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Electrocardiographic Systems with Reduced Numbers of Leads - Synthesis of the 12-lead ECG

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***Abstract*—Systems with reduced numbers of leads that can synthesize the 12-lead ECG with an insignificant or a small loss of diagnostic information have been proposed. The advantage over standard 12-lead ECG systems is the smaller number of measurement sites (i.e., electrodes) and, consequently, fewer wires. In this article we review all the important systems with reduced numbers of leads together with the methodology for synthesizing the leads. The fundamental theoretical background necessary to understand the most important concepts related to the synthesis is included. The presented theoretical and experimental justifications for the synthesis show that it is not necessary to measure a large number of leads directly, because the standard 12-lead ECG and arbitrary additional leads can be synthesized. Various approaches to evaluating the synthesized 12-lead ECG are defined and explained, and a number of systems that synthesize 12-lead ECG are presented as they were introduced in the literature. We cover the developments and improvements from the 1940s to the present day. The systems are classified on the basis of the synthesis method used, the approach to the evaluation of the synthesized ECG (depending on the measurement sites used), and on the number and types of leads employed. Based on a detailed assessment of state-of-the-art systems, open problems and challenges are highlighted, while further developments of electrocardiographic systems are envisaged.**

***Index Terms*—Electrocardiography, ECG synthesis, Derived 12-lead ECG systems, Reduced lead sets.**

I. INTRODUCTION

ACQUIRING a conventional 12-lead electrocardiogram (ECG) requires nine electrodes to be placed strategically on the human body and one electrode to be connected to ground [1]. However, it is a common characteristic of many ECG devices that they measure fewer than 8 leads, the number of independent leads in a standard 12-lead ECG system. We will refer to these devices as "electrocardiographic systems with reduced numbers of leads". The leads of such a device do not have to be a subset of the standard 12-lead ECG. Furthermore, there are systems that employ more than 8 leads, with some of them having more than 100 leads. Electrocardiograms produced by systems that employ more than 24 leads are referred to as multichannel ECGs (MECGs) [2] or body-surface maps (BSPMs) [3]. In between are the standard 12-lead systems extended with additional, precordial and posterior leads.

The systems with reduced numbers of leads that synthesize a 12-lead ECG are often called "derived 12-lead ECG systems" [4]. These systems can be divided into two classes: systems that employ subsets of the leads from a 12-lead ECG, referred to as "reduced-lead sets" [4], and systems that use special leads.

The development of systems with reduced numbers of leads started in the 1940s, but the first important derived 12-lead ECG system came in 1968 [5] with the introduction of a derived 12-lead ECG synthesized from the orthogonal lead system previously introduced by Frank [6]. Since 1968, many derived 12-lead ECG systems have been investigated. Only recently, however, have novel measurement technologies and systems emerged that significantly improve the acquisition of ECG recordings and the quality of the synthesized 12-lead ECG. The electrode positions are selected in such a way that they acquire the maximum amount of "information" about the heart's electrical activity. The development of new measuring systems is also motivated by the need for more wearing comfort, which is achieved by reducing the number of electrodes as well as the number and the length of the wires. The main aim of all new devices is to acquire the maximum amount of information about the heart's electrical activity while using the minimum number of electrodes [7].

As a result of improved reliability and wearing comfort, the new systems are not only applicable in hospital-based clinical practice; they also enable long-term monitoring of the heart during everyday activities, which is extremely important for applications like arrhythmia monitoring.

As most electrocardiographic diagnostic knowledge has been accumulated and described mainly on the basis of the 12-lead ECG, it is useful for any system with a reduced number of leads to be able to synthesize a 12-lead ECG. Even though there have been attempts to use neural networks for the purpose of this synthesis [8], the most common strategy is to construct a linear transformation [9] (most often described as a

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matrix) that can be universal, i.e., applicable to any person, or personalized.

This paper provides the theoretical background and summarizes the present state of knowledge in the field of derived ECG systems in order to provide a basis for future research. The derived 12-lead ECG systems are presented chronologically in terms of publication date. Special attention is given to the characteristics that are relevant for classifying the systems according to the leads employed, the methods of synthesis and the methods for evaluating the syntheses.

II. Electrocardiographic Systems

A. *Elements of Lead Theory*

Lead theory describes the relationship between the electrical sources in the heart and the potential differences on the surface of the body. Einthoven's classical lead theory [10], [11] is based on the assumption that the human body is part of an infinite, homogeneous conductor in which the heart's electrical sources are represented by a single, time-varying current dipole [12] fixed at the center of an equilateral triangle in the frontal plane, with apices corresponding to the functional positions on the limbs' measurements sites. Note that the terms "heart dipole" and "heart vector" are used as synonyms.

Burger and van Milaan developed a more precise lead theory, referred to as the volume-conductor theory [13], [14], which included an assumption that the human body is a three-dimensional, bounded, irregularly shaped and inhomogeneous volume conductor, that nevertheless still relied on a fixed dipole hypothesis under which the potentials anywhere on the surface of the body can be derived by projecting a heart vector in three-dimensional space. Burger also introduced an equation that, assuming the body to be a linear physical system, expresses the voltage on a given lead as a scalar product (i.e., a projection) of the heart dipole and the "lead vector", which is a vector in three-dimensional space that describes a certain lead. The introduction of the lead vector meant a lead could be interpreted as a monitored spatial direction of cardiac electrical activity [15].

1) *Lead Vector*

Burger's equation can be derived as follows. Let us presuppose there to be a three-dimensional coordinate system $(\vec{\imath},\vec{\jmath},\vec{k})$ with a zero reference potential at the origin. Let c_x be the potential at an arbitrary point Q caused by the unit dipole $\vec{\imath}$.

A dipole is a pair of a current source and a current sink of equal current strengths I_0 that is separated by a small displacement d. The strict definition requires $d \rightarrow 0$, $I_0 \rightarrow \infty$ with $p = I_0 d$ remaining finite. The quantity p is the moment or magnitude of the dipole. The dipole is a vector $\vec{p}$ with magnitude p and direction from the negative to the positive point source [12].

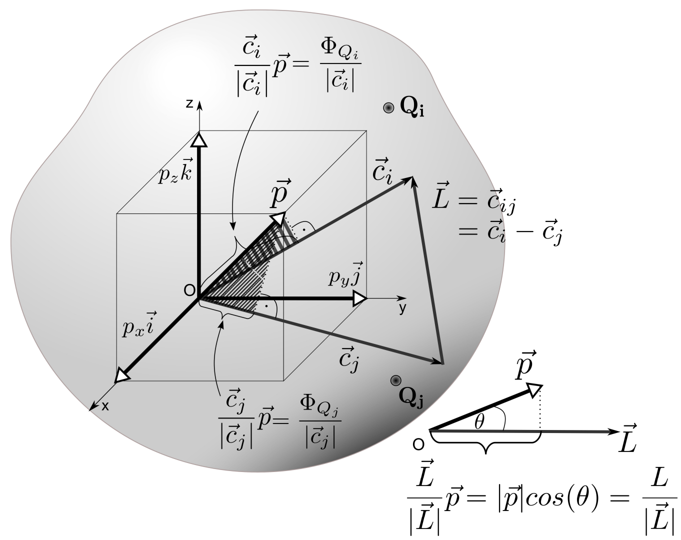

Fig. 1. Heart vector projections on axes and leads. $\vec{c_i}$ and $\vec{c_j}$ are the unipolar lead vectors for points Q_i and Q_j respectively, while $\vec{L}$ is the bipolar lead vector. The projection of the heart vector on a lead vector, multiplied by the lead vector's length, is the lead's voltage. The medium is generally inhomogeneous.

Because of the linearity assumption the potential $\Phi_Q^{p_x\vec{\imath}}$ corresponding to the dipole $p_x\vec{\imath}$ of an arbitrary magnitude p_x is

$$\Phi_Q^{p_x\vec{\imath}} = c_x p_x \,. \tag{1}$$

A similar expression holds for dipoles in the $\vec{\jmath}$ and $\vec{k}$ directions. The linearity assumption ensures the maintenance of the principle of superposition, which states that an electrical field arising from several sources is the sum of the fields that would be present for each source acting separately. The dipole $\vec{p}$ in three orthogonal components is expressed by $\vec{p} = p_x\vec{\imath} + p_y\vec{\jmath} + p_z\vec{k}$. Using the principle of superposition the potential at the point Q caused by the dipole $\vec{p}$ at the origin of the coordinate system is

$$\Phi_Q = c_x p_x + c_y p_y + c_z p_z \tag{2}$$

If the components c_x, c_y, c_z are interpreted as the components of the vector $\vec{c}$, equation (2) can be written as

$$\Phi_Q = \vec{c} \cdot \vec{p}. \tag{3}$$

The vector $\vec{c}$ is called the lead vector of a unipolar lead and $\vec{p}$ is the heart vector. In this case the lead is determined by the potential at the point Q and the zero potential at the origin of the coordinate system, but the zero reference potential may be any local or remote reference point.

Equation (2) can be used to find a lead vector for an arbitrary point Q by using a mathematical or physical torso model. The lead vector is found by energizing the unit dipoles in the model's heart region along the x, y, and z axes in sequence, and measuring the potential at point Q for each dipole. E.g. if the unit dipole is oriented in the x direction $p_y = p_z = 0$, it follows from (2) that $c_x = \Phi_Q$.

A bipolar lead whose electrodes are at points Q_i and Q_j measures the potential difference L between the two points:

$$L = \Phi_{Q_i} - \Phi_{Q_j}. \tag{4}$$

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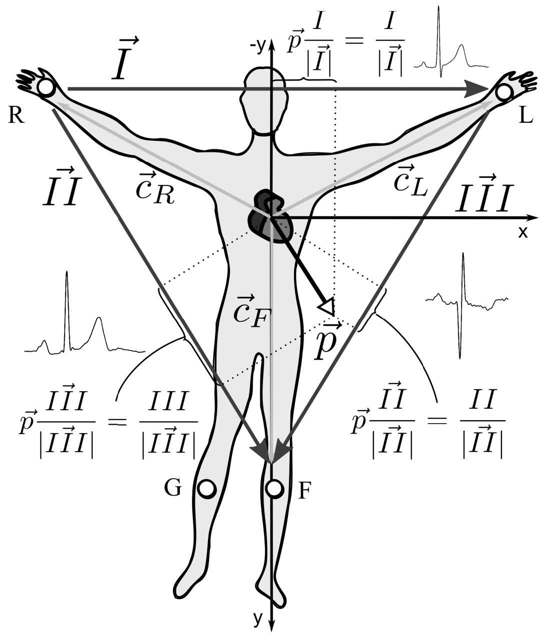

Fig. 2. Einthoven's triangle. All the lead vectors lie in the frontal plane defined by the x-y coordinate system vectors. The projections of the heart vector $\vec{p}$ on the sides of the triangle are equal to the scalar product of the heart vector to the normalized lead vectors (Burger equation).

Using equation (3), equation (4) becomes the Burger equation:

$$L = \vec{c_i} \cdot \vec{p} - \vec{c_j} \cdot \vec{p} = \vec{c_{ij}} \cdot \vec{p} = \vec{L} \cdot \vec{p} = |\vec{L}| \cdot |\vec{p}| \cdot cos(\theta), \quad (5)$$

where $\vec{c_i}$ and $\vec{c_j}$ are unipolar lead vectors for the points Q_i and Q_j, $\vec{L} = \vec{c_{ij}} = \vec{c_i} - \vec{c_j}$ is the bipolar lead vector, and θ is the angle between $\vec{L}$ and $\vec{p}$. The derivation of the Burger equation is illustrated in Fig. 1. It follows from (5) that for a normalized lead vector, i.e., for $|\vec{L}| = 1$, the lead voltage L is the projection of the heart vector $\vec{p}$ to the lead vector: $|\vec{p}| \cdot cos(\theta)$. The same follows for a unipolar lead vector from equation (3). Therefore, a lead vector can be interpreted as a monitored spatial direction of cardiac electrical activity.

The lead vector depends on the location of the dipole, on the locations of the lead electrodes, and on the electrical characteristics and the shape of the volume conductor, but not on the magnitude or the direction of the dipole [16]. Under Einthoven's assumptions, an unipolar lead vector is oriented in the direction of the radius (i.e., the position) vector of its measurement point, as is the case for the vectors $\vec{c_R}$, $\vec{c_L}$ and $\vec{c_F}$ in Fig. 2. The unipolar lead vectors $\vec{c_i}$ and $\vec{c_j}$ presented in Fig. 1 depart from the radius vectors for the points Q_i and Q_j as a consequence of the inhomogeneous medium assumed for the figure.

The concept of the Einthoven triangle, an example of a lead vector application, is presented in Fig. 2. (Note that the coordinate system introduced in Fig. 2, with x axis in the direction from the right to the left of the torso, the y axis from the head to the feet, and with an additional z axis oriented from front to back, is customary in electrocardiography.) As an example, we can select the two points determining a bipolar lead to be on the left and right arms.

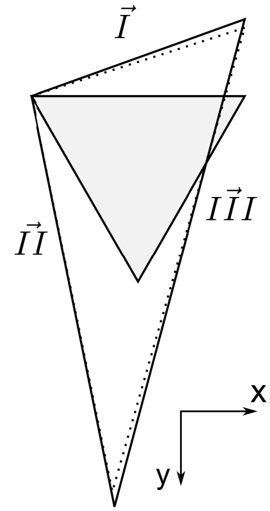

Fig. 3. Einthoven (shaded), Frank (line) and Burger (dashed line) triangles' relative proportions. The Einthoven triangle lies in the frontal plane, while the Burger and Frank triangles are tilted out of the frontal plane. Only their projections to the frontal plane are presented. (Note that since the measuring procedures for the Burger and Frank triangles were not calibrated, the vectors representing the triangles have been normalized by the x component to enable a comparison between the triangles.)

Equation (5) becomes $I = \vec{c_L} \cdot \vec{p} - \vec{c_R} \cdot \vec{p} = (\vec{c_L} - \vec{c_R}) \cdot \vec{p} = \vec{I} \cdot \vec{p}$. The lead vectors' $\vec{I}$, $\vec{II}$, $\vec{III}$ orientations, illustrated in Fig. 2, are a consequence of Einthoven's assumptions. The projections of the heart vector on the directions of Einthoven's lead vectors, multiplied by the corresponding lead vectors' lengths, are the lead voltages I, II, III. Einthoven did not consider the effect of the volume conductor on the lead vectors. The effect of the surface of the body on the leads for the limbs was reported by Ernest Frank [17], and the effect of the inhomogeneities of the volume conductor, by Burger and van Milaan [14]. The corresponding lead vector triangles are called the Frank triangle and the Burger triangle. To estimate the lead vectors of the limb leads, Frank and Burger both constructed a physical model of the volume conductor. Because of its simplicity, Einthoven's electrocardiographic model can be described mathematically, and therefore it requires no physical model. The similarity between the Burger and Frank triangles is remarkable (Fig. 3) if we consider that Burger's model was heterogeneous while Frank's was homogeneous.

It will be shown in Section III.B that Burger's equation allows the heart's electrical activity to be described by measuring the potentials on leads with known lead vectors. It is therefore desirable to determine the unipolar lead vectors for any point on a body's surface.

2) *Image Surface*

The concept of determining lead vectors using equation (2) can be applied at an arbitrary number of points on a model's surface. The tips of the acquired unipolar lead vectors determine the surface, which is known as the image surface, or image space. Since it consists of lead vectors, an image surface can be interpreted as an alternative, imaginary torso, in which lines connecting two points represent the true monitored spatial directions of the cardiac electrical activity.

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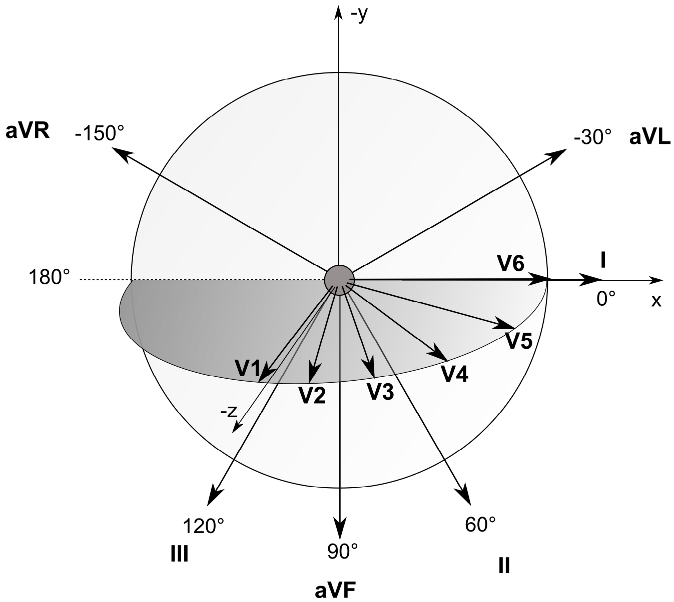

Fig. 4. Schematic presentation of the lead vectors of the 12-lead ECG system in the frontal (limb leads) and transverse (precordial leads) planes, when one assumes the volume conductor to be spherical and homogeneous with the cardiac source located in the center.

The departure of the image points from the points on the physical torso surface, can be regarded as a measure of the electrical distortion of the dipole behavior as seen on the torso surface [18].

The concept of image surface was introduced by Burger and van Milaan [15], but its first experimental determination was performed by Frank [17]. Although the image surface is dependent on the location of the dipole, Frank’s image surface, published in [17], is the main one used in the subsequent syntheses of leads. For that particular image surface a dipole was fixed in the center of the model’s region, which Frank assumed to be “occupied in life by the ventricular mass during very deep inspiration”. The frontal-view-triangle part of the Frank image surface (Fig. 3) can be seen to depart drastically from the equilateral Einthoven triangle. Since the apices of the Einthoven triangle represent the measurement points of the limb leads it is apparent that the directions of the Frank image surface lead vectors deviate from the spatial vectors connecting the measurement points. For a complete Frank image surface the reader is referred to [17] or [19].

Frank also concluded that the influence of the location of the dipole inside the model on the surface potentials, i.e. the lead vectors, is very pronounced, while the influences of the shape of the torso and the inhomogeneities introduced into the model are less important factors [20].

More recent image-surface studies were made on computer models and may include different inhomogeneities, such as the lungs, muscle layers etc. Computer models also make it easier to investigate the influence of the location of the dipole on the image surface [9].

B. Information Content of the 12-lead ECG

Previous studies showed that almost all cardiac electrical activity can be explained using the fixed-location dipole model [20], [21] (see Section III for details about testing the dipole source model). We will show in the next section that to evaluate the dipole it is sufficient to measure three independent leads. This implies that, if the cardiac source can be described as a dipole, a 12-lead ECG can be thought of as having only three independent leads. However, the non-dipolar content exists and the precordial leads (Fig. 4) detect more of it, because they are located closer to the heart. Therefore, the 12-lead ECG system has eight truly independent and four redundant leads. The basic idea behind all derived 12-lead ECG systems is thus to synthesize the 12-lead ECG from fewer than eight independent leads.

One of the techniques for testing the dipole hypothesis, the Becking-Burger technique [22], is based on measuring the non-dipolar components of the cardiac electrical activation by evaluating the quality of a lead, preferably close to the heart, synthesized from three independent leads, preferably some distance from the heart.

III. Synthesis of the 12-lead ECG – Theoretical Background

A. Heart Dipole

It has been shown that there are an infinite number of internal electrical heart sources (or their equivalent sources that by definition produce the same potential distribution as the actual heart sources) that can induce any given three-dimensional potential distribution [20], [23]. Therefore, to solve the inverse problem, an equivalent source has to be presupposed. One should keep in mind that the equivalent source is just a model, i.e., it does not exist physically There are different models of the volume source (i.e., the entire heart), e.g., dipole and quadrupole. A task of the inverse problem is to assess the models, i.e., to answer the question about how well the models represent the heart’s electrical sources.

For the purpose of describing the notion of the heart vector we start with Miller and Geselowitz’s source model [24], which is based directly on the generators associated with the activation of each cell. They considered a three-dimensional distribution of interconnected cells representing the myocardium. If gradients of the intracellular potentials exist, then it is assumed that a current flows in the intracellular network from regions of higher intracellular potential to those of lower intracellular potential, as given by:

$$\vec{J}^i = -\sigma_i \nabla \Phi_i, \qquad (6)$$

where $\vec{J}^i$ is the intracellular current density, σ_i the effective conductivity of the intracellular network, and Φ_i is the intracellular potential. Miller and Geselowitz also showed that $\vec{J}^i$ is the current density in the extracellular medium. Therefore, the current density in the myocardium is proportional to the spatial gradient of the intracellular potential distribution.

It was shown in [25] that for a homogeneous conductor the equivalent heart dipole is simply the integral of the vector function $\vec{J}^i$ over the heart volume:

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$$\vec{p} = \int_{V_H} \vec{J}^i dV. \tag{7}$$

$\vec{J}^i$ can be interpreted as the dipole moment per unit volume (or the dipole density) [26], which justifies the interpretation of $\vec{J}^i dV$ as a single dipole. Therefore, the heart vector $\vec{p}$ is obtained as the sum of all the elementary dipole contributions throughout the entire volume of the heart V_H.

Any complex source with a zero net current can be approximated by a dipole. The approximation improves as the observation distance becomes greater than the largest dimension of the source [21]. The condition of net current (i.e., the algebraic sum of currents) being equal to zero is satisfied by the heart, since no net charge is generated at any instant. As the observation distance increases, the dislocation of $\vec{p}$ from the heart centroid becomes negligible. Therefore, the vector $\vec{p}$ is usually placed at the center of the heart region, although its position is time dependent.

B. *Synthesis from Three Leads*

The most common method for synthesizing a 12-lead ECG is based on a linear transformation. It relies on the assumption that the heart-torso electrical system is linear and quasistatic.

Here, the term "quasistatic" implies that the electric field throughout the body is, at every instant, in equilibrium with the sources in the heart. Schwan and Kay [27] showed experimentally that the ratio of the capacitive to the resistive current components in body tissues is smaller than 0.1 for frequencies less than 1 kHz. Hence, it is justifiable to consider body tissues simply as resistive media, since the tissue capacitance is negligible. As the electromagnetic propagation effect can also be neglected [28], the heart-torso system can be expressed as quasistatic [29].

A consequence of such quasistatic conditions is that for a given distribution of sources at a given point in time, a corresponding extra-cardiac field can be determined without any regard to the source distribution at previous instants. Therefore, the ECG values recorded at a specific time instant in a synthesized 12-lead ECG are only a function of the values of the measured leads at the same time instant.

The linearity assumption justifies the utilization of a linear transformation for the purposes of the synthesis, i.e., for transforming from one lead system to another (see Appendix).

The single fixed-location dipole model assumes a dipole $\vec{p}$ at a fixed location within the heart region. The equation

$$L(i) = \overrightarrow{L(\iota)} \cdot \vec{p}, \tag{8}$$

that relates the dipole to the estimated potential $L(i)$ of a given i-th surface lead is the Burger equation, where $\overrightarrow{L(\iota)}$ is the lead vector of the i-th lead. 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, the three resultant equations (8) can be solved uniquely for the Cartesian components of $\vec{p}$. In other words, only three independent leads suffice for an accurate representation of a fixed-location dipole. This means that, given the assumption of the fixed-dipole being an applicable volume source model, any three linearly independent leads will suffice for an adequate synthesis of the 12-lead ECG or any other lead system. Although any three independent leads are acceptable, it can be shown [30] that three orthogonal leads are the desired form for a detector that measures the equivalent dipole.

Since there is no unique solution to the inverse problem, it is evident that not even a 12-lead ECG includes all the information about cardiac electrical sources. Therefore, it is not necessary to completely reassemble the heart's electrical sources for the reliable synthesis of a 12-lead ECG.

The lead vectors can be obtained from an image source. What prevents us from applying a universal image surface is the location of the dipole relative to the body surface, which has been shown to differ considerably between individuals [20]. If the dipole location is determined for a specific subject, a personal image surface may be obtained by placing a dipole at a personalized position in the model. However, such a method requires special equipment and would be too time consuming [20].

C. *Correctness of the Dipole Volume Source Model*

It was shown that the diagnostic performances of vectorcardiography (VCG) and the standard 12-lead ECG are practically the same [31]. Since VCG is both a measurement and a display of the heart dipole, this result is an important asset for the dipole hypothesis and for employing a reduced number of leads for the synthesis.

The Becking-Burger technique has most often utilized orthogonal lead systems (Section V.A). However, it is possible to use any set of three linearly independent reference leads to perform a Becking-Burger test of the dipole hypothesis. Therefore, any evaluation of the leads synthesized from a system of three linearly independent leads (Section V) is also an evaluation of the dipole hypothesis. One of the most comprehensive evaluations of a derived ECG system was that of the EASI lead system conducted by Horáček et al. [32], [9] on a population of 892 individuals, mostly consisting of patients with a previous myocardial infarction. This study supported the correctness of the dipole hypothesis.

IV. Methods for Synthesizing the 12-Lead ECG

Before the synthesis it is usual to do some preprocessing on measured leads. Most often this consists of filtering the base line and high-frequency noise. The resulting leads may be fed to the synthesis algorithm directly, or the average beat may be calculated for each lead and used in place of the source measurement.

On many occasions the Mason-Likar (M-L) [33] positions for the limb electrodes are used instead of the standard positions. Based on a limited study population, Mason and Likar asserted that their lead-placement system produces ECGs that are "essentially identical with those derived from standard peripheral electrode positions". However, subsequent studies have shown that the M-L positions may produce important changes in the ECG [34], and that they cannot substitute for the standard positions because they can lead to significant errors in the diagnostic interpretation [35].

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Therefore, when interpreting an ECG it is important to know if it has been recorded using an M-L electrode placement. Hence, when describing each derived ECG system it is important to indicate whether measurements according to the M-L specification are used for the synthesis algorithm or for the evaluation of the ECG system.

A. Linear Transformation Based Synthesis

Most of the derived 12-lead ECG systems employ a linear transformation for the synthesis of the 12-lead ECG. Let S be a system with a reduced number of leads:

$$\mathrm{S} = \{\mathrm{L}(1), \cdots, \mathrm{L}(i), \cdots, \mathrm{L}(m)\}, \tag{9}$$

where m is the number of leads employed by this system.

Hereafter, the lead potentials of one lead or of a system of leads are denoted in italics, so as to distinguish them from lead labels or labels representing systems of leads.

The standard 12-lead ECG system is:

$$\mathrm{E} = \{\mathrm{I}, \mathrm{II}, \mathrm{III}, \mathrm{aVR}, \mathrm{aVL}, \mathrm{aVF}, \mathrm{V1}, \mathrm{V2}, \mathrm{V3}, \mathrm{V4}, \mathrm{V5}, \mathrm{V6}\}. \tag{10}$$

The measured standard 12-lead ECG, E, constitutes a target ECG for the synthesis and is sometimes referred to as the "reference" 12-lead ECG. Given n samples $(S_1, E_1), \ldots, (S_n, E_n), (n > m)$, a linear model between E and S can be expressed as:

$$\boldsymbol{E} = \boldsymbol{M} \cdot \boldsymbol{\beta} + \boldsymbol{\varepsilon}, \tag{11}$$

where $\boldsymbol{E}$ is the matrix of the samples $E_i, (i = 1, \ldots, n)$, $\boldsymbol{\beta}$ is a transformation matrix formed by vectors of coefficients in its columns, and $\boldsymbol{\epsilon}$ is a matrix whose columns are vectors of errors. The matrix $\boldsymbol{M}$ is defined by:

$$\boldsymbol{M} = \begin{bmatrix} 1 & L(1)_1 & \cdots & L(\mathrm{m})_1 \\ \vdots & \vdots & & \vdots \\ 1 & L(1)_n & \cdots & L(\mathrm{m})_n \end{bmatrix}. \tag{12}$$

$\boldsymbol{M}$ does not necessarily contain a column of 1s, but if it does then we say that the model contains a constant term.

For the purpose of obtaining an estimate $\boldsymbol{b}$ of the transformation matrix $\boldsymbol{\beta}$, various methods have been used – statistical methods, deterministic methods [9], and a search method. The statistical approach is based on an analysis of the sampled data and on applying statistical methods to the data. The deterministic approach is based on understanding and modeling the heart's electrical source and the surrounding volume conductor.

The most frequently used deterministic approach is to employ an image surface (see Section II.A.2)). Because the image surface is a collection of described lead vectors, it can be used to form the transformation matrix $\boldsymbol{X}$, as described in the Appendix. By transposing equation (15) it is evident that $\boldsymbol{\beta}$ can be estimated as $\boldsymbol{X^T}$. It is shown in Section V.A that the first syntheses of leads were just rotations of the orthogonal system of leads. In this case $\boldsymbol{X^T}$ is a rotation operator and $\boldsymbol{S_1}$ is a diagonal matrix (see Appendix).

Using the statistical approach it is possible to estimate $\boldsymbol{\beta}$ by only using measurements from the two lead systems. In this approach $\boldsymbol{\beta}$ is most often estimated using the least-squares method [36] for each column of the matrix $\boldsymbol{E}$ (this method is also termed linear regression). The method yields the minimum-variance unbiased estimate $\boldsymbol{b} = (\boldsymbol{M^T M})^{-1} \boldsymbol{M^T E}$, which has the least variance of all the unbiased estimates. The best synthesized 12-lead ECG (in the least-squares sense) that can be obtained from S is

$$\widehat{\boldsymbol{E}} = \boldsymbol{M} \cdot \boldsymbol{b}, \tag{13}$$

where $\boldsymbol{b}$ is the estimate of $\boldsymbol{\beta}$ obtained with the least-squares method.

The search method is rarely used. Its basic concept is to form combinations of transformation parameters by incrementing each parameter by a predefined step. The best combination is the one that synthesizes a 12-lead ECG that is most similar to the target ECG in terms of the metrics used, e.g., the mean-squared distance or the correlation coefficient.

B. Synthesis Based on Artificial Neural Networks

Even though it has been shown on numerous occasions that a linear transformation provides a high-quality synthesized ECG, it is thought that nonlinear methods like artificial neural networks (ANNs) can further improve the quality of the synthesis [8]. The obvious advantage of ANNs is their ability to synthesize signals that are not outputs from a linear system. Therefore, the application of neural networks for the synthesis of a 12-lead ECG does not require us to assume the linearity of the heart-torso electrical system.

The basic ANN used for the purpose of the synthesis (Fig. 5) is a feed-forward ANN with an input layer composed of m neurons, each receiving samples of measured leads (9) as inputs. The output layer has 12 neurons that produce leads of the synthesized 12-lead ECG (10) on their outputs. The hidden layers make it possible to spread the data across the ANN and manage the relations between the input and output signals. The number of hidden layers is usually 1 or 2.

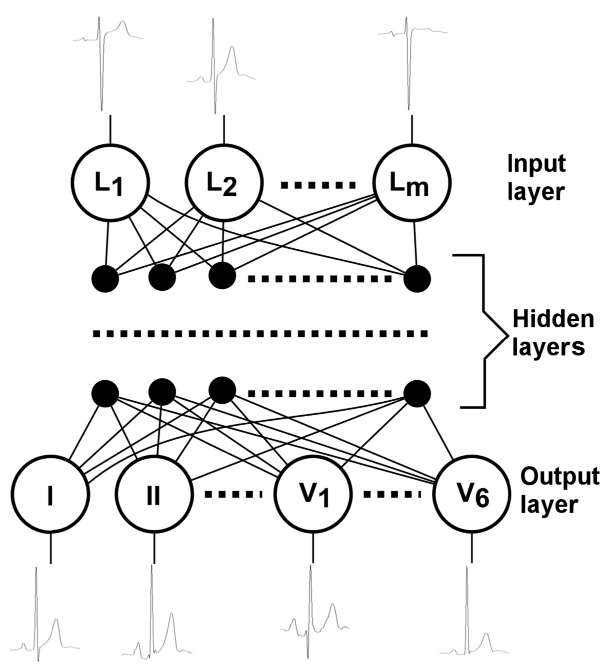

Fig. 5. General neural network architecture used for the synthesis of the 12-lead ECG.

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While the linear-transformation parameters are contained in the matrix $\boldsymbol{\beta}$, the transformation parameters of an ANN are the neurons' weights and biases that are determined in the ANN's learning process [37].

The disadvantage of using ANNs is that there is no general prescription about how to construct one ANN optimally, in terms of the number of hidden layers and the number of neurons per hidden layer. There is also no general prescription about how to optimally train one ANN with respect to the learning time and, more importantly, generalization, which is the output accuracy for the test data never used for training the network.

The methodology presented in the two previous sections can be used to synthesize any other lead system simply by replacing E with the lead set for that system.

C. The Synthesis Evaluation

The quality of the synthesized 12-lead ECG is evaluated by comparing it to the target 12-lead ECGs. The most commonly used metrics for automatic evaluation are the root-mean-square distance (RMSD) and the correlation coefficient (CC). The evaluation normally exploits a signal fragment that is not presented to the synthesis algorithm. This fragment is commonly referred to as the "test segment" or the "evaluation segment".

The RMSD and CC are the most commonly used methods for comparing waveforms, but they can be rather crude in expressing similarities or finding differences between detailed waveform patterns. A small RMSD or a large CC can lead to differences in the diagnostic content of the synthesized and the target 12-lead ECG.

Therefore, studies often use feature comparisons between the synthesized and the target 12-lead ECG. To do this it is necessary to extract features [38] from each lead of the two ECGs. Besides comparing the features directly, the evaluation is sometimes conducted by comparing the results arising from diagnostic rules based on the features. In such cases the synthesis is considered to be successful if the diagnostic rules produce the same diagnosis for the synthesized and the target 12-lead ECGs. The feature extraction and evaluations of the diagnostic rules are usually made with available software.

In parallel with these methods it is often helpful to engage an expert, i.e., a cardiologist, to examine independently the target and the synthesized ECGs. The synthesis is considered to be successful if the cardiologist makes the same diagnosis on the basis of each of the two ECGs. The engagement of an expert may be considered as the most important evaluation method because in clinical practice valid diagnoses are obtained from an expert analyzing the 12-lead ECG, and possibly using automatic rule-based diagnostics that modern ECG devices are often equipped with.

To make use of the CC and RMSD it is necessary to measure simultaneously the system with the reduced number of leads and the standard 12-lead ECG. However, the use of features, diagnostic rules and an expert do not necessarily need a simultaneous measurement on the two ECG systems.

Investigations of the vectorcardiographic features of extrasystoles [39], [40] imply that during an extrasystolic event the amplitude and orientation of the heart vector $\vec{p}$ change in a very different way compared to the changes during normal beats. More importantly, the same studies, together with an investigation using magnetocardiography [41], show that the electrical origin of an extrasystolic event differs significantly from that of normal beats, which implies that the location of the heart vector $\vec{p}$ for extrasystolic beats differs from the vector location for normal beats.

As noted in Section II.A.1) the lead vectors are independent of the magnitude or direction, but they do depend on the location of the heart vector. As a consequence of the changed location of the heart vector, the lead vectors of the system with a reduced number of leads S and the 12-lead ECG system E are also changed, which then causes the transformation (17) between the systems to be altered. The synthesis transformation parameters obtained by linear regression or ANNs are therefore potentially less effective for synthesizing an extrasystole if they are obtained from measurements lacking extrasystolic events.

Because of the above-noted specific properties of the extrasystole, any synthesis algorithms that have not "seen" the extrasystole during the calculation of the transformation parameters can be rigorously evaluated on a measurement segment containing an extrasystole. Fig. 6 shows a 12-lead ECG that contains an extrasystole that was successfully synthesized from three differential leads [42].

D. Universal versus Personalized Synthesis

Regardless of the use of either linear regression or ANNs, the synthesis of the 12-lead ECG can be universal, i.e., applicable for every person, or adjusted for any one person. Although, in general, both the transformation parameters and the electrode positions can be personalized, almost all existing derived 12-lead ECG systems employ universal electrode positions, i.e., predefined electrode positions, the same for every person. The transformation parameters are universal or personalized.

The transformation matrix is generally calculated from the lead vectors of a system with a reduced number of leads and the standard 12-lead system (see (17) in the Appendix). Any personalization of the transformation parameters can therefore be thought of as the employment of the personalized lead vectors that comprise the individual electrical characteristics and the shape of the volume conductor, as well as the individual locations of the dipole. Furthermore, the calculation of the personalized transformation parameters separately for each of the ECG waves or intervals allows the dipole location to be different for each of the waves or intervals in the same person (moving dipole).

Universal synthesis is sometimes referred to as "generic synthesis", while personalized synthesis is also called "person-specific synthesis". Therefore, the universal and personalized transformation parameters are accordingly referred to as "generic" and "person-specific" parameters.

One theoretically possible method for personalized synthesis is a calculation of the personal image surface, but

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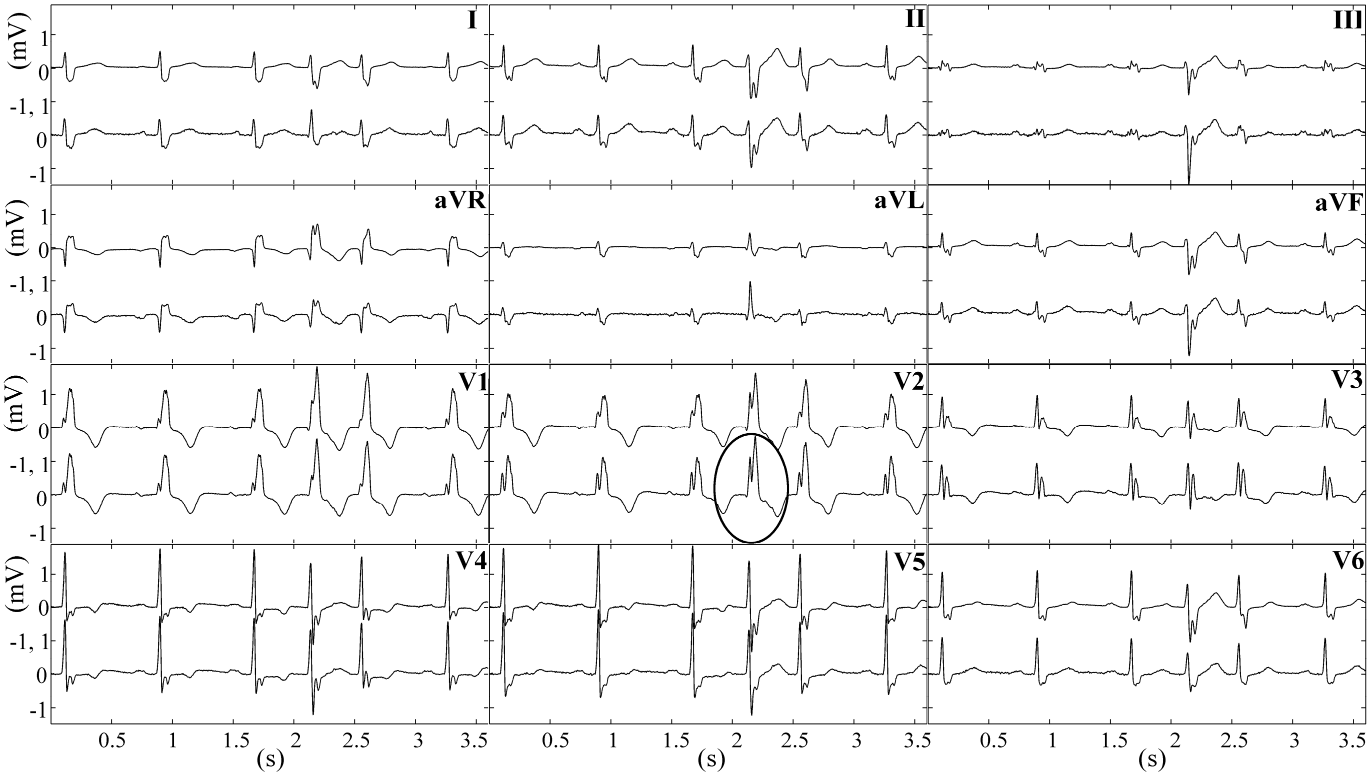

Fig. 6. Target (below) and synthesized (above) 12-lead ECG. Measurement contains a single extrasystole denoted by a circle on the target lead V2. The minimum CC is 0.87 for lead III and the maximum RMSD is 58.8 μV for lead V3. The 12-lead ECG is synthesized from three differential leads [42]. The transformation parameters were obtained from a measurement without extrasystolic events.

that approach is very impractical as it requires a volume source and volume conductor models to be constructed for each person.

The application of ANNs or the linear regression for personalized synthesis requires the simultaneous measurement of the 12-lead ECG and the leads used for the synthesis on each person before the systems can be used.

Universal synthesis can be obtained by using the image space, but for the application of the ANNs or the linear regression for the universal synthesis, a method of juxtaposing the measurements from different individuals is used. Usually, a set of ECGs made on several hundred people with different diagnoses and on healthy individuals is used. The 12-lead ECG and the leads used for the synthesis are simultaneously measured on each person. Equally long segments, or average beats, from the measurements taken from different persons are concatenated to form all-embracing measurements that are used as the inputs for the linear-regression algorithm, which results in a linear transformation that is potentially applicable to every person. The obtained measurements can also be used for training the ANN, which results in a universal ANN that can be used to synthesize a 12-lead ECG that is applicable for every person.

There are two further methods of universal synthesis, but they are only applicable in combination with linear regression. One is to form the universal transformation coefficients as the mean of the transformation coefficients obtained for each person. The other method is a generalization of the search method. Instead of assuming the best combination of parameters to be the one that produces the best synthesized ECG for a particular person, the chosen coefficients are those that result in the best synthesis, on average, over all the considered measurements.

In order to calculate the universal deterministic coefficients for deriving leads from the EASI lead system (Section V.C), Horáček et al. [9] used a realistic boundary-element model of a three-dimensional human torso. Three orthogonal unit dipoles were placed at a total of 1239 source locations within the torso's ventricular region. In this way they obtained 1239 image sources, i.e., 1239 lead vectors for each of the 352 points on the model surface. To apply the method of transforming one lead system to another, described in the Appendix, in this case it is possible to use the mean values of the obtained lead vectors as in [43] accompanying Horáček's paper, but Horáček et al. used regression to fit a linear model to the simulated data from the torso model in order to obtain a linear transformation from the EASI system to the 12-lead system, and to some other sets of leads. Even though it uses linear regression, this method is not to be considered statistical, because the data for it comes from a deterministic model. Horaček et al. also employed linear regression on the recorded ECGs from a population consisting of 892 individuals. Despite their evaluations using the CC and RMSD revealing the superiority of the coefficients derived statistically from recorded ECGs, suggesting that the lead transformations should be preferably designed by a statistical approach, they concluded that "model-derived deterministic transformations are compatible with statistically derived ones, provided that the distributed character of the cardiac sources is taken into account".

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The advantage of a universal synthesis is that once calculated, the transformation parameters can be applied to every person without the need for new measurements. The disadvantage is that a universal synthesis generally gives results that are inferior to those using a personalized approach, because the universal transformation parameters are not optimally adjusted to the uniqueness of each person.

On the other hand, a personalized synthesis has the disadvantage that, for its application, a simultaneous measurement of the target 12-lead ECG and of the leads used for the synthesis is needed for each person, before the derived ECG systems can be used. The personalized linear transformation is obtained exclusively with the least-squares method, while the universal linear transformation is obtained either with the juxtaposing approach or with the deterministic methods.

For the purpose of calculating the transformations from one VCG system to another, Burger et al. [44] were the first to apply linear regression for the syntheses of the universal and personalized leads. For the universal synthesis they were using the method of juxtaposing, although that is not immediately evident from their publication.

In addition to the universal and personalized syntheses, some studies benefit from a synthesis that is adjusted to a specific population. The populations can be chosen intentionally in various ways. They can contain, for example, subjects from the same geographical area, of the same age, or subjects with similar diagnoses.

V. Electrocardiographic Systems with Reduced Numbers of Leads that Synthesize 12-Lead ECG (Derived 12-Lead ECG Systems)

The lead theory was investigated intensively between 1945 and 1955. As a result, an understanding developed that although electrode systems might look orthogonal, this does not necessarily imply the mutual orthogonality of the lead vectors [18]. Such systems that were not measuring leads with lead vectors in precisely orthogonal directions, and of the same length, are referred to as “uncorrected orthogonal lead systems”. The most important step that advanced the assessment of electrocardiographic leads was the Frank image space [17].

A. Systems with Orthogonal Leads (Special Leads)

VCG systems with orthogonal and normalized lead vectors are called “orthonormal lead systems”. The term “normalized” means that all three components of the heart vector are detected with the same sensitivity. Such systems usually produce lead vectors that are approximately oriented in the directions of the axes of the Cartesian coordinate system and are accordingly denoted by the letters X, Y, Z. Thus, orthogonal lead systems with such leads are often referred to as XYZ lead systems. The XYZ lead systems that have been most often explored for the purpose of the synthesis are the SVEC III system [45] and the Frank VCG system [6].

At the time when the first VCG systems were designed, the methods for diagnostically analyzing the measurements of the orthogonal leads had not been established. The first attempts were therefore aimed at synthesizing the 12-lead ECG from VCG leads. Another motivation for these early syntheses was to evaluate the dipole hypothesis using the Becking-Burger principle [22].

The first syntheses of leads were based on a device often referred to as the “resolver”. The development of resolvers started in 1947 with the method described by Schmitt for the cathode-ray presentation of three-dimensional data [46].

Based on Schmitt’s principles, in 1953 Milnor et al. [47] designed an instrument for projecting the VCG, i.e., the heart vector, to any single axis directed from an estimated heart-vector origin. As an input to the device, the output from a custom VCG system was used. The elected directions for synthesized precordial leads were those that showed features most similar to the recorded standard precordial leads. Based on a study performed on 58 subjects, the authors concluded that the synthesized leads closely resembled the recorded precordial leads.

In 1957 Helm published the design of a custom VCG device that he claimed to be orthonormal, and a switch box capable of linearly transforming any XYZ lead system to one of 13 leads [48]. The switch box was limited to one angular step between two or three orthogonal leads. However, in 1959 Helm published details of another, more effective switch box, which he used for synthesizing various groups of leads from his custom system of seven electrodes [49]. He synthesized the standard precordial leads using the Frank image space.

Pipberger et al. [50] developed a resolver capable of rotating any XYZ lead system in steps of 15°. The resolver details were published in 1958, but the answer to the question about whether the precordial leads provide clinical information that was not contained in ECGs obtained from XYZ systems was published [51] in 1961. As a source of orthonormal leads they used the SVEC III system with measurements from 261 patients. In 92.7 % of the group, the same diagnoses were obtained from the standard 12-lead ECG as from the XYZ leads. The next step was to compare the 12 standard leads with the synthesized leads. In 18 of the 19 cases for which clinically significant details could not be recovered from the XYZ leads, the synthesized leads revealed this information, resulting in a total of 99.6 % of measurements with recognized details.

Okada et al. [52] synthesized precordial leads with respect to a mid-back electrode for seven locations on the chest that the authors assumed to be approximately in the zone of standard precordial leads. The components of the SVEC III system where used as the input to a resolver based on Schmitt’s principles [46]. Based on a study of 28 subjects, the authors concluded that there is a distinct possibility that non-dipole potentials are large enough to be of clinical value for some patients.

In 1963 Abildskov and Wilkinson [53] employed a resolver (described in [54]) to rotate the axes of the McFee-Parungao orthogonal lead system (described in [55]). The synthesized precordial leads were chosen from a set of leads obtained by rotations, using a critical four-step selection procedure. The

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TABLE I,
MAIN CHARACTERISTICS OF THE DERIVED 12-LEAD ECG SYSTEMS

Source ECG system	Synthesis system	Year	Source leads	Synthesis method	Personalization	Evaluation	No. of measurements with accompanied diagnoses
SVEC III (1955)	Okada et al.[52]	1959	3 orthonormal	rotating XYZ to precordial lead vectors[b]	yes	signals diff. and visual comparison	28 (20 normal subjects[a], 8 MI)
SVEC III (1955)	Pipberger et al.[50], [51]	1961	3 orthonormal	rotating XYZ to precordial lead vectors[b]	no	features comparison	261 (conduction defects, hypertrophies, MI)
Frank (1956)	Dower [5]	1968	3 orthonormal	universal linear trans.	no	visual comparison	200
Frank (1956)[c]	Uijen et al. [56]	1988	3 orthonormal	universal linear regression	no	RMSD and max. absolute difference	106 (54 normal[a], 52 chronic MI)
McFee-Parungao (1961)	Abildskov and Wilkinson [53]	1963	3 orthogonal	rotating XYZ to precordial lead vectors[b]	yes	features comparison	35 (5 normal ECGs, 30 patients with miscellaneous abnormalities)
12-lead ECG	Scherer et al. [57]	1989	I, II, V2	pers. linear trans. per segments	yes	CC, RMSD	12 (MI)
12-lead ECG (M-L)	Wei [58], [59]	2002	I, II, V1, V6	universal linear transformation	no	CC, ST-segment center	113 (normal subjects[a])
12-lead ECG (M-L)	Drew et al. [60]	2002	I, II, V1, V5	N/A	N/A	visual comparison, RMSD, expert	649 (ischemia or malignant arrhythmias)
12-lead ECG (M-L)	Robertson et al. [61]	2002	2 systems of 3 bipolar leads	universal linear transformation	no	RMSD, ST-level, diagnoses comparison	65 (ischemia/MI)
12-lead ECG (M-L)	Nelwan et al. [62]	2000	all subsets of precordial leads	universal and personalized linear regression	yes	CC	2372 (chest pain suggestive for acute MI.)
12-lead ECG (M-L)	Nelwan et al. [63]	2004	all subsets of precordial leads	universal and personalized linear regression	yes	CC, ST-level, results from diagnostic rules	234 (ischemia)
12-lead ECG	Nelwan et al. [64]	2004	I, II, V2, V5	universal and personalized linear regression	yes	CC, ST-level, comparison to EASI synthesis	38 (percutaneous coronary intervention induced ischemia)
“Transtelephonic System” [65]		2004	3 bipolar	personalized linear regression	yes	RMSD, experts	192 (normal[a], various chronic disorders, balloon angioplasty)
“Eigenleads“ [66]		2010	3 bipolar	universal linear regression	no	RMSD, CC, comp. to EASI and Nelwan (3)	744 (229 normal[a], 278 MI, 237 left-ventricular hypertrophy) – 185 used for evaluation
12-lead ECG	Atoui et al. [8]	2010	I, II, V2	NN and linear regression (personalized and universal)	yes	RMSD, CC	157 (120 cardiac patients from an intensive care unit)
Trobec and Tomašić [42]		2011	3 bipolar (differential leads)	personalized linear regression	yes	RMSD, CC, extrasystole, comp. to EASI	99 (30 normal[a], 34 patients with miscellaneous cardiac diagnoses)

[a] subjects with no previous medical record regarding heart disease.
[b] lead vectors under the assumptions of the volume conductor being spherical homogeneous and the cardiac source centrally located.
[c] other evaluations of the syntheses from the Frank lead system have also been reported: [67], [68], [69].

VCG and the standard 12-lead ECGs were obtained from 35 patients. The authors state that only one of the synthesized leads did not contain the same clinically significant features as the target lead.

Several other syntheses from the VCG systems have been investigated; nevertheless, we will concentrate on the Frank system as it was the cornerstone of further development for the derived 12-lead ECG systems.

Of the three most popular VCG lead systems—Frank, McFee-Parungao, and SVEC III—that of Frank uses 7 electrodes, SVEC III uses 14 and McFee uses 9. Because it has the smallest number of electrodes and also because it is the most easy to apply, the Frank system has superseded the other two in clinical practice, even though they had some desirable properties that were more pronounced [70].

Dower [5] was the first to derive a 12-lead ECG system from the Frank lead system by using the Frank image surface to estimate the parameters of the linear transformation. In the original paper [5] Dower obtained two sets of parameters, one for each of his two hypotheses, relating to where the electrode sites of the 12-lead ECG system are located on the Frank torso model. From a visual comparison of the target and the synthesized 12-lead ECGs Dower concluded that his simulated ECG could provide a very useful method for displaying the X, Y, Z signals. Dower et al. later published another set of parameters, also based on Frank’s image surface [71]. Uijen et al. [56] applied linear regression on juxtaposed Frank orthogonal leads measured on 54 subjects free of significant cardiac diseases and 52 patients with chronic infarctions. The resulting universal synthesis was evaluated by its RMSD and the maximum absolute difference, and compared with the syntheses obtained using Dower’s transformation matrices. It was shown that the 12-lead ECG synthesized by Dower’s matrices can differ significantly from the target 12-lead ECG. Even though the universal matrix obtained by linear regression appeared to perform somewhat better than the Dower

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matrices, the authors concluded that this was not sufficient evidence to advocate its use.

Other evaluations of the syntheses from the Frank lead system have been reported. Those performed by Zywietz et al. [67] and Wolf et al. [68] also indicated that universal linear transformations do not perform sufficiently well. The explicit forms of the transformation matrices used were not reported in these two papers. A recent study [69] shows that the population-specific transformations, obtained by linear regression, also perform better than the Dower transformation.

Further work on enhancing the synthesis from the Frank lead system was overshadowed by the emergence of the EASI and other modern lead systems (Section V.C), which appeared to be more practical and easier to use.

B. Systems that employ a Subset of Leads from the 12-lead ECG (Reduced Lead Sets)

Scherer et al. [57] used measurements on 12 patients to investigate the synthesis from the lead set: I, II, V2. Scherer did not describe the details for calculating the parameters of the linear transformation. The personalized transformation parameters were calculated for the entire beat, but separate transformation parameters were also calculated for the PR interval, the QRS complex and the ST interval. Based on the available measurements, universal transformations for each segment were also estimated by averaging the personalized transformations.

Nelwan et al. [62] investigated how well a missing precordial lead can be synthesized from the remaining precordial leads of the 12-lead ECG. All possible subsets of the precordial leads, obtained in such a way that one or more precordial leads are excluded, were studied. In this way they investigated $2^6 - 1$ (i.e., 63) distinct subsets of the precordial leads, with up to five precordial leads excluded. They used universal synthesis, personalized synthesis and population-specific synthesis. The coefficients of the linear models were estimated using the least-squares method. The CC was used for the evaluation. The authors concluded that the missing precordial leads can be sufficiently well synthesized, although the personalized approach generally gave better syntheses than the universal approach.

In another study [63] they used 236 measurements, each of 24 hours, obtained during a study of myocardial ischemia. They showed that it is possible to synthesize up to four missing precordial leads by using a personalized linear transformation. Secondly, they showed that it is possible to synthesize up to two missing precordial leads by using universal linear transformation synthesis. The difference from the preceding study lay in the way the evaluation was performed. As well as the CC, a features comparison was used, specifically the amplitude of the ST segment at 60 ms after the J-point. Furthermore, they applied an evaluation based on comparing the results from diagnostic rules.

Nelwan et al. conducted one additional study [64] in which they used simultaneously measured reduced-lead sets, EASI leads and conventional 12-lead ECG leads. The measurements were obtained from 38 patients during percutaneous coronary occlusion. The 12-lead ECG was synthesized from I, II, V2 and V5 leads by using a personalized linear transformation and universal transformation coefficients obtained from the available population. By comparing the synthesized 12-lead ECG with the one obtained from the EASI system, they showed that the reduced lead set synthesizes the 12-lead ECG even better than the EASI system. The CC over the QRS-T interval and the ST60 feature were used for the evaluation.

Wei [58], [59] also used a reduced lead set for synthesizing the 12-lead ECG, but the explored subset was I, II, V1 and V6. In order to obtain benefits similar to those from the EASI system's electrode positioning, Wei positioned the limb electrodes according to the M-L specification. The 12-lead measurements from 113 young, healthy people were used for the synthesis. Wei first applied the linear model with universal transformation coefficients obtained from the Frank image space. In the second case the universal coefficients were determined as the mean values of the coefficients obtained by the least-squares method for each person. The CC and the comparison of the potential in the center of the ST segment were used for the evaluation in both cases. Wei concluded that the least-squares method results in a significantly better synthesis than the deterministic method. Furthermore, he stated that the synthesized 12-lead ECG may be good enough for clinical applications. The advantage of his lead system over the EASI system was also emphasized, since most of the leads from the synthesized 12-lead ECG are measured directly and therefore need no synthesis.

Drew et al. [60] explored a lead system that only differs from Wei's in terms of one lead. They used V5 instead of V6 in assembling a lead set I, II, V1 and V5. The synthesis was evaluated in three ways: 1) by visually rating the synthesized and target leads as identical, similar, or clearly different; 2) by calculating the RMSD; and 3) using the diagnostic interpretation of an expert. The system was evaluated on 649 patients with various diagnoses. It was concluded that the synthesized 12-lead ECG is useful for diagnosing diverse pathophysiological disorders, including wide QRS complexes, tachycardia, acute myocardial ischemia and myocardial infarction (MI). Drew's lead system, just like that of Wei, also offers the same advantage over the EASI system, i.e., 8 of the 12 leads are measured directly.

Atoui et al. used leads I, II and V2 [8]. For the analysis they used measurements of the 12-lead ECG and of the reduced lead set, both of 10 seconds. They obtained 157 measurement pairs recorded on 120 patients. For the synthesis they used a set of 50 ANNs, each incorporating one hidden layer with 15 neurons and an output layer of 5 neurons, to produce the missing independent leads of the 12-lead ECG {V1, V3, V4, V5, V6}. ANNs were trained for both universal and personalized synthesis by means of a supervised back-propagation algorithm. The synthesized 12-lead ECGs were compared to the target 12-lead ECGs, by calculating the CCs and RMSDs, and also to the 12-lead ECGs obtained by universal and personalized linear transformations. The parameters of the linear transformations were obtained using the least-squares method. As with the universal ANN training,

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the method of juxtaposing individual measurements was used to obtain the universal linear transformation. The authors concluded that the universal ANN synthesis yields a slightly better 12-lead ECG than the universal linear transformation. In addition, they concluded that the superiority of ANNs is more pronounced in the case of a personalized synthesis.

The systems presented in this section that use reduced lead sets all emerged after the systems with orthogonal leads presented in the preceding section. Recently, new systems with special leads have been proposed, the most popular being the EASI system, but others are expected to prove their clinical usability.

C. Modern Systems with Special Leads

The EASI system [72] is composed of four signal electrodes and a fifth ground electrode (Fig. 7). From four measured signals, three approximately orthogonal leads are formed: E-S, A-S and A-I.

Compared with the majority of other derived 12-lead ECG systems, the EASI system is less sensitive to artifacts that are a consequence of body movement, since the measurement sites are located exclusively on the torso. Accurate positioning of the electrodes is relatively easy since the recording locations are at prominent anatomical landmarks.

The 12-lead ECG is synthesized as a linear combination of the three EASI leads but Dower—the inventor of the system—did not explicitly publish the original transformation coefficients [72]. Feild et al. in 2002 published various sets of universal transformation coefficients obtained using measurements on 983 adults [43]. To find the universal linear transformation coefficients Feild used the universal search method with the mean-squared distance as the metric for evaluating the synthesis. The best combination of coefficients was the one that resulted in the minimum mean-squared distance over all the available measurements. From 1988, when the EASI system was introduced, until the introduction of Feild's parameters in 2002, publications regarding the EASI system evaluation mostly referenced the Dower conversion box [73] as the source of the transformation parameters.

There have been a number of evaluations of the quality of the 12-lead ECG synthesized from the EASI lead system. The studies of Klein et al. [74] and Drew et al. [75], [76] showed that EASI accurately detects the right/left bundle branch block and the fascicular blocks, and that it is diagnostically equivalent to the standard 12-lead ECG for the detection of cardiac arrhythmias. The detection efficiencies of the EASI system were found to be equivalent to the standard 12-lead ECG for the detection of acute ischemia [77], [76], [78], [79], [80], acute MI [81], and prior MI [74], [76], [78], [82]. Sejersten et al. [83] tested the hypothesis that precordial waveforms in EASI-derived ECGs have no greater deviation from those in gold standard ECGs than do the precordial waveforms in paramedic-acquired standard ECGs. The results suggested that the EASI lead system may provide an alternative to the standard ECG in emergency situations. The EASI system was also evaluated in other cardiac abnormalities. The most prominent evaluations of the EASI

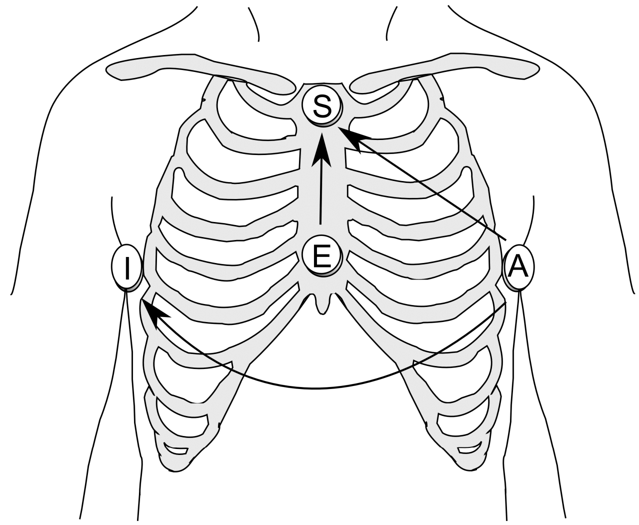

Fig. 7. EASI system's electrode positioning.

system are summarized in Table II.

Studies in children [84], [85] support the suggestion that the EASI lead system is a potential alternative to the standard ECG also for children. The studies included 221 children, both healthy children and those with varying cardiac diagnoses.

Robertson et al. [61] introduced two systems of bipolar leads. The first system forms the leads as potential differences between the precordial electrodes V2, V4 and V6, on one side, and the M-L modified electrode positioned on the right arm, on the other. The second lead system also uses the potential on the right arm as one side of the bipolar leads, but the V1, V2 and V4 precordial electrodes for the other side. Measurements recorded on 65 patients were used for the study. Robertson did not go into specifics about the synthesis, but stated that the 12-lead ECG was, in both cases, synthesized by a universal linear transformation. The authors concluded that the tested lead systems, coupled with universal synthesis, do not give satisfactory results.

The "Transtelephonic System" [65] consists of two distinct parts: a stationary calibration device and a mobile ECG device with integrated electrodes. The calibration device simultaneously measures the 12-lead ECG and three special leads. The electrodes of the mobile ECG device are later placed at the positions held by the electrodes of the calibration device that measure special leads. The calibration device is connected to a personal computer on which a personalized transformation matrix is calculated by the least-squares method on measurements of 4.5 s. When the calibration is finished, the mobile ECG device can be used, which, by utilizing a mobile phone, sends measurements recorded from the three special leads to a diagnostic center. Here, the transformation matrix calculated in the calibration process is applied to the received measurement, which results in the synthesized 12-lead ECG. Besides calculating the RMSD, the synthesis was evaluated by independent observers on measurements from 192 subjects. The authors also analyzed the errors in the synthesized ECG that could appear as a consequence of inaccurate mobile-device positioning. In order to investigate the ability of the synthesized ECG to reconstruct

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TABLE II.
EASI SYSTEM EVALUATIONS

Year	Authors	Population	Diagnoses	Coefficients	Evaluation	Target 12-lead
1992	Drew et al. [75]	49	wide QRS complex tachycardia, varying cardiac diagnoses	N/A	2 investigators compared features, features comparison, diagnostic rules	standard simultaneous
1997	Drew et al. [77]	93	coronary angioplasty induced ischemia	converter device[b]	ST-level	standard simultaneous
1997	Klein et al. [74]	50	miscellaneous diagnoses	Dower conversion box [73]	features comparison, diagnostic rules	standard simultaneous
1999	Drew et al. [76]	426	multiple cardiac abnormalities	converter device[c]	features and diagnoses comparison supported by a computer, expert analyses	M-L simultaneous
2000	Horáček et al. [82]	780	290 normal[a], 490 prior MI	universal by linear regression	CC, features comparison, MI injury score – composite feature	standard simultaneous
2002	Feild et al. [43]	983	normal[a], post-MI, ventricular arrhythmias, induced ischemia	universal linear trans. (search)	RMSD and CC	standard and M-L
2002	Rautahar. et al. [78]	894	prior MI (472) and induced ischemia (40), no history for MI (382)	Field et el.	2 ECG readers and features comparison by a Philips ECG analysis program	standard and M-L
2003	Sejersten et al. [83]	N/A	normal subjects[a]	From [73]	features comparison by a Philips Medical System analysis program	standard simultaneous
2003	Pahlm et al. [84]	221 children	normal subjects[a] and varying cardiac diagnoses	age-specific and coeff. from [82]	RMSD	standard simultaneous
2006	Welinder et al. [85]	221 children	normal subjects[a] and varying cardiac diagnoses	calculated for age groups	interpretations from 2 pediatric cardiologists	standard simultaneous
2006	Wehr et al. [81]	203	acute coronary syndromes	Philips EASI device	2 independent cardiologists	standard simultaneous
2007	Sejersten et al. [80]	88	balloon inflation angioplasty induced ischemia	Field et el.	ST-level	M-L simultaneous

[a] subjects with no previous medical record regarding heart disease.
[b] Zymed Medical Instrumentation, Camarillo, California
[c] Totemite, Inc., Point Roberts, WA

the ischemic ST segment changes, the synthesis was also evaluated on a population of 72 patients with provoked myocardial ischemia during the balloon angioplasty procedure. The authors also present a test of 50 mobile devices used in real-life situations over a time period of two months. On the basis of all the tests the authors concluded that the synthesized 12-lead ECG is, in general, very accurate, while being slightly sensitive to small positional variations of the mobile device. More importantly they note that the observed errors in the synthesized 12-lead ECG are not diagnostically significant.

Another promising lead system with special leads is closely related to the development of smart textiles [86]. Smart textiles integrate the measurement devices, wires and electrodes into clothing, thereby enabling the convenient acquisition of ECG recordings. A drawback of these devices is that the measurements obtained are susceptible to noise and artifacts caused by the movement of the electrodes.

The lead system named “Eigenleads” [66] attempts to resolve the imperfections in smart textiles by employing principal component analysis, a multivariate statistical technique, to identify the measurement sites at which the signal-to-noise ratio is a maximum. The authors used MECGs with 117 unipolar leads and the measurements were obtained from 744 people. The universal bipolar leads, named by the authors “eigenleads”, are determined by analyzing the extremes of the first few principal components. Using linear regression, two universal linear transformations were calculated, one transforming the 3 eigenleads to a 117-lead MECG, and the other transforming the 3 eigenleads to a 12-lead ECG. The applicability of the resulting eigenleads was assessed, not only by calculating the RMSD and CC between the synthesized and the target ECGs (both 12-lead and 117-lead), but also by considering the measured variances of the eigenleads. The results of synthesizing the 12-lead ECG from the eigenleads were compared to the syntheses from the EASI and Nelwan $\{I, II, V2, V5\}$ lead systems in terms of the RMSD and CC between the target and the synthesized 12-lead ECGs. It was found that the proposed leads can be used to reconstruct the 12-lead system with an accuracy comparable to those for other systems with a reduced numbers of leads. The authors concluded that the eigenleads perform very well in synthesizing precordial leads, while the limb leads are synthesized slightly less well; nevertheless they consider the eigenleads to be a viable system.

Trobec and Tomašić [42] investigated the utility of wireless electrodes (WEs) for synthesizing the 12-lead ECG. A WE [87] measures the potential difference between two proximal electrodes on the body surface. The WEs’ leads were emulated by taking the differences of the neighboring unipolar leads belonging to MECGs. The leads are termed “differential leads” (DLs). An algorithm was proposed that, when using an MECG recorded for a person, yields the optimum personalized positions of the WEs with a personalized transformation matrix. The algorithm is based on linear regression, while the synthesis is conducted by a linear transformation. The authors tested and evaluated the algorithm on 99 MECGs obtained from 30 healthy subjects and 35 patients scheduled for elective cardiac surgery. The evaluation was conducted by calculating the RMSD and CC between the synthesized and target 12-lead

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ECGs on measurement segments that were not "seen" by the algorithm, i.e., evaluation segments. It was shown that the algorithm significantly outperforms the synthesis from the EASI lead system with medians of the correlation coefficients greater than 0.954 for all twelve standard leads. Moreover, a measurement containing extrasystoles was used for an additional evaluation of the synthesis algorithm.

The algorithm for obtaining the optimal personalized positions of the DLs and the personalized linear transformations was executed for 2, 3 and 4 DLs. The authors demonstrated that just three DLs are sufficient for a reliable synthesis of the 12-lead ECG and concluded that three is the optimal number for practical applications.

The main characteristics of the described derived 12-lead ECG systems are presented in Tables I and II.

VI. Summary

The 12-lead ECG is a reliable diagnostic tool that is widely used in routine clinical practice for screening, for outpatient and emergency evaluation, for evaluating complicated cardiac arrhythmias, and for diagnosing other cardiac disorders. However, since its conventional acquisition requires long wires and 10 electrodes, the recording of the 12-lead ECG can be inconvenient, particularly for long-term and mobile applications. Moreover, because the standard positions of the precordial electrodes are often difficult to locate accurately, particularly in women and children, the application of the conventional 12-lead ECG device can be impractical in certain emergency situations that, on the basis of a diagnosis obtained from an ECG recording, demand urgent therapeutic intervention. The progress in developing derived 12-lead ECG systems has allowed the acquisition of the 12-lead ECG with a small or insignificant loss of diagnostic information. However, despite numerous studies that demonstrate favorable efficiency and good accuracy of certain derived 12-lead ECG systems, the conventional 12-lead ECG still dominates clinical practice.

The systems with reduced numbers of leads employ universal or personalized synthesis, but all use universal measurement sites (i.e., universal electrode positions). The only exception is the system of DLs that enables person-specific WE positions. The systems of DLs and of eigenleads are the only two that make use of a statistical method for deriving the electrode positions. All the other systems presented use a subset of the conventional 12-lead ECG lead set, or attempt to guess the optimum electrode positions by seeking to make leads orthogonal and less susceptible to electrode misplacement, and/or seeking to make the system as easy to use as possible.

One of the most important factors in selecting measurement sites is the sensitivity to a possible misplacement of the electrodes, which has not been investigated for all the systems presented. The sensitivity to misplacement is particularly important for systems with a reduced number of leads because reducing the number of electrodes for a particular lead system potentially increases the misplacement sensitivity of the remaining electrodes [30]. The sensitivity to misplacement can be reduced by placing the electrodes further from the source [30], with the drawback that the distant leads may pick up less non-dipolar content.

As explained in Section IV.D, personalization of the transformation parameters encompasses individual characteristics and the shape of the volume conductor, as well as the individual location of the dipole. At first the personalization was achieved partially by an approximate personalized selection of the directions of leads that best assemble the target leads, but later it became technically possible to calculate and employ individual transformation parameters by linear regression or by using ANNs. Few of the presented syntheses of the 12-lead ECG that were used for testing the dipole hypothesis, or for evaluating the diagnostic capabilities of vectorcardiography, lead to the conclusion that the dipole hypothesis is questionable [52], or that vectorcardiography is not an appropriate diagnostic technique [56], but these conclusions are unfounded because they did not take the personalization into account. Moreover, there are numerous studies that support the dipole hypothesis (Sections II.B and III.C).

The system of DLs supported by WEs is so far the only one for which the authors presented personalized measurement sites and personalized synthesis parameters (Approach I). The development of technologies like wireless technology and smart clothing may motivate the development of additional systems that exploit personalized measurement strategies with which it might be possible to obtain the best possible synthesized 12-lead ECGs, given that every human body is unique.

The fact that the universal measurement sites, together with universal synthesis parameters (Approach II), can be used without additional measurements, calibrations or calculations, makes them an important field of research that may benefit from nonlinear methods like ANNs, which have not yet been widely tested for this purpose. Fig. 8. A. shows that ANNs have been used in a very small proportion of measurements compared to linear transformations.

The third approach is to keep the electrode positions universal but obtain a personalized synthesis in a process of calibration. An example of a system making use of a calibration is the transtelephonic system [65]. This paradigm remains to be investigated for other systems.

It can be observed in Tables I and II that there is a great variation in the evaluation methods employed by the studies. Some of the studies employ the CC and/or RMSD, together with a comparison of the features and diagnostic rules (or the employment of an expert) on the same data set. Although the CC and RMSD are rough estimations of the similarity in diagnostic content between measured leads (Section IV.C), those studies show that favorable values of the CC and RMSD correlate with the situations in which the synthesized and target 12-lead ECG contain the same diagnostic information [63], [64], [59], [60]. Graphs B, C and D in Fig. 8 illustrate the mean CCs, the mean diagnostics concordance percentage and the mean RMSDs, aggregated from the subset of studies in Tables I and II for which these evaluation measures are

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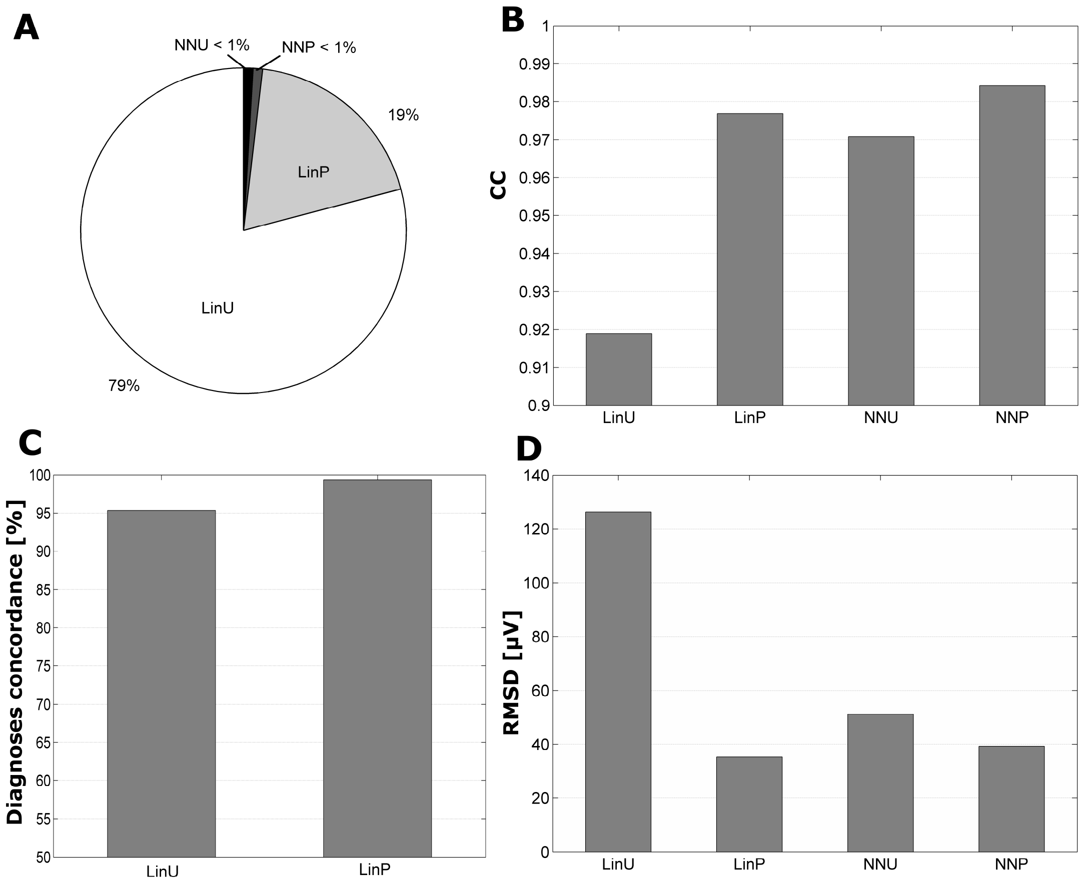

Fig. 8. A comparison between synthesis methods (LinU – linear universal, LinP – linear personalized, NNU – neural network universal, NNP – neural network personalized). **A** – Proportions of measurements employed for each method, **B**- Average CCs, **C** – Average diagnoses or features concordance, **D** – average RMSDs. In panels B, C and D the evaluation metrics are calculated between the synthesized and standard 12-lead ECG. The panels present data aggregations from the subset of studies presented in Tables I and II for which the presented evaluation metrics are available. There are no evaluations based on diagnoses or ECG features for ECGs synthesized with ANNs.

available. The graphs show an obvious advantage of the employment of personalized transformation parameters and the superiority of ANNs, except in the personalized case measured by the RMSD in which the linear transformation is better. Note that as the source for the data of ANN syntheses evaluations, only the data from the study by Atoui et al. [8] was used.

The authors of eigenleads and DL systems have discussed the possibility of obtaining optimum measurement sites for the synthesis of a specific ECG segment, the demand for which can emerge from some specific tasks like monitoring arrhythmia. The DL system retains the possibility of both electrode positions and transformation parameters being adapted for specific tasks. A calculation of the personalized transformation parameters, separately for each of the waves or intervals of the ECG, can improve the synthesis quality (see Section IV.D), but so far only Scherer et al. have investigated that possibility [57], although Burger et al. [44] were the first to report the idea.

The syntheses from reduced lead sets, presented in Section V.B, have all shown satisfactory results in the synthesis of the 12-lead ECG. It is a tendency in today's electrocardiography, however, to introduce additional unipolar leads to the standard 12-lead ECG, which seem to add valuable information for specific patient groups [3]. It is also possible to find additional clinically relevant information with the use of a large number of leads [3], but the question is: is it necessary to directly measure the additional leads? Under the acceptable assumption of a dipole as the volume source model, we have shown (Section III) that it is necessary to measure only three independent leads, while the others can be synthesized. Indeed, the investigation by Finlay et al. [66] showed that the BSPMs synthesized (by using a universal linear transformation) from three eigenleads, standard 12-lead ECG, EASI and Nelwan {I,II,V2,V5} system, have the median correlations with the target BSPM: 0.907, 0.941, 0.878, 0.913 respectively, which shows that systems with reduced numbers of leads can perform well in synthesizing BSPMs, and that the quality of the synthesis is comparable to the BSPM synthesis from the standard 12-lead ECG. Furthermore, universal coefficients have been developed that derive the right-sided, posterior and vessel-specific leads from the EASI system, with acceptable quality [9], [43]. The personalized synthesis of an arbitrary set of leads is expected to be of even higher quality; nevertheless, these examples confirm the dipole hypothesis and its consequence: the possible synthesis of arbitrary, not directly measured, leads.

It was shown in Section III that the synthesis of leads is

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based on the dipole source model, but every evaluation of a lead system derived from three leads is also an evaluation of the dipole model. Waller, who was the first to measure human cardiac electrical activity, was also the first to perceive the heart's dipole concept. Although not using the term "dipole", it is obvious from his choice of measurement sites, discussion and illustration of the heart's isopotential maps [88], that he understood the meaning and foresaw the significance of the dipole concept.

APPENDIX

Calculations of linear transformations from one lead system to another, by using a-priori-known lead vectors, are mostly presented sequentially [22], [5], [43]. The direct formula is presented here, that not only eases the calculation of the transformation, but more importantly allows certain conclusions to be made directly from it, as they were obtained through this paper.

In order to describe a transformation from one lead system to another, let us assume that there are two lead systems S_1 and S_2 with m_1 and m_2 leads.

Under the fixed-location dipole hypothesis and the assumption of a body being a linear physical system, we may employ Burger's equation for every lead in both systems:

$$S_1 = \boldsymbol{S_1} \cdot \vec{p},\ S_2 = \boldsymbol{S_2} \cdot \vec{p}, \tag{14}$$

where S_1 and S_2 are one-column matrices of lead values, $\boldsymbol{S_1}$ and $\boldsymbol{S_2}$ are the matrices with corresponding lead vectors in rows and $\vec{p}$ is the fixed-location heart dipole.

The matrices $\boldsymbol{S_1}$ and $\boldsymbol{S_2}$ have dimensions $m_1 \times 3$ and $m_2 \times 3$. Since three leads are necessary for describing the fixed-location dipole source (see Section III.B) we will assume that the rank of the matrices $\boldsymbol{S_1}$ and $\boldsymbol{S_2}$ is 3.

Equations (14) represent two linear systems with the same input. We are searching for a linear transformation $\boldsymbol{X}$ that transforms S_1 to S_2:

$$S_2 = \boldsymbol{X} \cdot S_1. \tag{15}$$

By combining (14) and (15) we obtain $\boldsymbol{S_2} \cdot \vec{p} = \boldsymbol{X} \cdot \boldsymbol{S_1} \cdot \vec{p}$, which is true only if $\boldsymbol{S_2} = \boldsymbol{X} \cdot \boldsymbol{S_1}$. It was proven in Section III.B that, under the above assumptions, just three independent leads are sufficient for uniquely obtaining the dipole $\vec{p}$. Therefore, only three independent leads from $\boldsymbol{S_1}$ are sufficient to obtain the transformation $\boldsymbol{X}$. We will denote the matrix with three arbitrary, linearly independent leads from $\boldsymbol{S_1}$ as $\boldsymbol{S_1^*}$ so we can write:

$$\boldsymbol{S_2} = \boldsymbol{X} \cdot \boldsymbol{S_1^*}, \tag{16}$$

where $\boldsymbol{S_1^*}$ is a square 3×3 matrix with the full rank and hence has the inverse $(\boldsymbol{S_1^*})^{-1}$. By multiplying (16) by $(\boldsymbol{S_1^*})^{-1}$ from the right we obtain

$$\boldsymbol{X} = \boldsymbol{S_2} \cdot (\boldsymbol{S_1^*})^{-1}. \tag{17}$$

Consequently, the linear transformation $\boldsymbol{X}$ between the lead systems S_1 and S_2 can be calculated directly from the lead vectors of both lead systems by employing equation (17). Equation (15) can now be used to transfer the measurements obtained from one lead system to another.

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