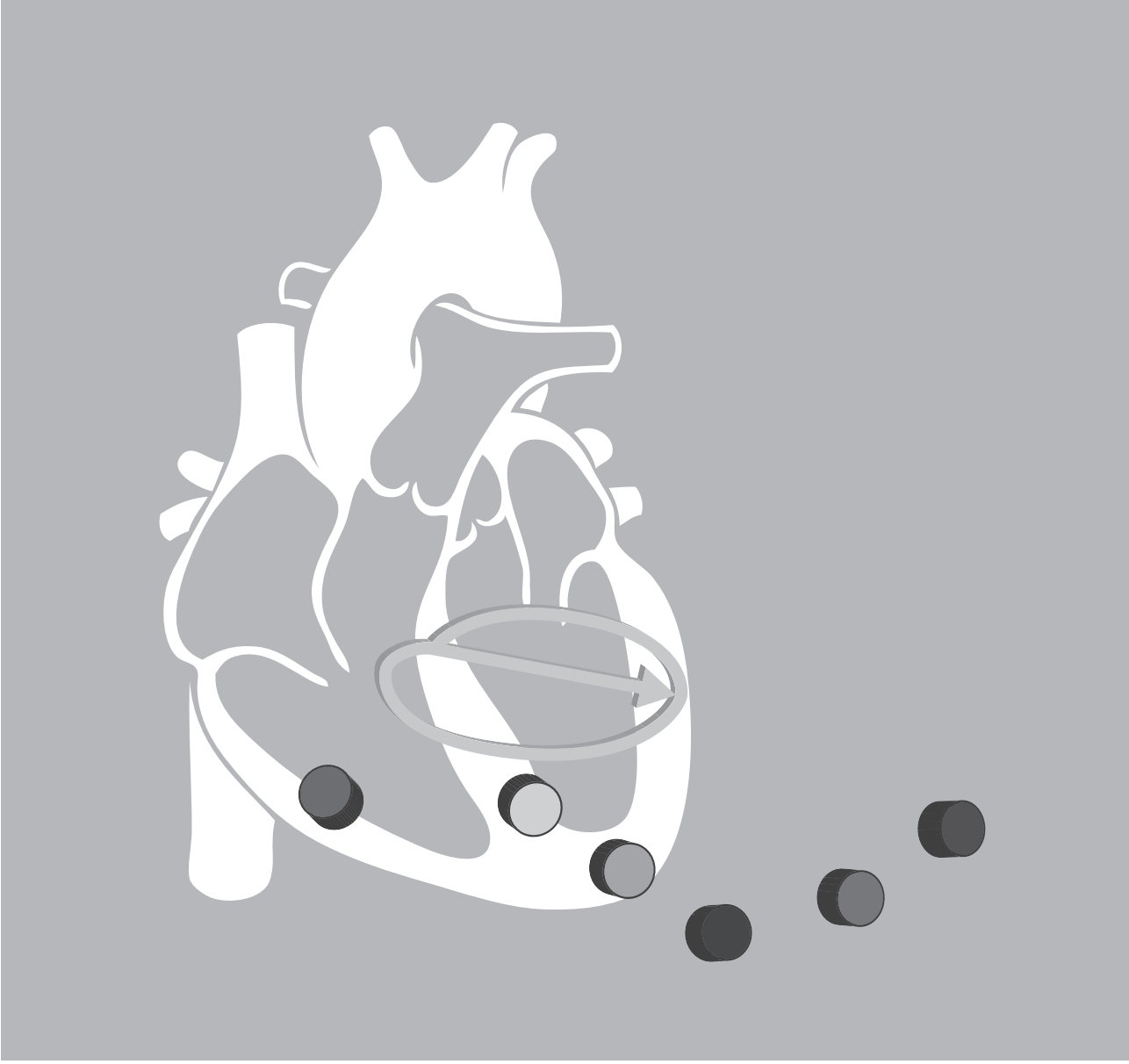

Chapter 2

Reconstruction of standard 12-lead electrocardiograms from 12-lead electrocardiograms recorded with the Mason-Likar electrode configuration

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Abstract

Background

Electrocardiograms (ECGs) made with Mason-Likar electrode configuration (ML-ECGs) show wellknown differences from standard 12-lead ECGs (Std-ECGs).

Methods

We recorded, simultaneously, Std-ECGs and ML-ECGs in 180 subjects. Using these ECGs, 8 × 8 individual and general conversion matrices were created by linear regression, and standard ECGs were reconstructed from ML-ECGs using these matrices. The performance of the matrices was assessed by the root mean square differences between the original Std-ECGs and the reconstructed standard ECGs, by the differences in major ECG parameters, and by comparison of computer-generated diagnostic statements.

Results & Conclusion

As a result, we conclude that, based on the root mean square differences, reconstructions with 8 × 8 individual matrices perform significantly better than reconstructions with the group matrix and perform equally well with respect to the calculation of major electrocardiographic parameters, which gives an improved reliability of the QRS frontal axis and the maximal QRS and T amplitudes. Both types of matrices were able to reverse the underdiagnosis of inferior myocardial infarctions and the erroneous statements about the QRS frontal axis that arose in the ECGs that were made by using the Mason-Likar electrode positions.

Introduction

At various instances, the text of the recently published "Recommendations for the standardization and interpretation of the electrocardiogram[1]" points to the fact that 12-lead ECGs obtained with the 10 electrodes positioned according to Mason and Likar[2] (ML-ECGs) are essentially different from 12-lead ECGs obtained with standard electrode positioning (Std-ECGs). Originally, Mason and Likar proposed their alternative electrode positioning (extremity electrodes on the thorax and abdomen instead of on wrists and ankles) with the purpose to reduce muscle noise and movement artifacts during exercise tests. Nowadays, the Mason-Likar electrode positions are also routinely used for emergency ECGs (ambulance) and for continuous 12-lead intensive care unit ECG monitoring.

Electrode positioning according to Mason and Likar gives the inferiorly directed ECG leads II, III and aVF a more lateral character[3], thereby causing a rightward shift in the orientation of the QRS axis in the frontal plane and reduced Q wave amplitudes in multiple leads. In addition, the ST segment is affected[4]. An extra complication is that the differences between ML-ECGs and a Std-ECGs vary strongly from person to person[4].

Inevitably, the ML-ECG based–diagnosis is sometimes erroneous. Rautaharju *et al.*[4] noted a tendency to overdiagnose left ventricular hypertrophy, codable Q waves and QS patterns in healthy men. Sejersten *et al.*[5] studied 20 patients with chest pain and signs of acute coronary syndrome: the ML-ECG missed signs of ischemia in the form of negative T waves in leads V2-V4 in 1 case, and there was an average 18 μV difference in the ST-segment amplitude in lead V2. Pahlm *et al.*[6] reported that the duration of the Q waves in patients with anterior and inferior infarctions were significantly shorter in lead aVF of the ML-ECG. Several studies[7-9] report that in ML-ECGs, a large fraction of inferior and posterior infarcts is missed.

Based on their own findings and the studies cited above, Sejersten *et al.* state that an ML-ECG–based diagnosis must therefore be considered as preliminary[5], and should be confirmed/corrected on the basis of a Std-ECG. However, a Std-ECG is, in many circumstances, not available. In these cases, a possible solution is the mathematical reconstruction (by matrix conversion[10-25]) of the Std-ECG based on the original recorded ML-ECG.

Attempts to reconstruct a standard ECG from an ML-ECG were so far restricted to the synthesis of the Einthoven extremity leads I and II from the Mason-Likar extremity leads I and II by a 2 x 2 conversion matrix. Such matrices were published by Bartosik *et al.*[10] and by Nelwan *et al.*[23;25]. Generation and performance testing of the conversion matrix was done with ECGs recorded according to the electrode placement strategy described by Pahlm *et al.*[6] In this approach, ECGs are recorded with a regular 12-lead electrocardiograph, while placing the precordial electrodes C1, C4 and C6 at the Mason-Likar extremity electrode positions right arm, left arm and left leg, respectively. In this way, it is possible to compute off-line the simultaneously recorded standard and Mason-Likar extremity leads from the recorded signals.

As the central-terminal voltages of the standard ECG and the Mason-Likar ECG differ, the standard and Mason-Likar precordial leads differ as well. However, the sacrifice of electrodes C1, C4 and C6 in the above-described recording technique precludes the computation of the standard and Mason-Likar precordial leads V1, V4 and V6 in this setting. To overcome this limitation, we recorded in our here-described study 13-electrode ECGs in a population of patients. Thus, we were able to compute and compare complete and simultaneously recorded 12-lead Std-ECGs and ML-ECGs, and to investigate how well a full 3-dimensional (3D) reconstruction of a standard ECG based on an ML-ECG approaches the originally recorded Std-ECG.

Methods

Study population

Study data were a series of consecutively recorded ECGs in subjects visiting the outpatient clinic of the Cardiology Department of our hospital to perform an exercise test for diagnostic or screening purposes. Because of possible deformation of the body surface potential distribution close to the Mason-Likar infraclavicular electrodes, patients with implanted devices were not included in our study. The study group consisted of 180 subjects (101/79 men/women), 54±17 (19–87) years

old, with body mass index (BMI) 26±4 (17–39) kg/m^2 and body surface area (BSA) 1.94±0.22 (1.37–2.60) m^2.

Recording and computation of standard and Mason-Likar ECGs

In each subject, a supine resting ECG was recorded with the "standard 15-lead, 13-electrode placement" modality of a CASE-8000 electrocardiograph (GE Medical Systems, Milwaukee, Wis). The 3 extra chest electrodes C3R, C4R and C7 were, for the purpose of our study, placed at the Mason-Likar positions: C3R and C4R in the right and left infraclavicular fossae, respectively, medial to the border of the deltoid muscle and 2 cm below the lower borders of the clavicles, and C7 at the left iliac crest.

Afterwards, the recorded signals were exported to a PC, and the 8 independent leads I, II, V1 to V6 of the Std-ECGs and of the ML-ECGs were calculated from the 11 simultaneously recorded leads I, II, V1 to V6, V3R, V4R and V7 (the latter 3 leads called after their electrode names, but actually representing the Mason-Likar extremity leads) similar to the calculus described by Pahlm *et al.*[6]. All computations in this study were done in the MATLAB (The MathWorks, Natick, Mass; version R2006b) programming environment.

Computation of conversion matrices; reconstruction of standard ECGs

Subjects were sorted by age and grouped into equally-sized learning (subjects 1&4, 5&8, etc.) and test (subjects 2&3, 6&7, etc.) sets.

For all subjects, individual 8 x 8 Mason-Likar-to-Standard (ML2Std) conversion matrices were generated by multiple linear regression (with the constant = 0), thus minimizing the root mean square differences (RMSD) between the reconstructed standard ECG (ML2Std-ECG) and the originally recorded Std-ECG. This approach, which can be solved by the method of normal equations[26], was first applied for ECG lead transformation by Burger and colleagues[12]. In effect, this method minimizes the RMSD for each reconstructed lead separately, each time generating one 8 x 1 column vector that, after transposition, constitutes one row of the conversion matrix.

Finally, a general 8 x 8 ML2Std conversion matrix (the "Leiden conversion matrix") was generated by applying the multiple linear regression to the concatenated ECGs of the learning set (concatenation of the 10-second ECGs of the 90 subjects in the learning set yielded a 900-second 8-lead "meta–ML-ECG" and a 900-second 8-lead "meta–Std-ECG").

Having computed the individual conversion matrices in all subjects in the learning and in the test sets, and having computed the learning set–based general conversion matrix, individual and general ML2Std-ECG reconstructions were made in all participants. In addition to the minimized RMSD errors per subject per lead that resulted from the individual matrix computations, we computed the overall RMSD errors per subject with individual reconstruction. In addition to the minimized RMSD errors per lead that resulted from the computation of the general conversion matrix, we computed the RMSD errors per subject per lead and the overall RMSD errors per subject with general reconstruction. To assess the amount of RMSD reduction after individual or general reconstruction, we computed also the uncorrected RMSD errors per subject per lead (uncorrected RMSD errors are the RMSD errors between the originally recorded Mason-Likar ECG and the originally recorded standard ECG) and the uncorrected overall RMSD errors per subject. In all cases, the overall RMSD errors per subject were computed by taking the square root of the average of the summed squared differences of all samples in all leads.

Computation of general ECG characteristics

All ECGs (ML-ECG, Std-ECG, the individually reconstructed ML2Std-ECG, and the ML2Std-ECG reconstructed by the general Leiden conversion matrix) of all subjects in the study group were analyzed with the LEADS program, our locally developed computer program for 3D ECG/VCG analysis[27]. The following general ECG characteristics were computed in LEADS: QRS frontal axis ($QRS_{frontal\ axis}$ (°)), magnitude of maximal QRS vector (QRS_{max} (μV)), magnitude of the maximal T vector (T_{max} (μV)), QRS-T spatial angle (SA (°)), spatial ventricular gradient magnitude (magnitude of the spatial ventricular gradient, irrespective of its orientation; SVG_{mag} (mV·ms)), and spatial ventricular gradient magnitude plus orientation (the distance between two spatial ventricular gradients in 3D space; $SVG_{m\&o}$ (mV·ms)). The spatial ventricular gradient is a vector with a magnitude (mV·ms) and spatial orientation (elevation and azimuth (°)). ML-ECGs and ML2Std-ECGs are likely to have errors in both.

Therefore, we choose to express the Mason-Likar induced errors in the ventricular gradient as errors in the ventricular gradient magnitude alone (hence, irrespective of its orientation) as well as in errors in the combination of its magnitude and orientation (3D distance between the spatial ventricular gradient in the uncorrected ML-ECG and the ML2Std-ECG on one hand and the Std-ECG on the other hand).

ECG diagnosis

Finally, all ECGs were transferred to our departmental ECG management system (Dräger Megacare VF3.0) and then analyzed by the University of Glasgow ECG Analysis Program[28]. The Glasgow diagnostic statements were grouped into the following categories (more then one category possible per ECG):

- normal (NML);
- borderline normal (BN);
- any statement about an abnormal frontal plane axis (AX);
- any statement relating to the diagnosis of a myocardial infarction, divided into inferior myocardial infarction (IMI), anterior myocardial infarction (AMI), lateral myocardial infarction (LMI), widespread myocardial infarction (WMI);
- any statement concerning ST-T changes relating to ischemia (STT);
- left or right ventricular hypertrophy (HYP);
- any other statement (OTH).

Statistical analysis

The comparison of performances in terms of RMSD errors, in terms of errors in general ECG characteristics and in terms of ECG diagnostic errors was done with paired or unpaired t-tests, when appropriate. P-values <0.05 were considered significant.

Results

The learning set consisted of 90 subjects (56/34 male/female), aged 54±17 [19–87] years, BMI 25±4 [17–39.1] kg/m^2 and BSA 1.94±0.22 [1.40–2.49] m^2, the test set consisted of 90 subjects (45/45 male/female), aged 54±17 [19–83] years, BMI 26±4 [17–39.4] kg/m^2 and BSA 1.93±0.23 [1.37–2.60] m^2. There were no significant differences between these characteristics of the subjects in the learning set and in the test set.

TABLE 1. The Leiden 8 x 8 general Mason-Likar to standard ECG conversion matrix as computed on the basis of the ECGs in the learning set.

	Mason-Likar leads							
Reconstructed standard leads	I	II	V1	V2	V3	V4	V5	V6
I	1.085	-0.082	-0.027	-0.028	0.034	-0.004	-0.099	0.312
II	-0.035	0.782	0.024	0.022	-0.032	0.012	0.013	-0.030
V1	0.263	-0.108	0.987	-0.020	0.045	-0.020	0.060	-0.153
V2	0.263	-0.108	-0.013	0.980	0.045	-0.020	0.060	-0.153
V3	0.263	-0.108	-0.013	-0.020	1.045	-0.020	0.060	-0.153
V4	0.263	-0.108	-0.013	-0.020	0.045	0.981	0.060	-0.153
V5	0.263	-0.108	-0.013	-0.020	0.045	-0.020	1.060	-0.153
V6	0.263	-0.108	-0.013	-0.020	0.045	-0.020	0.060	0.847

The coefficients of the general Leiden 8 x 8 Mason-Likar to standard ECG conversion matrix, computed on the basis of the learning set, are given in Table 1. The minimized lead-dependent RMSD values that resulted from the linear regression procedure were 33 μV for lead I, 25 μV for lead II, and 18 μV for leads V1-V6.

Descriptive statistics of the RMSD errors per subject, per lead and overall for all leads, for the uncorrected Mason-Likar ECG and for the generally and individually reconstructed standard ECG, as computed in the learning and test sets, are given in Table 2. Conversion of the ECGs in the learning set by the Leiden matrix reduced the original, uncorrected overall RMSD per subject between the standard ECG and the Mason-Likar ECG from 34 ± 17 μV to 18 ± 13 μV (reduction by 48%, $P<0.001$). In the test set, the original, uncorrected overall RMSD between the standard ECG and the Mason-Likar ECG was 35 ± 14 μV; after application of the Leiden conversion matrix, this was reduced to 16 ± 9 μV (reduction by 55%, $P<0.001$). ECG reconstruction with individual matrices further reduced the overall RMSD per subject to 8 ± 9 μV ($P<0.001$) in the learning set and to 8 ± 4 μV ($P<0.001$) in the test set. The uncorrected RMSD errors in leads I and II were significantly ($P<0.001$) larger that the uncorrected RMSD errors in leads V1-V6. All RMSD errors after general or individual reconstruction were significantly ($P<0.001$) smaller than the uncorrected RMSD errors. All RMSD errors after individual reconstruction were significantly (all $P<0.001$, except $P=0.016$ for lead I in the learning set) smaller than the RMSD errors after general reconstruction.

TABLE 2. RMSD errors per subject: overall (All leads), and for lead I, II, and V1-V6. RMSD errors were computed between the standard ECGs and the uncorrected Mason-Likar ECGs (Uncorrected), the individually corrected ECGs (Individual) and the generally learning-set based reconstructed ECGs (General), respectively. The overall RMSD errors per subject were computed by taking the square root of the average of the summed squared differences of all samples in all leads. Data are from the learning and test sets. All uncorrected RMSD errors of lead I and II are significantly larger than the uncorrected RMSD errors of leads V1-V6 (P<0.001). All RMSD errors after individual and general reconstruction are significantly smaller than the uncorrected RMSD errors (P<0.001). All RMSD errors after individual reconstruction are significantly smaller than after general reconstruction (All P<0.001, except P=0.016 for lead I in the learning set).

Learning Set		**RMSD errors (μV)**		
		Mean ± SD	**Median**	**Range**
Lead I	Uncorrected	41±25	38	14-234
	General	23±24	17	9-230
	Individual	15±22	11	6-212
Lead II	Uncorrected	49±24	43	20-169
	General	21±15	16	7-96
	Individual	13±8	11	6-73
Lead V1-V6	Uncorrected	27±19	22	6-134
	General	15±11	11	4-57
	Individual	5±4	4	2-34
All leads	Uncorrected	34±17	30	13-118
	General	18±13	13	7-84
	Individual	8±9	7	4-76
Test Set		**RMSD errors (μV)**		
		Mean ± SD	**Median**	**Range**
Lead I	Uncorrected	42±18	38	18-133
	General	21±10	18	9-57
	Individual	13±6	11	6-35
Lead II	Uncorrected	50±22	45	12-163
	General	19±11	16	9-85
	Individual	13±7	11	6-60
Lead V1-V6	Uncorrected	28±16	22	6-97
	General	13±9	10	4-74
	Individual	4±3	4	2-28
All leads	Uncorrected	35±14	32	12-98
	General	16±9	15	7-73
	Individual	8±4	7	4-34

TABLE 3. Differences in general ECG parameter values between the standard ECGs and the uncorrected Mason-Likar ECGs, the standard ECGs as reconstructed with the general, learning-set-based conversion matrix, and the standard ECGs as reconstructed with the individual matrices, respectively. Data are from the test set. Data in each cell are: mean ± SD of the signed errors (upper line), range of the signed errors (upper line, between brackets) and mean ± SD of the absolute errors (lower line, between parentheses). QRS_{max} (μV) = maximal QRS vector; T_{max} (μV) = maximal T vector; SA(°) = spatial QRS-T angle; SVG_{mag} = spatial ventricular gradient magnitude; $SVG_{m\&o}$ = spatial ventricular gradient magnitude and orientation.

Performance measure	Original Uncorrected error	Error after General reconstruction	Error after Individual reconstruction	$P_{General\ reconstruction}$	$P_{Individual\ reconstruction}$
$QRS_{frontal\ axis}$ (°)	22±15 [-29–57] (23±13)	1±8 [-14–32] (5±6)	0±2 [-4–2] (1±1)	<0.001 (<0.001)	<0.001 (<0.001)
QRS_{max} (μV)	113±126 [-144–455] (134±104)	-2±42 [-138–122] (30±29)	3±19 [-67–106] (10±16)	<0.001 (<0.001)	<0.001 (<0.001)
T_{max} (μV)	26±38 [-71–164] (34±31)	1±11 [-31–25] (8±8)	0±8 [-17–51] (4±7)	<0.001 (<0.001)	<0.001 (<0.001)
SA (°)	-3±8 [15–22] (7±4)	1±3 [-11–9] (2±2)	1±1 [-3–6] (1±1)	<0.001 (<0.001)	<0.001 (<0.001)
SVG_{mag} (mV·ms)	6±7 [-11–31] (7±6)	0±2 [-8–4] (2±1)	0±1 [-4–3] (1±1)	<0.001 (<0.001)	<0.001 (<0.001)
$SVG_{m\&o}$ (mV·ms)	10±5 [2-28]	3±2 [0-14]	2±2 [0-17]	<0.001	<0.001

TABLE 4. Diagnostic statements, learning set. The statements generated by the Glasgow program in the standard (Std), individually reconstructed (Ind), generally reconstructed with the Leiden conversion matrix (Gen) and Mason-Likar (ML) ECGs were grouped into the following categories: NML = normal; BN = borderline normal; AX = any diagnostic statement about the frontal QRS axis; IMI = inferior myocardial infarction; AMI = anterior myocardial infarction; LMI = lateral myocardial infarction; WMI = widespread myocardial infarction; ST-T changes related to ischemia; HYP = left- or right ventricular hypertrophy; OTH = any diagnostic statement that does not fit into one of the other categories. An ECG may have more than 1 diagnostic statement. The majority of the false positive values for NML and BN are due to crossover between these groups.

		Correct Positive			False Positive		
	Std	Ind	Gen	ML	Ind	Gen	ML
NML	40	39	40	37	3	3	2
BN	12	7	9	11	0	2	3
AX	12	12	10	7	0	0	0
IMI	8	7	6	5	0	0	0
AMI	3	3	3	3	0	0	0
LMI	4	4	4	4	0	0	0
WMI	1	1	1	1	0	0	0
STT	13	12	10	11	0	0	1
HYP	6	6	6	6	0	0	0
OTH	7	7	7	5	1	0	0

Descriptive statistics of the differences in the general ECG parameter values ($QRS_{frontal\ axis}$, QRS_{max}, T_{max}, SA, SVG_{mag} and $SVG_{m\&o}$) between the uncorrected Mason-Likar ECGs, the generally and individually reconstructed standard ECGs on one hand, and the recorded standard ECGs on the other hand are given in Table 3. All parameter differences after general or individual reconstruction were significantly ($P<0.001$) smaller than the uncorrected parameter differences.

The correct and false positive diagnostic statements in the Mason-Likar ECGs, the standard ECGs reconstructed with the general conversion matrix and the standard ECGs reconstructed with the individual conversion matrices are given in Tables 4 (learning set), 5 (test set) and 6 (complete study group).

TABLE 5. Diagnostic statements, test set. See legend of Table 4 for explanation.

		Correct Positive			False Positive		
	Std	Ind	Gen	ML	Ind	Gen	ML
NML	40	34	33	30	2	3	3
BN	17	14	14	16	6	5	10
AX	6	6	5	5	1	1	1
IMI	4	4	4	1	2	3	1
AMI	3	3	3	2	0	0	0
LMI	2	2	1	0	0	0	0
WMI	0	0	0	0	0	0	0
STT	13	13	12	11	1	2	3
HYP	6	5	6	5	0	0	2
OTH	5	5	5	4	0	1	1

TABLE 6. Diagnostic statements, total study group. See legend of Table 4 for explanation.

		Correct Positive			False Positive		
	Std	Ind	Gen	ML	Ind	Gen	ML
NML	80	73	73	67	5	6	5
BN	29	21	23	27	6	7	13
AX	18	18	15	12	1	1	1
IMI	12	11	10	6	2	3	1
AMI	6	6	6	5	0	0	0
LMI	6	6	5	4	0	0	0
WMI	1	1	1	1	0	0	0
STT	26	25	22	22	1	2	4
HYP	12	11	12	11	0	0	2
OTH	12	12	12	9	1	1	1

Discussion

Genesis of ECG conversion matrices by the normal equations method

Multiple studies report about the transformation of ECGs from one lead set into another lead set[10-25]. Such transformation is usually done by matrix multiplication; the rows in the transformation matrix (or conversion matrix) are commonly computed by multiple linear regression, a procedure that minimizes the squared amplitude differences between the reconstructed and the recorded ECG leads. For the computation of the conversion matrix, original samples of the leads to be transformed as well as of the leads to be reconstructed are required. The here presented conversion matrix is the first to reconstruct the complete (10-electrode) standard ECG from the complete (10-electrode) Mason-Likar ECG.

The regression procedure is separately executed for each lead to be reconstructed. Given an *m*x*n* matrix *A* (with *n* the number of leads in the ECG to be transformed, *m* the number of samples/amplitudes in each lead, and *A* the ECG to be transformed), the algorithm finds, for each lead **b** to be reconstructed (with **b** a *m*x1 column vector with the original samples in the reconstructed lead), a *n*x1 column vector **x** in such a way that the residue vector $\mathbf{r} = \mathbf{b} - A\mathbf{x}$ (with **r** a *m*x1 column vector with the *m* amplitude differences between the original and reconstructed samples for the reconstructed lead, and $A\mathbf{x}$ the reconstructed samples in the reconstructed lead) is as small as possible. The normal equations theorem states that the residue vector **r** has its minimal size (square root of summed squared amplitude differences in all samples) when $\mathbf{x} = (A^T A)^{-1} A^T \mathbf{b}$.

The seminal publication that introduced the multiple linear regression method to transform ECGs from one lead set into the other was the 1962 paper by Burger and colleagues[12]. They computed matrices to transform four alternative VCG lead systems into each other. Importantly, the original measurements (columns of matrix *A*, column vectors **b**) were composed of concatenated groups of ECG amplitudes of all 169 subjects (41 normal subjects and 128 patients with heart disease) in the study. In this way, an "averaged transformation" matrix was computed for the group. Since then, concatenation of data of multiple subjects has become the standard in the computation of generalized, group based matrices[10-12;17;20-25]; this concept was also applied in our current study.

Burger stresses the importance of taking "isophasic" ECG amplitudes (*i.e.*, measurement points that are temporally coincidental in the cardiac cycle) for the transformation. This is especially important when the originally recorded lead sets (in matrix *A* and in the column vectors **b**) have not been obtained simultaneously. In that case, the ECG amplitudes that represent the ECG to be transformed (in matrix *A*) are derived from another heart beat than the ECG amplitudes that represent the ECG to be reconstructed (in column vectors **b**). Burger and colleagues characterized each VCG lead by five equidistant amplitudes taken at corresponding points in the QRS loops of the VCG to be transformed and of the VCG to be reconstructed (Figure 5 in [11]). The number of samples, five, was purposely kept small to limit the computational burden, while the condition of isophasic data points was considered to be met best when taken from the QRS complex.

Burger *et al.* recognized the potential problem that a QRS-based transformation matrix might not be fully valid for the reconstruction of other parts of the ECG, like the P wave or the T wave. This was checked, and the authors found "satisfactory" results for T wave reconstruction with a QRS-based transformation matrix (no numerical data were presented, however). In our study, the coincidental, isophasic, nature of the ECG samples to be transformed and to be reconstructed is perfect, because these ECGs were recorded simultaneously. This frees our approach from the burden of incompatibilities, caused by beat-to-beat variability in the ECG, between the data to be transformed and the data to be reconstructed. Also, our conversion matrix is representative for the complete ECG as we entered in the regression procedure the full 10s ECG recording, which is not associated with a specific part of the ECG cycle. The large number of 450000 equations (10 seconds x 500 samples/second x 90 subjects) for each reconstructed lead should yield a stable general matrix, of which the value for the reconstruction of a standard ECG from a Mason-Likar ECG should mainly depend on the representativeness of the learning set and on the question how well a general, "averaged", transform can handle individual variations in a population.

Representativeness of the learning set for the test set

The ECGs were divided into a learning set and a test set of equal size by an algorithm based on age order. Age order has no relationship with any of the

anthropomorphic characteristics of the subjects or with any ECG property. From the data presented in the Results section it is obvious that this objective algorithm to distribute subjects over the learning and test sets was effective for the equal distribution of length, weight, BMI, and BSA, and (less so) for gender. Also, the RMSD errors of the learning and the test sets were not different. However, the distribution of the diagnostic statements over the learning and the test sets is not very well matched (compare Tables 3 and 4). We believe that this is no drawback in our study, and have not done further attempts to get a more even distribution of diagnostic statements over the learning and the test set. Indeed, the Mason-Likar distortion of the ECG is a consequence of the volume conduction properties of the torso and extremities and not of the underlying heart disease.

Reduction of Mason-Likar-induced RMSD errors by general and individual reconstruction

Table 2 shows that the uncorrected RMSD errors were larger in the limb leads than in the chest leads ($P<0.001$). The extreme values show that the uncorrected lead I and II RMSD errors may assume very large values in certain individuals, indeed. Obviously, the contributions of the QRS-T complex to the RMSD error are larger than that of the remaining part of the cardiac cycle, where amplitudes in all leads are relatively small. Hence, the RMSD error values as listed in Table 2 (averaged over the complete cardiac cycle) must be interpreted as considerable differences between Mason-Likar and standard ECGs.

The fact that the uncorrected RMSD errors in the precordial leads are >0 illustrates that Mason-Likar electrode positioning affects not only the limb leads but also the precordial leads, because of a difference in central terminal potential. The smaller amount of RMSD error in the Mason-Likar precordial leads as compared to the RMSD error in the limb leads can be explained by the fact that the precordial electrode positions remain unaffected in the Mason-Likar ECG, and by the fact that the central terminal potential, being an average of the limb electrode potentials, is less sensitive to limb electrode displacements than the individual limb electrode potentials are.

The data in Table 2 show that individual reconstruction of the standard ECG strongly reduces the Mason-Likar induced RMSD errors: mean and median values

were reduced by a factor 3 or more. Large part of this RMSD error reduction is already achieved by general reconstruction.

Reduction of Mason-Likar-induced errors in global ECG parameter values by general and individual reconstruction

Table 3 shows that reconstruction by individual conversion matrices strongly reduces errors in the general ECG parameters. Part of this error reduction can already be achieved by reconstruction with the general conversion matrix. Apart from bias removal (*e.g.*, in the $QRS_{frontal\ axis}$) also extreme errors in single individuals (as apparent from the ranges in the errors in Table 3) are reduced by general and individual reconstruction.

Reduction of Mason-Likar induced diagnostic errors by general and individual reconstruction

Realizing that the matrices were not optimized for diagnosis but for RMSD error, and given that the size of the learning and test set (90 subjects both, which means that the ECG of one given subject has only limited influence on its own successful diagnosis) it is unlikely that the diagnostic error in a given individual is better compensated by general reconstruction in the learning set (Table 4) than in the test set (Table 5). Hence, in our opinion, the best impression of how well diagnostic improvements can be achieved by general or individual reconstruction is by considering the pooled data of the study group (Table 6).

Table 6 underscores what has been observed earlier[7-9], *i.e.*, that the false negative diagnosis of inferior infarctions is the most striking problem in Mason-Likar ECGs. In our study group, of the 12 inferior infarctions present, 6 (50%) were missed in the Mason-Likar ECG. Reconstruction by the general Leiden conversion matrix reduced the false negative diagnosis to 2 cases (16%), while individual reconstruction led to 1 missed case only. Although individual reconstruction is the best possible reconstruction, the general reconstruction by the Leiden conversion matrix reached a high degree of effectiveness in the diagnosis of inferior infarction. A certain toll has to be paid, however, in terms of false positive diagnosed inferior infarctions.

Similar reasonings, but less outspoken, can be held for other diagnostic categories. Of note: individual reconstruction could not prevent that in several cases diagnostic errors were still made.

Limitations

It is a limitation of our study that no ECGs with acute ischemia have been studied; therefore the diagnostic improvement after ECG reconstruction with the Leiden matrix in those conditions could not be estimated. This is an important issue, as according to current insight, the triage of patients with acute coronary syndrome should already occur in the ambulance[29], where usually a Mason-Likar ECG is recorded.

Conclusion

In conclusion, Mason-Likar ECGs lead to ECG distortion and diagnostic errors that can partly be reduced by mathematical reconstruction of the standard ECG by a conversion matrix. General reconstruction by the Leiden conversion matrix removes already most of the errors that can be removed by individual reconstruction. In cases where ECG diagnosis is decisive for triage and a standard ECG is not available, a standard ECG could be reconstructed from the Mason-Likar ECG by using a general conversion matrix like our here proposed Leiden matrix. By combining the Mason-Likar and the reconstructed ECG diagnoses clinical decision making could be improved. Future research should be done to assess the value of this approach.

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Appendix: Stability of the Leiden conversion matrix

The Leiden 8 x 8 general Mason-Likar to standard ECG conversion matrix (Table 1) was computed from the ECGs recorded in the 90 subjects in the learning set. Ideally, when the matrix would be computed from the ECGs recorded in the 90 subjects in the test set, the matrix coefficients should be the same. No or little change in the matrix coefficients would indicate that the learning and test sets are representative samples and that the conversion matrix is stable. A potential danger of instability of the matrix is constituted by the fact that ECG leads do not bear completely independent information. *E.g.*, leads I and V6 generally look very similar. Hence, a small modification in the composition of the group that is used for the generation of a general conversion matrix could eventually result in lead V6 taking over (by getting a larger coefficient) from lead I (that gets a smaller coefficient), or vice versa. Although the operational reconstruction properties of the matrix could remain almost unchanged in such cases, such instability of matrix coefficients is not an attractive feature. Therefore, we did some additional experiments to investigate the stability of the Leiden conversion matrix: alternative matrices were computed based on the test set and based on all ECGs of the study group, respectively.

Changes in the matrix coefficients with respect to the conversion matrix in Table 1, when the matrix is based on the test set instead of on the learning set are listed in Table 7. This Table shows that all coefficients changed little (the maximum change was 0.053).

TABLE 7. Changes in the conversion matrix coefficients with respect to the matrix in Table 1, when the conversion matrix is based on the test set instead of on the learning set. Positive/negative differences mean that the coefficients in the test-set based matrix are larger/smaller than the coefficients in Table 1.

	Mason-Likar leads							
Reconstructed standard leads	I	II	V1	V2	V3	V4	V5	V6
I	-0.042	-0.021	0.013	-0.012	0.035	-0.050	0.047	0.037
II	-0.027	0.013	-0.012	-0.010	0.035	-0.038	0.041	-0.030
V1	-0.053	-0.034	-0.040	0.046	-0.051	0.034	-0.005	0.026
V2	-0.053	-0.034	-0.040	0.046	-0.051	0.034	-0.005	0.026
V3	-0.053	-0.034	-0.040	0.046	-0.051	0.034	-0.005	0.026
V4	-0.053	-0.034	-0.040	0.046	-0.051	0.034	-0.005	0.026
V5	-0.053	-0.034	-0.040	0.046	-0.051	0.034	-0.005	0.026
V6	-0.053	-0.034	-0.040	0.046	-0.051	0.034	-0.005	0.026

The impact of these matrix coefficient changes can be assessed by comparing the descriptive statistics of the RMSD errors in the learning and in the test set, after ECG reconstruction with either the learning-set based or with the test-set based matrix (see Table 8). The RMSD performances of both matrices are strikingly

TABLE 8. Comparison of the RMSD errors between the generally learning-set based reconstructions (Learning-set based) and the generally test-set based reconstructions (Test-set based). Descriptive statistics of the RMSD errors per subject overall (All leads), and for lead I, II, and V1-V6. RMSD errors were computed between the standard ECGs and the uncorrected Mason-Likar ECGs (Uncorrected) and the generally test-set based reconstructed ECGs, respectively. The overall RMSD errors per subject were computed by taking the square root of the average of the summed squared differences of all samples in all leads. All uncorrected RMSD errors of lead I and II are significantly larger than the uncorrected RMSD errors of leads V1-V6 ($P<0.001$). All RMSD errors after general reconstruction are significantly smaller than the uncorrected RMSD errors ($P<0.001$). All RMSD errors after generally test-set based reconstruction are significantly not different from the RMSD errors after generally learning-set based reconstruction.

Learning Set		**RSMD errors (μV)**		
		Mean ± SD	**Median**	**Range**
Lead I	Uncorrected	41±25	38	14-234
	Learning-set based	23±24	17	9-230
	Test-set based	24±24	18	9-231
Lead II	Uncorrected	49±24	43	20-169
	Learning-set based	21±15	16	7-96
	Test-set based	21±15	17	7-97
Lead V1-V6	Uncorrected	27±19	22	6-134
	Learning-set based	15±11	11	4-57
	Test-set based	15±12	10	4-58
All leads	Uncorrected	34±17	30	13-118
	Learning-set based	18±13	13	7-84
	Test-set based	18±13	13	6-85
Test Set		**RSMD errors (μV)**		
		Mean ± SD	**Median**	**Range**
Lead I	Uncorrected	42±18	38	18-133
	Learning-set based	21±10	18	9-57
	Test-set based	21±9	19	9-49
Lead II	Uncorrected	50±22	45	12-163
	Learning-set based	19±11	16	9-85
	Test-set based	19±11	16	9-87
Lead V1-V6	Uncorrected	28±16	22	6-97
	Learning-set based	13±9	10	4-74
	Test-set based	12±10	9	3-80
All leads	Uncorrected	35±14	32	12-98
	Learning-set based	16±9	15	7-73
	Test-set based	15±9	13	6-77

similar: for RMSD error reduction it seems irrelevant by which of the two general matrices the reconstruction of the standard ECG was performed.

Alternatively, to investigate matrix stability, we can compute the conversion matrix on the basis of the data of all 180 subjects. The extra value of this matrix would be that it is computed on the basis of a larger group of subjects; the disadvantage of using this matrix would be that no validation is possible (validation would require doubling of the study group to create a test set). Changes in the matrix coefficients with respect to the conversion matrix in Table 1, when the matrix is based on the data of all 180 patients in the study group instead of on the learning set are listed in Table 9. As expected, the changes in the matrix coefficients were smaller (maximum change was 0.030). Descriptive statistics of the RMSD errors in the total study group, after ECG reconstruction with the total study group based matrix are given in Table 10. Again, no improvement of the RMSD error reduction can be seen.

Because the changes in the matrix coefficients, when the matrix is computed on the basis of a different group of subjects, do not result in substantial changes in RMSD error reduction performance, we may assume that the Leiden matrix for reconstruction of a standard ECG from a Mason-Likar ECG is stable, and that not much improvement can be expected when the amount of subjects in the study group would be increased.

TABLE 9. Changes in the conversion matrix coefficients with respect to the matrix in Table 1, when the conversion matrix is based on the data of all 180 patients in the study group instead of the learning set. Positive/negative differences mean that the coefficients in the complete study group based matrix are larger/smaller than the coefficients in Table 1.

		Mason-Likar leads							
		I	II	V1	V2	V3	V4	V5	V6
Reconstructed standard leads	I	-0.019	-0.012	0.005	-0.007	0.020	-0.029	0.030	0.016
	II	-0.011	0.006	-0.004	-0.009	0.020	-0.021	0.027	-0.023
	V1	-0.022	-0.018	-0.014	0.024	-0.029	0.018	-0.007	0.021
	V2	-0.022	-0.018	-0.014	0.024	-0.029	0.018	-0.007	0.021
	V3	-0.022	-0.018	-0.014	0.024	-0.029	0.018	-0.007	0.021
	V4	-0.022	-0.018	-0.014	0.024	-0.029	0.018	-0.007	0.021
	V5	-0.022	-0.018	-0.014	0.024	-0.029	0.018	-0.007	0.021
	V6	-0.022	-0.018	-0.014	0.024	-0.029	0.018	-0.007	0.021

TABLE 10. Descriptive statistics of the RMSD errors per subject overall (All leads), and for lead I, II, and V1-V6. RMSD errors were computed between the standard ECGs and the uncorrected Mason-Likar ECGs (Uncorrected) and the generally total-group based (Total-group based) reconstructed ECGs, respectively. The overall RMSD errors per subject were computed by taking the square root of the average of the summed squared differences of all samples in all leads. All uncorrected RMSD errors of lead I and II are significantly larger than the uncorrected RMSD errors of leads V1-V6 (P<0.001). All RMSD errors after general reconstruction are significantly smaller than the uncorrected RMSD errors (P<0.001).

Total study group		RSMD errors (μV)		
		Mean ± SD	Median	Range
Lead I	Uncorrected	41±22	38	14-234
	Total-group based	22±18	19	9-230
Lead II	Uncorrected	49±23	44	12-169
	Total-group based	20±13	16	7-97
Lead V1-V6	Uncorrected	28±18	22	6-134
	Total-group based	13±11	10	4-77
All leads	Uncorrected	35±16	30	12-118
	Total-group based	16±11	13	6-84

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