

Synthesis of the 12-lead Electrocardiogram from Differential Leads

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Abstract—A new approach is proposed for synthesizing the standard 12-lead ECG from three differential leads formed by pairs of proximal electrodes on the body surface. The method is supported by a statistical analysis that gives the best personalized positions of electrodes. The measurements from multichannel ECGs were used to calculate the differential leads. Our algorithm searches for optimal differential leads and the corresponding personalized transformation matrix that is used to synthesize the standard 12-lead ECG. The algorithm has been evaluated on ninety-nine multichannel ECGs measured on thirty healthy subjects and thirty-five patients scheduled for elective cardiac surgery. It is shown that the algorithm significantly outperforms the synthesis based on the EASI lead system with medians of correlation coefficients greater than 0.954 for all twelve standard leads. To determine the optimal number of differential leads, the syntheses for two, three and four differential leads were calculated. The analysis shows that three is the optimal number of differential leads for practical applications. Because of the proximity of the differential electrodes, the proposed approach offers an opportunity for the synthesis of a standard 12-lead ECG with wireless electrodes.

Index Terms—Derived electrocardiograms, ECG synthesis, Electrocardiography, Differential leads, Wireless electrodes.

I. INTRODUCTION

ALTHOUGH imperfect, the 12-lead electrocardiogram (ECG) is the gold standard in cardiology, and lies at the center of the decision pathway for the evaluation and management of patients. The conventional 12-lead ECG is obtained from ten electrodes placed strategically on the patient's body. Recently, however, novel measurement technologies and systems have emerged that improve the acquisition of ECG recordings in terms of the number of recording sites and their positions. The obtrusion of the devices, with its effect on patient comfort, has also become an important issue for both home care and clinical practice, motivating the development of devices that involve the minimum number of electrodes and minimal length of wires. The main goal for all the devices is to acquire the maximal amount of information about the cardiac electrical activity

from as few recording sites as possible [1].

Possibly the most promising type of wearable ECG device is that using wireless electrodes (WEs) [2], [3] that enables the minimal use of wires on the body and consequently maximal wearing comfort. A WE enables the measurement and transmission of only local potential differences, i.e. bipolar measurements, from two closely placed skin electrodes. A number of WEs can constitute a body wireless sensor network (BWSN), eliminating the need for additional wires and therefore improving their applicability [2]. The measurements thus form a limited lead system that can potentially be used for reconstruction of the 12-lead ECG.

Existing limited lead systems [4] can be divided into two groups – lead systems that use a subset of the 12-lead ECG set of leads, and systems that use special leads. The most widely studied limited lead system is the EASI system [5], which is commercially available from Philips Medical Systems. In this system, four special electrodes and a single ground electrode are applied at predefined positions on the body surface. Another device that also exploits predefined positioning is the trans-telephonic system [6] that measures lead “I” from the standard 12-lead ECG plus two special bipolar leads. A further promising lead system is “eigenleads” [7], which is closely related to the development of smart textiles [8] and enables bipolar lead measurements acquired from distant recording sites on the body surface.

Even though there have been attempts to use neural networks for synthesis of the 12-lead ECG [9], the predominant strategy is to estimate a transformation matrix [10] that can be universal, i.e. applicable to every person, or personalized.

In order to obtain the best synthesis, positions and transformation matrices both have to be personalized, since every human body is unique. One of the advantages of WEs is that their positions can be completely arbitrary, which enables maximal personalization of the recording sites. Previous attempts to find the optimal positions of small bipolar devices, to give a reliable and strong ECG signal, involved analysis solely of signal to noise ratio (S/N) ratio [11], [12]. Although not attempting to synthesize a 12-lead ECG, those studies showed that S/N is acceptable for all bipolar leads measured at an inter-electrode distance of at least 5cm. This motivated our previous study [13] in which we presented a synthesis of the 12-lead ECG from three WEs whose positions were determined by respecting the S/N criterion.

In this paper, we present a new methodology by which the

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optimal personalized positions of an arbitrary number of WEs are determined in terms of the smallest root mean square (RMS) error and of the highest correlation coefficients (CCs) between the synthesized and target 12-lead ECGs. A method for synthesis of the standard 12-lead ECG from a limited number of optimally positioned WEs is also presented.

II. METHODS

Regression analysis is often used for the synthesis of the 12-lead ECG from both reduced [14] and special [6], [7] lead sets. In the current study we use it as part of a novel algorithm that suggests the optimal and personalized locations of WEs.

WE measurements can be emulated by differences between unipolar leads of a multichannel electrocardiograph (MECG) [15]. From these differences, i.e. differential leads (DL), the 12-lead ECG is synthesized and compared to the target 12-lead ECG. The proposed algorithm provides optimal DLs on whose positions the WEs have to be placed for the best synthesis. The algorithm is described in detail in the following sections.

A. Study Population

Thirty healthy volunteers with no previous medical record related to heart disease and with normal 12-lead ECG, one subject with an untreated conduction abnormality, and thirty-four patients scheduled for elective cardiac surgery were included in the present study. Informed consent was obtained from all the subjects before the study. Age, gender, and clinical data are shown in Table I. A single MECG measurement was obtained from each volunteer and two MECG measurements from each patient who underwent surgery: the first, one day before the surgery and the second, in the period from the fifth to seventh day after the surgery. No attempt was made to exclude any measurements, therefore a few measurements have arrhythmic events. The measurements were obtained during our previous studies [16], [17], [18] in various medical institutions. A complete list is included in the Acknowledgment.

TABLE I
DATA FOR THE SUBJECTS INCLUDED IN THE STUDY

Medical status	Num. of subjects	Age (mean \pm SD)	Gender (female:male)
NPMR	30	45.6 \pm 9.6	9:21
RBBB	1	56	0:1
B-VALR	6	63.0 \pm 10.7	3:3
A-VALR	6	63.0 \pm 10.7	3:3
B-CABG	15	60.3 \pm 9.7	6:9
A-CABG	15	60.3 \pm 9.7	6:9
B-CABG+VALR	5	67.0 \pm 7.3	2:3
A-CABG+VALR	5	67.0 \pm 7.3	2:3
B-PLV	7	52.2 \pm 6.4	2:5
A-PLV	7	52.2 \pm 6.4	2:5
B-LVA	1	50	1:0
A-LVA	1	50	1:0

Acronyms used: no previous medical record (NPMR), right bundle branch block (RBBB), coronary artery bypass grafting (CABG), valve repair or replacement (VALR), partial left ventriculectomy (PLV), left ventricle aneurysmectomy (LVA), standard deviation (SD). Measurements before and after surgery are denoted by B and A.

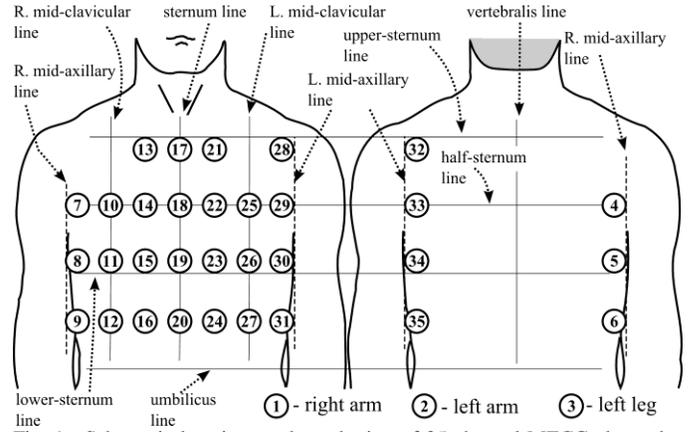


Fig. 1. Schematic locations and numbering of 35-channel MECG electrodes on the chest (left) and the back (right).

B. Data Acquisition and Preparation

We have developed a custom MECG device with 35 electrodes, all referenced to the Wilson central terminal potential (see [15] for details). The electrodes are not placed with regard to a reference spatial point; instead, their positions are adapted to the body size. Consequently, the distances between electrodes in DLs differ slightly for different subjects. The locations of electrodes are shown schematically in Fig. 1. All MECG measurements also incorporate all the electrodes for the simultaneous measurement of a standard 12-lead ECG.

The measured analog signals were sampled at 1000 Hz and digitized with 0.73 μ V resolution (14-bit analogue-digital converter). The length of each measurement was 360 seconds. The bandwidth of the recording system was 0.05 Hz - 250 Hz. All data were immediately examined for quality of the signals from each individual electrode. In the case of a defective measurement, the cause of disturbance was identified and the problem immediately solved. Data acquisition was then restarted, following the same protocol. The measurements with acceptable quality, and with removed baseline wandering, were used for further processing.

Baseline wandering was removed from all measurements with the efficient procedure described in [19]. Each signal was processed with a median filter of 200 ms window width to remove QRS complexes and P-waves. The resulting signal was then processed with a median filter of 600 ms window width to remove T-waves. The signal resulting from the second filter operation contained the baseline of the ECG signal, which was then subtracted from the original signal to produce the baseline corrected ECG signal.

From every MECG measurement and every related simultaneously measured standard 12-lead ECG, two ten second long non-overlapping segments were extracted. Positions of the segments were chosen randomly for every MECG measurement. The first segment was used as the input to our algorithm while the second was used for evaluation of the synthesized results. In general, the second segment differs from the first due to the beat-to-beat variability [17] within the recorded ECG. In that context the segment with extrasystole is of great significance, due to the fact that vectorcardiographic features of extrasystolic events have been shown to differ

drastically from vectorcardiographic features of normal beats [20], [21].

We denote each MECG measurement (complete or a segment) as a set of leads:

$$X = \{X(1), \dots, X(i), \dots, X(j), \dots, X(k)\}, \quad (1)$$

where $X(i)$, and $X(j)$ are the i th and j th leads, and k is the total number of leads, in our case 35.

We use MECG measurements as a data source for the emulation of bipolar measurements that can be measured by WEs.

C. Differential Leads

For the 35 leads of an MECG there are $\binom{35}{2} = 595$ possible differences between them. However, in BWSN applications, implementation of a small WE dictates the minimization of the distance between MECG electrodes. That requirement restricts the set of all possible differences to that formed by a selected electrode and its nearest neighbors on the body surface.

The differential lead (DL) is defined as

$$DL^{i,j} = X(i) - X(j), \quad i, j = 1, \dots, k, \quad (2)$$

where pairs of i and j are chosen such that only differences of neighboring MECG leads are taken into account. For example, referring to Fig. 1, electrode pair (18,22) determines differential lead $DL^{18,22}$, but electrode pair (18,25) does not determine any DL since electrodes 18 and 25 are not neighboring electrodes on the body surface.

This results in 91 DLs that are candidates for the synthesis. The fact that the minimal inter-electrode distance of MECG is 5 cm [16] ensures an acceptable S/N ratio [11], [12].

D. Synthesis of the Standard 12-lead ECG from Special Leads (theoretical background)

The problem of transformation from one leads system to another is closely related to forward and inverse problems in electrocardiography [22], [23]. The forward problem addresses the influence of the irregular torso shape and the non-homogenous torso conductivity on the surface potentials, while the inverse problem provides an assessment of different electrical models of the heart.

The most common method for synthesizing the 12-lead ECG is based on linear transformation. It relies on the assumption that the electrical system heart-torso is linear and quasi-stationary, and on the approximation that electrical activity of the heart can be represented as a single fixed-location dipole. The widely accepted [6] assumption of a linear and quasi-stationary heart-torso system justifies the utilization of a linear transformation for the purposes of synthesis.

The single fixed-location dipole model assumes a fixed location for a dipole vector (also called ‘‘heart vector’’) \vec{H} within the heart region. The equation relating the dipole to the estimated potential $L(i)$ of a given surface lead i is

$$L(i) = \overline{L(i)} \cdot \vec{H}, \quad (3)$$

where $\overline{L(i)}$ is the lead vector. If the lead vectors of three independent leads are known *a priori* and their three measured potentials are denoted as $L(i)$, $i=1,2,3$, then, in the absence of noise, three resultant equations (3) can be solved uniquely for the Cartesian components of \vec{H} . In other words, only three independent leads suffice for an accurate representation of a fixed-location dipole. The leads used in our work are differential leads.

The vectorcardiographic features of the extrasystole imply that amplitude and orientation of the heart vector \vec{H} during an extrasystolic event change very differently from the changes during normal beats. Furthermore, investigation by magnetocardiography [24] shows that a single dipole approximation is adequate only for the early excitation phase of the extrasystolic event, while it becomes inadequate when the excitation reaches the epicardium. Any synthesis algorithm that did not see the extrasystole during calculation of the transformation operator is therefore very strongly evaluated on a measurement segment containing the extrasystole.

For the Frank orthogonal leads system [25], known also as vectorcardiography (VCG), it has been proved that it contains the essential information for ECG interpretation [26]. In contrast to the VCG and its successors, like the EASI system which exploits deterministic leads’ positions, our algorithm determines personalized optimal DLs and therefore compensates maximally for eventual violations of the assumptions of the forward and inverse problems.

E. Multiple Linear Regression (MLR) Synthesis

One combination, C , of m DLs calculated from the first MECG segment is denoted as

$$C = \{DL(1), \dots, DL(m)\}. \quad (3)$$

The measured standard 12-lead ECG constitutes a target ECG for the reconstruction:

$$ECG12 = \{I, II, III, aVR, aVL, aVF, V1, V2, V3, V4, V5, V6\}. \quad (4)$$

Given n samples $(C_1, ECG12_1), \dots, (C_n, ECG12_n)$, a model between $ECG12$ and C can be represented in the form:

$$ECG12 = M \cdot \alpha + \epsilon, \quad (5)$$

where $ECG12$ is the matrix of samples $ECG12_i$ ($i=1, \dots, n$), M is the design matrix of the system, α is a matrix whose columns are vectors of coefficients, and ϵ is a matrix whose columns are vectors of errors. We have explored the straight line model for which the matrix M is

$$M = \begin{bmatrix} 1 & DL(1)_1 & \dots & DL(m)_1 \\ \vdots & \vdots & & \vdots \\ 1 & DL(1)_n & \dots & DL(m)_n \end{bmatrix}. \quad (6)$$

M contains a column of “1”s so that the model contains a constant term.

α is estimated by the least squares method [27] for every column of ECG_{12} , which results in the minimum variance unbiased estimate α . The best synthesized 12-lead ECG (in the least squares sense) that can be obtained from C is:

$$\overline{ECG_{12}} = M \cdot \alpha, \quad (7)$$

where α is the estimate of α obtained with the least squares method. For the purpose of algorithm verification, coefficients from α will be used to multiply matrix M filled with data from the second MEGG segment to produce a synthesized 12-lead ECG that is compared to the second segment of the corresponding target 12-lead ECG. α can be used in all subsequent syntheses of 12-lead ECGs applied on acquired measurements from WEs placed at the same positions as DLs used for the algorithm. To obtain the best possible synthesis, the optimal combination of DLs can be determined for each individual.

F. Differential Leads Selection

In order to find the best combination of DLs, we have developed a “brute force” algorithm that applies MLR for every combination of DLs. The correlation coefficient (CC) [28] is often used with the linear regression. For every combination of DLs, MLR results in 12 CCs between the leads of the target and the synthesized ECG.

The most significant CC among the 12 values is the minimum one (CC_{min}), since it represents the worst synthesized lead. We considered that the best combination of differential leads is the one that provides the largest value of CC_{min} . The algorithm for the selection of m DLs is illustrated in Fig. 2.

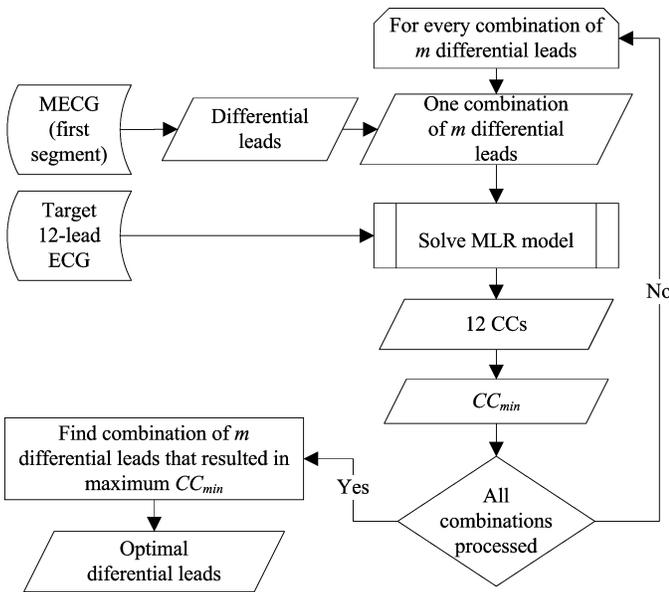


Fig. 2. Best differential leads selection algorithm.

G. Conducted Experiments

For every measurement in Table I we have applied the differential leads selection algorithm for two, three and four DLs. Transformation coefficients α for the selected optimal DLs were used to synthesize a 12-lead ECG from the second (evaluation) segments of corresponding MEGGs. RMS error and CCs were calculated between the target and the synthesized 12-lead ECGs. Our ECGs, synthesized from DLs, were compared with those synthesized from the EASI lead system. EASI transformation coefficients were taken from the literature [29].

The statistical significance of differences in performance between DLs and the EASI lead system was evaluated using the Wilcoxon signed rank test (with significance level 5%).

III. RESULTS

The results of 12-lead ECG synthesis from two, three and four DLs, together with synthesis from the EASI lead system, are illustrated in Fig. 3. On each box, the central mark is the median; the edges of the box are the 25th and 75th percentiles.

It follows from Fig. 3 that both three and four DLs completely outperform EASI synthesis by a significant margin for all leads except the V6 precordial lead, for which the difference in RMS error is not significant for three DLs. The difference in CC between three DLs and EASI is significant for the lead V6. The latter is due to the fact that EASI synthesis is extremely good for this lead (CC median = 0.993) but, nevertheless, the synthesis from three and four DLs is very close (CC medians: 0.979 and 0.985 respectively).

Syntheses from three and four DLs exhibit a consistent level of reconstruction accuracy across all reconstruction leads, on the basis of both RMS error and CCs. This makes them good candidates for an application. RMS error medians are all less than 40.24 μV and CC medians are all larger than 0.954 for both three and four DLs.

To evaluate the gain in synthesis introduced by a fourth DL we calculated the consequent reduction in RMS error and the increase of CC for every MEGG measurement in the studied data set. The ranges between standard deviations (SDs) of calculated values are presented in Table II for each lead.

A fourth DL potentially improves synthesis, but by only a small amount (Table II). Nevertheless, the lower SD limits are negative for all leads, revealing that a small decrease in synthesis performance for some leads is also possible. It can be concluded that, in practice, the optimal number of WEs is three, since the additional obstruction caused by a fourth WE on a person wearing the device cannot be justified by the negligible improvement in the synthesis.

The quality of the synthesized 12-lead ECG of two MEGG datasets is illustrated with two test cases shown in Figs. 4. and 5. For each lead, the target lead is shown below and the synthesized lead above. In both cases synthesis has been performed on the second MEGG’s segment that was not seen by the MLR algorithm.

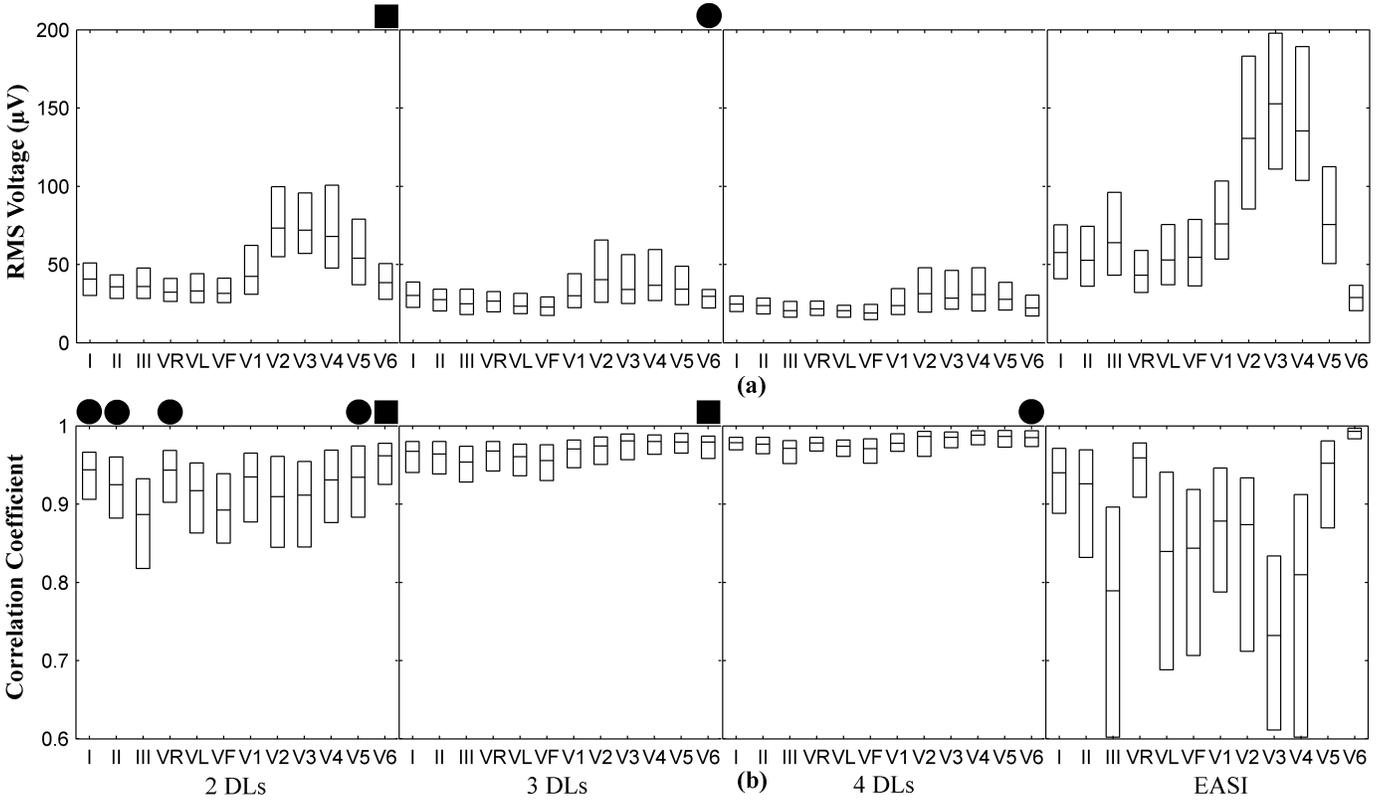


Fig. 3. Performance of two, three and four DL syntheses compared to EASI leads synthesis as (a) RMS voltage error, (b) correlation coefficient. A square indicates that a particular lead was more accurately reconstructed with the EASI system by a significant margin. A filled circle indicates that a difference was not significant. Leads that are not marked are more accurately reconstructed with DLs by a significant margin. Significance level used is 5%.

The first case in Fig. 4. shows an ECG measured on a healthy person with a normal sinus rhythm. The best set of DLs used for the synthesis comprises electrode pairs $\{(21,22), (22,26), (26,27)\}$. For the position of each electrode refer to Fig. 1.

To illustrate the importance of finding the optimal DLs, a histogram is shown in Fig. 5, with the distribution of combinations of three DLs that result in a particular CC_{min} (minimum from all twelve synthesized leads). The histogram is generated for the measurement shown in Fig. 4. It has forty bins distributed between minimal and maximal CC_{min} that arise from all combinations of DLs. Every bin is 0.0242 wide. The rightmost bin, for the highest CC s, has a center at

0.9589 and contains 16 DLs combinations. It can be seen that there are a lot of “bad combinations” of DL and very few “good ones”, which provides support for the personalized approach.

The second case in Fig. 6. shows an ECG measured five days after CABG surgery. It contains a single extrasystole that was not present in the MEKG’s segment used by the MLR algorithm. This case enables additional evaluation of the synthesized 12-lead ECG by means of the extrasystole reconstruction ability. For this case the leads selection algorithm resulted in the set of DLs: $\{(14,11), (14,19), (22,25)\}$.

TABLE II
ADDITIONAL DL SYNTHESIS GAIN

Leads	RMS error (μ V)		Correlation coefficient	
	mean-SD	mean+SD	mean-SD	mean+SD
I	-7	7	-0.008	0.032
II	-5.7	5.7	-0.005	0.025
III	-5.9	5.9	-0.005	0.032
aVR	-5.6	5.5	-0.006	0.028
aVF	-5.7	5.7	-0.007	0.031
aVL	-4.4	4.3	-0.004	0.029
V1	-14.1	14.1	-0.01	0.026
V2	-26.5	26.5	-0.019	0.035
V3	-20.4	20.4	-0.018	0.038
V4	-17.8	17.8	-0.016	0.038
V5	-14.3	14.3	-0.011	0.031
V6	-14	13.9	-0.01	0.024

Columns are lower and upper limits of RMS error and CC standard deviation (SD) ranges respectively.

IV. CONCLUSION

We have shown that a small number of bipolar measurements from pairs of proximal electrodes can reliably reproduce a standard 12-lead ECG and are therefore suitable for real wireless applications. An algorithm is proposed that finds the best combination of DLs and also evaluates all other combinations in terms of CCs. This enables other combinations of DLs to be selected if, for some anatomic or ergonomic reasons, the best combination is inconvenient for WE placement.

We have used the EASI lead system for comparative evaluation of our algorithm and showed that it is outperformed by differential leads. While the EASI lead system exploits fixed and easy to locate anatomic landmarks, WE can be

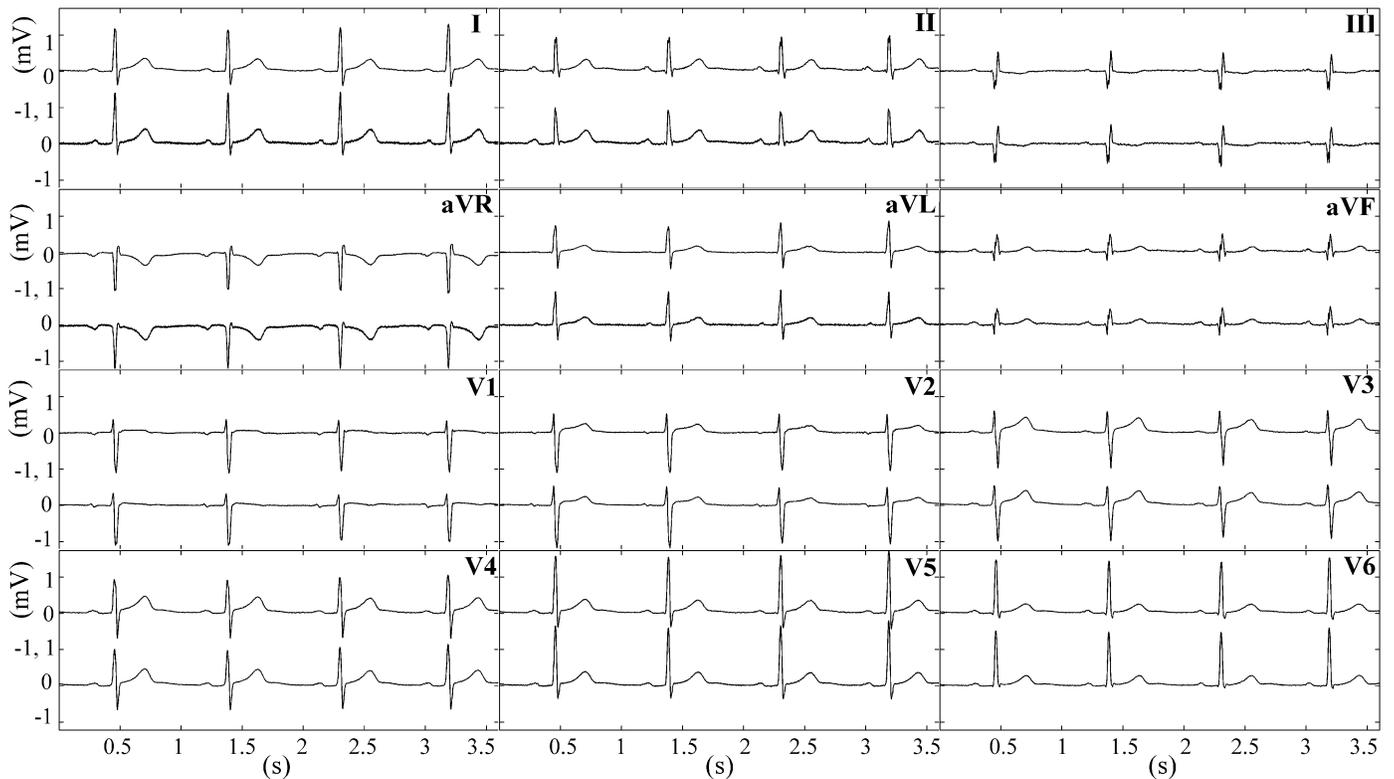


Fig. 4. Target (below) and synthesized (above) 12-lead ECG. Measurement is performed on a healthy person. Minimal CC is 0.971 for lead III and maximal RMS error is $41.9 \mu\text{V}$ for lead I.

placed at arbitrary positions on a body surface, improving patient mobility and comfort.

We have demonstrated that just three WEs suffice for the reliable synthesis of the 12-lead ECG. This result confirms the assumption that a single fixed-location dipole provides an adequate representation of a heart's electrical activity.

The proposed approach is personalized, in the sense that optimal positions of WEs and transformation matrices are calculated for each individual. An alternative approach that remains to be investigated would be to determine fixed

positions of WEs and a universal transformation matrix.

In developing this approach we have assumed that WEs are placed at positions defined by DLs. Although this assumption is easy to accomplish by some kind of skin marking [30], the effect of wireless electrodes misplacement on the synthesis quality and reconstruction sensitivity will be addressed in future work, as well as the impact of artifacts and high frequency noise.

The proposed algorithm always gives the best synthesis in terms of the smallest RMS factor across the entire cardiac cycle. For some specific tasks, like arrhythmia monitoring, it is likely that some individual segment of the cardiac cycle will require particular analysis. For example, the detection of atrioventricular block may rely on PR interval analysis, while the detection of abnormalities associated with ventricular recovery will require scrutiny of the ST interval. Starting with a preposition of abnormality, selective criteria for the synthesis of a specific ECG segment can be introduced [31]. Additionally, personalized positions of WEs that are optimal for the synthesis of a specific ECG segment can be found with the methodology proposed in this paper. We plan to investigate, with further experiments performed with prototype WEs, the clinical diagnostic ability of the synthesized 12-lead ECG.

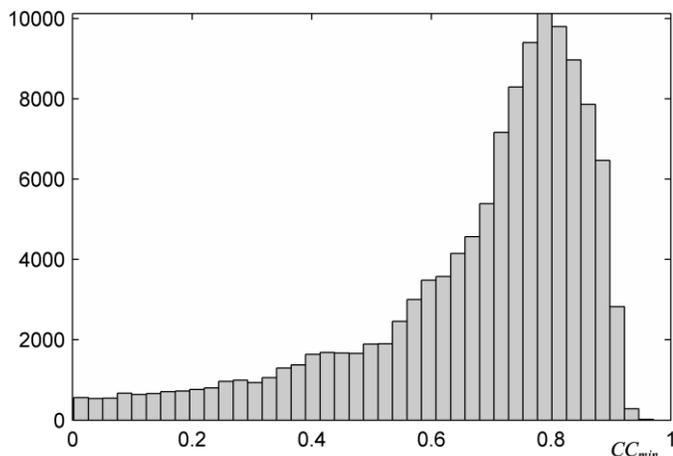


Fig. 5. Histogram of CC_{min} for the case from Fig. 4. Y axis shows the number of DLs' triplets that result in a particular CC_{min} interval.

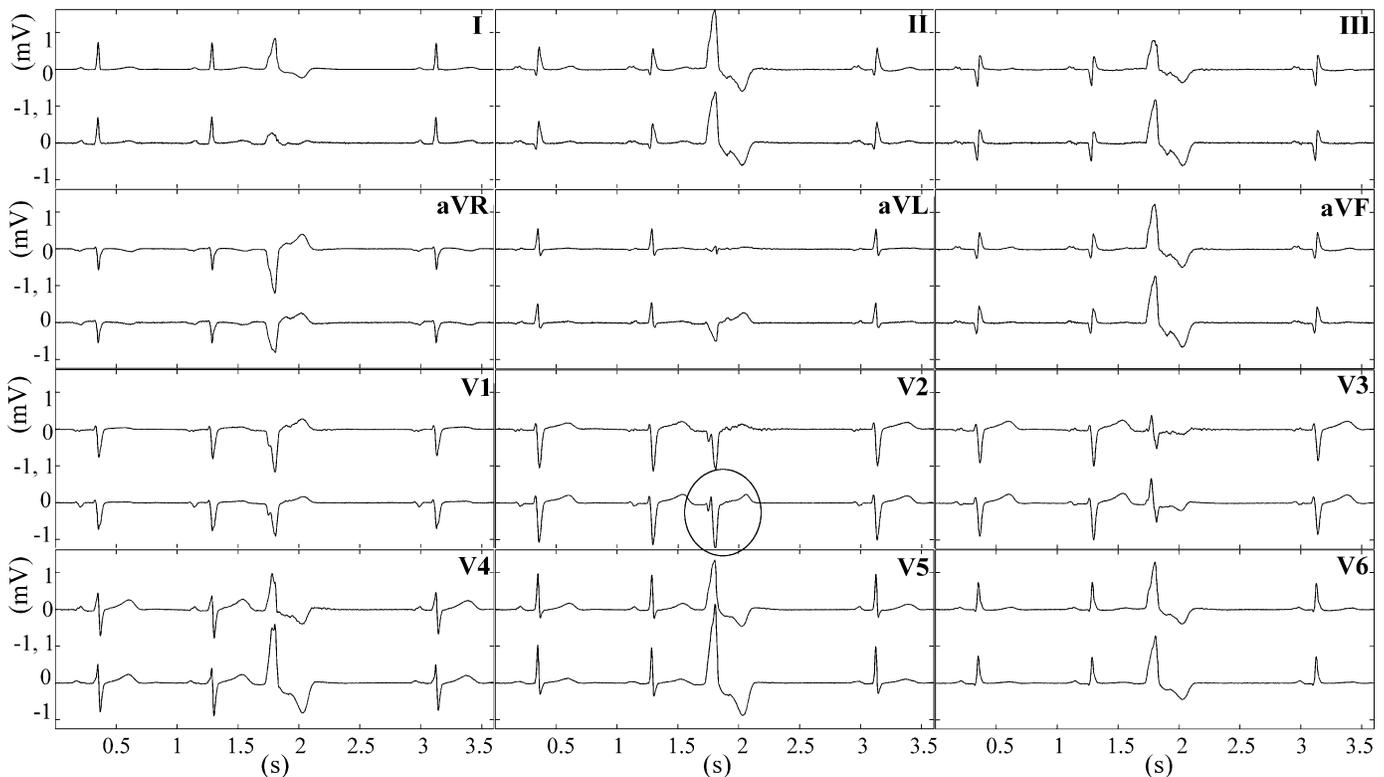


Fig. 6. Target (below) and synthesized (above) 12-lead ECG. Measurement is taken five days after CABG surgery and contains a single extrasystole denoted by a circle on the target lead V2. Minimal CC is 0.71 for lead aVL and maximal RMS error is 115.3 μ V for lead V5.

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