patient monitoring

Two well-known problems that may occur during long-term continuous ECG monitoring are described and addressed by methods similar to and based on the earlier described ECG reconstruction methods.

First, it is well-known that a body position change (BPC) may alter the 12-lead ECG, resulting in changes in QRS and ST amplitudes and T-waves. It is likely that these ECG changes can be interpreted as ischemia and may trigger false positive patient-monitoring alarms. Chapter 7 presents a study which aim was to quantify these body position changes and to develop a detection method and a patient-specific correction method. The study was carried out on a set of 114 patients admitted to the coronary care unit at the Thoraxcentrum. Each patient underwent a body position test (supine, left, right, and upright position). A body position change detector was developed using the EXPLORE automated rule induction algorithm. To distinguish positional from ischemic changes, a separate set of 71 PCI recordings was used including ECGs recorded at rest and during balloon inflation. The ECG variations were corrected using a patient-specific reconstruction method based on a combination of leads. Performance of the correction method was assessed by Pearson's correlation coefficient and by similarity coefficient. ST changes of $\geq 100\ \mu V$ in ≥ 1 lead caused by BPC were observed in 50 (43%) patients. The most pronounced changes were found in the left-lateral position. With a fixed specificity at 95%, sensitivity of the detection rules was for left 97.4%, right 69.9%, upright 64.3% and combined: 66.1%. False alarm rate per hour in the PCI set was 2.22 at rest and 4.31 during balloon inflation. Performance of the patient-specific correction method yielded an overall correlation coefficient of 0.970 and similarity coefficient of 0.889.

Second, electrode positions for continuous monitoring are different from those for recording of a standard 12-lead ECG, because the standard sites at the wrists and ankles may introduce noise and artifacts. Therefore, most institutions move the limb electrodes to the chest and lower abdomen on monitoring positions defined by Mason and Likar. However, this change may alter the ECG significantly and may produce alterations in the frontal QRS axis, Q waves in the inferior leads, and R amplitudes. A study was set up to develop a method to correct for these changes. With a data set of 93 subjects with a simultaneously recorded 9-lead ECG in standard and monitoring positions, patient-specific and generalized methods were developed and evaluated. The main results are that general reconstruction can be used to map the monitoring leads to the standard leads with high accuracy.

Discussion and conclusions

Chapter 9 contains a general discussion of the described reconstruction methods. In conclusion, the methods developed and clinically validated in this thesis may alleviate problems encountered during ECG monitoring. Reconstruction of up to four precordial leads with general or patient-specific coefficients was shown to be accurate. It was found that patient-specific reconstruction is superior over general reconstruction over time, and during known ST changes caused by balloon inflation. In pre-hospital decision making, a general reconstruction method with a reduced lead subset containing leads I, II, V_2, and V_5 might be considered. ST-T changes caused by body position changes can be distinguished from ischemic changes and correction methods have been developed to correct for these changes with high reconstruction performance. General and patient-specific correction methods have been developed and evaluated to correct changes caused by repositioning the standard limb electrodes to the monitoring electrode positions.

Samenvatting

Het elektrocardiogram is één van de meest gebruikte diagnostische methoden voor de evaluatie en behandeling van patiënten met (acute) cardiale klachten. Continue 12-afleidingen ECG-bewakingstechnieken hebben inmiddels een belangrijke plaats gekregen op intensive en medium care afdelingen, maar hebben praktische en technische beperkingen. Zo kan de kwaliteit van de ECG-registratie worden verstoord door bewegingsartefacten en ruis. Tevens worden elektroden doorgaans verwijderd of verplaatst ten behoeve van diagnostische onderzoeken, zoals echocardiografie of röntgenfoto's. Tenslotte is 12-afleidingen ECG-bewaking op telemetrische en medium care afdelingen onpraktisch vanwege de hoeveelheid aan kabels en elektroden en het verlaagde patiëntcomfort.

De onderzoeksdoelen van dit proefschrift bestaan uit het onderzoeken, ontwikkelen en valideren van ECG-reconstructiemethoden op basis van deelverzamelingen van het 12-afleidingen elektrocardiogram en het aanpakken van problemen bij continue ECG-registratie, die kunnen voorkomen als gevolg van houdingsveranderingen en de verschillen die optreden na het verplaatsen van de extremiteitselektroden van de standaardposities (polsen en enkels) naar de patiëntbewakingsposities.

Deel I: ECG reconstructie

In hoofdstuk 2 is een reconstructiemethode ontwikkeld en geëvalueerd op een verzameling van 2484 12-afleidingen ECG's van 10 seconden. Deze ECG's zijn verkregen van patiënten die gediagnosticeerd zijn met een acuut myocardinfarct, angina pectoris of atypische pijn op de borst. Een totaal van 62 deelverzamelingen van het 12-afleidingen ECG werden gedefinieerd door het systematisch verwijderen van één of meerdere precordiale afleidingen, maar waarbij afleidingen I en II altijd waren opgenomen. Na het opsplitsen van de dataset in een leer- en testset werden algemene en patiëntspecifieke coëfficiënten berekend. Reconstructieprestaties werden beoordeeld met correlatiecoëfficiënten en root-mean-square fouten tussen de originele en gereconstrueerde afleidingen. Algemene reconstructie maakt het mogelijk om drie precordiale afleidingen van het 12-afleidingen ECG te reconstrueren, terwijl het met patiëntspecifieke reconstructie mogelijk is om vier precordiale afleidingen goed te reconstrueren.

In hoofdstuk 3 was de onderzoeksvraag hoe goed de reconstructieprestaties van de generale en patiëntspecifieke methoden zouden zijn over een langere periode. Voor dit doel werden de algemene en patiëntspecifieke methoden toegepast op een dataverzameling van continue 24-uurs, 12-afleidingen ECG-opnamen van patiënten met ischemische episodes. Algemene en patiëntspecifieke methoden werden toegepast op de testverzameling. Reconstructieprestaties werden beoordeeld met correlatiecoëfficiënten bere-

kend tussen de originele en gereconstrueerde afleidingen over de QRS- en T-golven. Gemiddelde en maximum absolute ST-verschillen ($|\Delta ST|$) werden bepaald tussen de originele en gereconstrueerde afleidingen. Nauwkeurige reconstructie van het 12-afleidingen ECG is mogelijk gebleken gedurende een periode van 24 uur. Reconstructieprestaties met algemene coëfficiënten bleven op een gelijk nivo. Prestaties van patiëntspecifieke reconstructie namen initieel af, maar stabiliseerden na verloop van tijd. Prestaties van patiëntspecifieke reconstructie bleven over de hele periode hoger dan algemene reconstructie.

Deel II: Klinische evaluatie

Het tweede deel van het proefschrift bestaat uit drie hoofdstukken, waarin de reconstructiemethoden worden geëvalueerd in een klinische omgeving. De studies in hoofdstuk 4 en 6 zijn prospectief uitgevoerd in samenwerking met het Duke Ischemia Core Laboratory (Durham, NC, VS). Hoofdstuk 4 presenteert een validatiestudie met opnamen voor en tijdens een percutane coronaire interventie. De studie is uitgevoerd in het catheterisatielaboratorium van het VA Medical Center (Durham, NC, VS), waarbij algemene en patiëntspecifieke reconstructiemethoden werden gebruikt. In elk van de 39 opnamen werden één of meerdere balloninflaties uitgevoerd, wat ischemie en ST-T veranderingen op het ECG tot gevolg kan hebben. De balloninflaties werden gemarkeerd en vergeleken met een eerder gedefinieerd basislijn-ECG. Nauwkeurigheid van de ST-T metingen werd beoordeeld in de gereconstrueerde afleidingen. Het is gebleken dat de algemene en patiëntspecifieke reconstructiemethoden, met de extremiteitsafleidingen en twee precordiale afleidingen, nauwkeurig de afwezige afleidingen kunnen reconstrueren op het basislijn-ECG en het ECG tijdens balloninflatie.

Hoofdstuk 5 bevat een evaluatie voor prehospitale toepassing van de algemene ECG-reconstructiemethode met een gereduceerde afleidingenverzameling bestaande uit alle extremiteitsafleidingen en precordiale afleidingen V_2 en V_5. In deze spoedeisende situaties kan vroege diagnose, risicostratificatie en start van een therapeutische behandeling op locatie door het ambulancepersoneel de mortaliteit en infarctgrootte verkleinen. Het gebruik van een gereduceerde afleidingenset kan tijd besparen en kan worden geïmplementeerd in apparatuur zonder een 12-afleidingenoptie, zoals defibrillatoren. De algemene reconstructiemethode is toegepast op een dataverzameling van 12-afleidingen ECG's, die zijn verkregen van de ambulancedienst in Rotterdam. Deze dataverzameling, die eerder gebruikt is om een computerondersteunend algoritme voor prehospitale thrombolyse te ontwikkelen, bestaat uit een leer- (n=1435) en testverzameling (n=825). Reconstructieprestaties werden beoordeeld met absolute ST-verschillen en misclassificaties. Hoge tot zeer hoge sensitiviteit en specificiteit werd gevonden, met drie misgeclassificeerde (vals negatief) gevallen, die geen therapie zouden krijgen, maar gestuurd zouden worden naar de spoedeisende hulp. De algemene reconstructiemethode kan in overweging worden genomen voor gebruik in prehospitale situaties.

In hoofdstuk 6 is een vergelijkende studie gedaan naar de algemene en patiëntspecifieke reconstructiemethoden en het EASI afleidingensysteem. Het EASI systeem gebruikt vijf elektroden op goed gedefinieerde elektrodelocaties, waarmee alle 12 afleidingen berekend kunnen worden. De drie methoden werden beoordeeld op een set van 44 opnamen van patiënten die een percutane coronaire interventie ondergingen. Reconstructieprestaties werden bepaald met absolute ST-verschillen, root-mean-square fouten en ver-

schillende klinische beslisregels. De grootste absolute ST-verschillen, root-mean-square fouten en misclassificaties werden gevonden bij de ECG-reconstructies van EASI. De prestaties van de algemene reconstructiemethode waren beter dan EASI; patiëntspecifieke reconstructie bleek de hoogste prestatie te hebben.

Deel III: Patiëntbewaking

In hoofdstuk 7 en 8 is onderzoek gedaan naar oplossingen voor twee veelvoorkomende problemen tijdens langdurige en continue ECG-patiëntbewaking. Voor deze oplossingen zijn methoden ontwikkeld die gebaseerd zijn op de eerder beschreven reconstructiemethoden.

Ten eerste, een lichaamspositieverandering (LPV) kan het 12-afleidingen ECG zodanig veranderen dat er verschuivingen kunnen optreden in het QRS-complex, het ST-segment en de T-golf. Deze ECG-veranderingen kunnen geïnterpreteerd worden als ischemie en kunnen als gevolg hiervan onterechte alarmen veroorzaken. In hoofdstuk 7 is een studie uitgevoerd met als doel om ECG-veranderingen als gevolg van een LPV te kwantificeren en om een detectie- en correctiemethode te ontwikkelen. Hierbij is gebruik gemaakt van een dataverzameling van 114 patiënten die waren opgenomen op de coronary care unit van het Thoraxcentrum. Elke patiënt heeft een lichaamspositietest ondergaan, waarbij de patiënt verschillende posities (liggend op de rug, linkerzij, rechterzij en rechtop-zittend) moest aannemen. Een LPV-detector werd ontwikkeld met het EXPLORE beslisregel-inductiealgoritme. Om ischemische veranderingen te onderscheiden van lichaamspositieveranderingen, is een aparte verzameling gebruikt van 71 opnamen die zijn gemaakt voor en tijdens een percutane coronaire interventie procedure. Tijdens elke opname zijn één of meerdere balloninflaties uitgevoerd. ECG-variaties kunnen worden gecorrigeerd door een patiëntspecifieke reconstructiemethode gebaseerd op een aantal afleidingen. Reconstructieprestaties werden beoordeeld op basis van Pearson's correlatiecoëfficiënt en similarity coefficient. ST-veranderingen van ≥ 100 µV in ≥ 1 afleiding veroorzaakt door een LPV werden gevonden bij 50 patiënten (43%). De meest geprononceerde ST-veranderingen werden gevonden in de links-laterale posities. De sensitiviteit van de beslisregels met een gefixeerde specificiteit van ten minste 95% was voor links: 97.4%, rechts: 69.9%, rechtop: 64.3% en gecombineerd: 66.1%. Het aantal onterechte alarmen per uur in de PCI-verzameling was 2.22 bij rust en 4.31 tijdens balloninflatie. Voor patiëntspecifieke correctie voor alle posities gecombineerd was de correlatiecoëfficiënt 0.970 en de similarity coefficient 0.889.

Ten tweede worden de extremiteitselektroden voor gebruik bij continue patiëntbewaking op een andere manier geplaatst dan voor het standaard 12-afleidingen ECG, omdat de standaardposities op de polsen en enkels ruis en artefacten op het ECG kunnen veroorzaken. Daarom verplaatsen veel instellingen de extremiteitselektroden naar locaties op de borstkas en de onderbuik, zoals aanbevolen door Mason en Likar. Echter, deze elektrodeverplaatsingen kunnen het ECG veranderen. Er kunnen veranderingen optreden in de R-toppen en frontale QRS-as en Q-golven kunnen zichtbaar worden of verdwijnen in de onderwandafleidingen. Hoofdstuk 8 bevat een studie met als doel een correctiemethode te ontwikkelen en te evalueren op basis van een dataverzameling van 93 ECG's met gelijktijdig opgenomen extremiteitsafleidingen op standaard- en bewakingsposities. Patiëntspecifieke en algemene reconstructiemethoden zijn ontwikkeld en geëvalueerd. Uit de resultaten van het onderzoek is naar voren gekomen dat algemene

reconstructiecoëfficiënten gebruikt kunnen worden om bewakingsafleidingen met een hoge nauwkeurigheid te corrigeren naar de standaardafleidingen.

Discussie en conclusies

Hoofdstuk 9 bevat een algemene bespreking van de beschreven reconstructiemethoden. Samengevat kunnen problemen tijdens patiëntbewaking verminderd worden met behulp van de reconstructiemethoden. Nauwkeurige reconstructie tot en met vier precordiale afleidingen met algemene of patiëntspecifieke coëfficiënten is mogelijk gebleken. Patiëntspecifieke reconstructie is nauwkeuriger dan reconstructie met algemene coëfficiënten, zowel over een langere periode als tijdens ST-veranderingen die door een balloninflatie worden veroorzaakt. Bij prehospitale besluitvorming zou een algemene reconstructiemethode met een gereduceerde afleidingenverzameling van I, II, V_2, en V_5 overwogen kunnen worden. ST-T veranderingen, die door lichaamspositieveranderingen zijn veroorzaakt, kunnen worden onderscheiden van ischemische veranderingen. De ontwikkelde correctiemethoden kunnen deze ST-T veranderingen corrigeren met hoge reconstructieprestaties. Algemene en patiëntspecifieke correctiemethoden zijn ontwikkeld waarmee het mogelijk is om de bewakingsafleidingen te corrigeren naar de standaardafleidingen.

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Lieve *Sas*, je bent een continue steun en stimulans geweest tijdens de afgelopen drukke, maar mooie periode. Aan jou is dit proefschrift opgedragen.

Curriculum Vitae

Stefan Nelwan was born on April 13, 1973 in Hoek van Holland (Rotterdam), The Netherlands. After attending the Zandevelt College in 's-Gravenzande, he studied Medical Informatics at the Haagse Hogeschool, The Hague, which he completed in 1995. He has been a staff member at the Thoraxcentrum, Erasmus MC from 1995 to present. In the period 1995–1999, he worked under a research contract of the Thoraxcentrum and Siemens Medical Systems (Danvers, MA, USA) for the joint development of several commercially available clinical systems, including the Cardiology Review Station, Infinity Gateway, and (Pocket) WinView. In 2001, he completed the Master of Medical Informatics programme as part of the NIHES curriculum of the Erasmus University. PhD work was started during this period under the guidance of ir. Simon Meij of the Thoraxcentrum and dr.ir. Jan Kors of the Department of Medical Informatics.

Publications

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Awards

- International Society for Computerized Electrocardiology 2004 Young Investigator Travel Award
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