Influence of the Training Set Size on the Subject-to-Subject Variability of the Estimation Performance of Linear ECG-Lead Transformations

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Abstract

Linear ECG-lead transformations (LELTs) are used to estimate unrecorded leads by applying a number of recorded leads to a LELT matrix. Such LELT matrices are commonly developed using a training dataset and linear regression analysis. An important performance metric of LELTs is the subject-to-subject variability (SSV) of their estimation performance. In this research, we assess the relationship between an increasing training set size (from n=10 to n=370 subjects) and the SSV of LELTs.

A total of 200 LELT matrices were developed for each training sets size. The developed LELT matrices and 12-lead ECG data of a testing dataset (n=123 subjects) were used for the estimation of Frank VCGs. Root-mean-squared-error (RMSE) values between recorded and estimated Frank VCG leads were used for the quantification of the estimation performance. The SSV associated with each LELT matrix was quantified as the standard deviation of the corresponding RMSE values. This was followed by an analysis of the relationship between the training set size and the associated SSV values.

Increasing the training set size from 10 to 180, to 160 and to 200 subjects, for Frank VCG leads X, Y and Z respectively, was associated with a reduction of the observed SSV. Further increases in training set size were found to only have a marginal effect on the observed SSV.

1. Introduction

Linear electrocardiographic (ECG) lead transformations (LELTs) are used to estimate or derive unrecorded target leads by applying a number of recorded basis leads to a LELT matrix [1], [2]. A LELT matrix is commonly developed using a training dataset that is assembled using ECG data from different subjects. One set of target leads and basis leads is included for each subject in the training dataset. Multivariate linear regression analysis is typically used to develop the LELT matrixes from the ECG data of the training dataset [1], [3].

LELT matrices are frequently used to derive target leads that are not recorded in clinical practice but are thought to provide additional prognostic or diagnostic value. Examples of such target leads are the leads of the Frank VCG [2] – [4] or the so-called vessel specific leads [5]. The 12-lead ECG is frequently used as the basis lead set of LELT matrices. This is the because it is the most widely adopted ECG recording format [6] and therefore allows for an easy integration of LELT derived target leads into clinical practice without the need of recording additional non-standard ECG leads.

It is desirable that LELT matrices are capable of producing accurate estimates of the target leads for all members of the target population. Increasing the size of the training set up to a certain limit has been shown to increase the mean estimation performance of LELTs [7]. However, well performing LELT matrices should not only have an acceptable mean estimation performance, they should ideally also perform equally well for all members of the target population. The subject-to-subject variability (SSV) of the estimation performance is therefore an important performance metric of LELTs.

Recording a large training set in an attempt to minimize the SSV of a new LELT matrix is potentially a time and cost expensive procedure. It would therefore be desirable to have an understanding of the relationship between the training set size and the SSV of LELTs. However, an analysis of this relationship has, to the best of our knowledge, not previously been reported in the literature.

The aim of our research is twofold. First, we aim to assess the relationship between the size of the training set and the SSV of LELT matrices. Second, we aim to quantify a sufficient training set size that allows for the development of LELT matrices with low associated levels of SSV.

2. Material and methods

2.1. Study population

Our study population was composed of 228 normal

subjects and 265 subjects with myocardial infarction. Random sampling was used to partition the study population into a test dataset ($DTest$) and a training dataset ($DTrain$). The ECG data of 123 subjects was used to assemble $DTest$. Data from the remaining 370 subjects was used to assemble training datasets of varying size. Table 1 details the composition of $DTest$ and $DTrain$.

Table 1. Composition of the test data ($DTest$) and the train data ($DTrain$).

	Normal	MI	Total
$DTest$	57	66	123
$DTrain$	171	199	370

Notes. ***Normal****, Subjects with no abnormalities in their ECGs;* ***MI****, Subjects with myocardial infarction.*

2.2. BSPM data

One body surface potential map (BSPM) was recorded for each of the 493 subjects in the study population. Each BSPM used in this research contains electrocardiographic data of 120 BSPM leads. A representative average QRS-T complex was calculated for each of the 120 BSPM leads. Three of the 120 leads were recorded from electrodes placed on the right and left wrist and the left ankle (VR, VL and VF respectively). Electrodes situated at 81 anterior and 36 posterior locations were used to record 117 thoracic leads. All thoracic leads were recorded with reference to the Wilson central terminal (WCT). A comprehensive description of the recording procedure can be found in [8]. A Laplacian 3D interpolation procedure [9] was applied to the 117 thoracic BSPM leads. This was performed to obtain body surface potentials at the locations of the 352 Dalhousie torso [10] nodes. Body surface potentials from electrode locations that were not a direct subset of the 352 Dalhousie torso nodes were obtained using linear interpolation [11].

2.2. Target and basis leads of the LELTs

The standard 12-lead ECG is the most widely adopted ECG recording format [6]. This has made the eight independent leads I, II, V1 to V6 of the standard 12-lead ECG a popular basis lead set that is used in different LELTs. We have therefore, used the eight independent leads of the standard 12-lead ECG as the basis lead set of the LELT matrices that were assessed in this research. The leads of this basis lead set were extracted form the BSPM data of each subject in the study population.

Currently, LELT matrices are used to estimate a variety of different target leads [1],[5],[12]. The aim of our research was to assess the relationship between the training set size and the SSV of LELTs such that the findings provide an insight into this relationship that is independent of the particular target lead. In an attempt to obtain a target lead independent inside of this relationship, we have chosen the three orthogonal leads of the Frank VCG [4] as the target lead set. This choice was based upon the heart-vector model [13] of the cardiac electrical activity that allows the expression of any ECG lead as a weighted sum of the three orthogonal Frank VCG leads.

Average QRS-T complexes of the basis leads and target leads were extracted from the interpolated BSPM data. More precisely, body surface potentials on the right wrist, the left wrist, the left ankle and from the location of the six precordial electrodes were used for the determination of the basis leads. In addition, body surface potentials at the A, C, E, F, H, I and M electrode locations of the Frank lead system [4] were used to determine the target leads using a matrix of published coefficients [14].

2.3. Development of the LELT matrices

The data in $DTrain$ was used to assemble training datasets of different sizes. More precisely, training datasets staring from n = 10 to n = 360 subjects were generated in steps of 10 subjects. Random sampling with replacement was used to compose 200 different instances of each training set size using the data in $DTrain$. The different training dataset instances were used to generate a total of 200 LELT matrices for each training set size. The LELT matrices that allow for the estimation of the Frank VCG from the standard 12-lead ECG were developed using the multivariate linear regression based approach in (1).

$$ {}_{m}\boldsymbol{AVCG_i} = \left({}_{m}\boldsymbol{BL_i^T} \cdot {}_{m}\boldsymbol{BL_i} \right)^{-1} \cdot {}_{m}\boldsymbol{BL_i^T} \cdot {}_{m}\boldsymbol{TL_i}. \quad (1) $$

Where $[\cdot]^{\boldsymbol{T}}$ and $[\cdot]^{-\boldsymbol{1}}$denote the transpose and the inverse of a matrix respectively, ${}_{m}\boldsymbol{AVCG_i}$ refers to a 8×3 matrix of transformation coefficients that allows for the transformation of the basis leads into the target leads, $m \in \{10, \dots, 370\}$ denotes the size of the training dataset, n refers to the number of QRS-T sample values in the training dataset of size m, $i \in \{1, \dots, 200\}$ denotes the instance of the training dataset that was used for the development of ${}_{m}\boldsymbol{AVCG_i}$, ${}_{m}\boldsymbol{TL_i}$ refers to a $n \times 3$ matrix that contains n sample values of the target leads and ${}_{m}\boldsymbol{BL_i}$ refers to a $n \times 8$ matrix that contains n sample values of the basis leads.

2.4. Derivation of the target leads

The ${}_{m}\boldsymbol{AVCG_i}$ matrices were used to derive the target leads of the 123 subjects in $DTest$. This was performed using the approach in (2) and for all LELT matrices with $i \in \{1, \dots, 200\}$ and $m \in \{10, \dots, 370\}$.

$$ {}_{m}\boldsymbol{dTL_i} = \boldsymbol{BL} \cdot {}_{m}\boldsymbol{AVCG_i}. \quad (2) $$

Where ${}_{m}\boldsymbol{AVCG_i}$, m and i are as defined in (1), $\boldsymbol{BL}$ is a $n \times 8$ matrix that contains the n sample values of the QRS-T complex from the basis leads of one subject in $DTest$ and ${}_{m}\boldsymbol{dTL_i}$ is $n \times 3$ matrices that contain the derived target leads.

2.5. Performance assessment

The relationship between the training set size and the SSV of the associated LELT matrices was assessed as detailed subsequently.

First, root mean square error (RMSE) values were calculated between the QRS-T complexes of the recorded and the derived target leads. This was performed for each $_{m}\boldsymbol{AVCG_i}$ matrix and for each of the 123 subjects in $DTest$. Second, the SSV of the estimation performance of each $_{m}\boldsymbol{AVCG_i}$ matrix was quantified by calculating the standard deviation of the associated RMSE values. This was performed separately for each of the three Frank VCG leads. The outcome of this assessment was a 200×37 matrix of $^{SSV}_{m}\boldsymbol{VCG}_i$ elements. Where each $^{SSV}_{m}\boldsymbol{VCG}_i$ contains a SSV value for each of the three Frank VCG leads, $i \in \{1, \dots, 200\}$ and $m \in \{10, \dots, 370\}$ respectively denote the instance and size of the training dataset hat was used for the development of the $_{m}\boldsymbol{AVCG_i}$ matrix associated with the values in $^{SSV}_{m}\boldsymbol{VCG}_i$. Third, the median and the span (difference between the 97.5th and 2.5th percentile) of the SSV values were calculated for each of the Frank leads. This was performed across the 200 different SSV values associated with each training set size $m \in \{10, \dots, 370\}$.

2.6. Quantification of a sufficient training size

Well preforming LELT matrices should ideally be able to estimate the target leads of all subjects in the target population with a similar level of accuracy and therefore show low levels of SSV. It follows, that the training set size has to be chosen such that each particular instance of the training set leads to a LELT matrix with similar low levels of SSV. Based upon these considerations we define a sufficient training set size as one that fulfills the following two requirements.

First, the training set size $N_1 \in \{10, \dots, 370\}$ must ensure that the developed LELT matrices are associated with low SSV values. This corresponds to a low median value calculated across the 200 different SSV values associated with the $i \in \{1, \dots, 200\}$ different training set instances of a given size N_1. We therefore quantified N_1 as the smallest size at which the right-tailed bootstrapped hypothesis test (significance level alpha = 0.05; 20000 bootstrap replicates) for the hypothesis H_{01} was rejected.

H_{01}: The observed reduction in the median SSV value between the training set size of 10 and the training set size of N_1 is ≤ 95 % of the observed reduction in the median SSV value observed between training set sizes of 10 and 370 subjects.

Second, the training set size $N_2 \in \{10, \dots, 370\}$ must ensure that all $i \in \{1, \dots, 200\}$ different instances of the training set produce LELT matrices with similar SSV values. This corresponds to a low span of the SSV values across the $i \in \{1, \dots, 200\}$ different training set instances of a given training set size N_2. We therefore quantified N_2 as the smallest size at which the right-tailed bootstrapped hypothesis test (significance level alpha = 0.05; 20000 bootstrap replicates) for the hypothesis H_{02} was rejected.

H_{02}: The observed reduction in the span of the SSV values between a training set size of 10 and a training set size of N_2 is ≤ 95 % of the observed reduction in the span of the SSV values observed between training set sizes of 10 and 370 subjects.

The two hypothesis tests for H_{01} and H_{02} were conducted separately for each of the three Frank leads and for training set sizes $N_1, N_2 \in \{10, \dots, 370\}$. We defined a sufficient training set size for each Frank lead as the size $N_* = \max(N_1, N_2)$.

3. Results

A summary of the findings from our analysis is provided in Table 2. In addition, an example of the relationship between an increasing training set size and the SSV of a LELT is provided in Figure 1.

Table 2. Median and span of SSV values for training set sizes 10, N_1, N_2, 370 and value of the sufficient training set size N_* for derived Frank VCG leads X, Y and Z.

derived lead	10[a]	N_1[b]	N_2[b]	370[a]	N_*
X	[18.9; 6.0]	150 [17.3; 0.9]	180 [17.4; 0.7]	[17.4; 0.4]	180
Y	[13.3; 7.0]	160 [11.7; 0.7]	160 [11.7; 0.7]	[11.6; 0.5]	160
Z	[26.8; 12.4]	160 [22.8; 1.5]	200 [22.7; 1.1]	[22.6; 1.1]	200

[a][median; span] of the SSV values; [b]training set size [median; span] of the SSV values; all SSV values are in µV they were quantified using the ECG data in DTest and based upon LELT matrices that were developed using 200 bootstrap samples of size 10, N_1, N_2 and 370 obtained from DTrain.

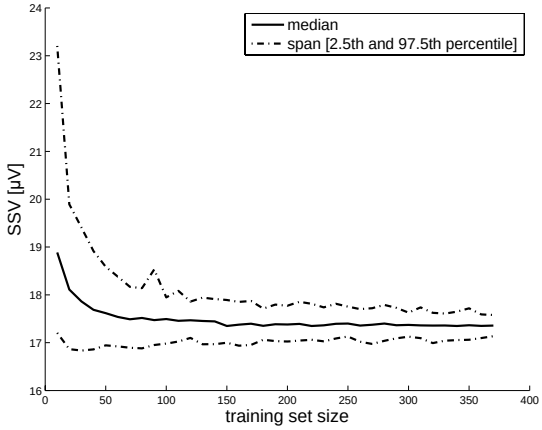

Figure 1. Median and span of the SSV values associated with Frank VCG lead X in µV quantified using the ECG data in DTest and based upon 200 different LELT matrices that were derived for each training set size $m \in \{10, \dots, 370\}$ using 200 bootstrap samples of the ECG data in DTrain.

4. Discussion and conclusion

In this research, we have assessed the influence of the training set size on the SSV of LELT matrices. In addition, we have identified a sufficient training set size for the development of LELT matrices as one that leads to a low median SSV value and ensures a low span of SSV values across different training set instances.

The relationship between the training set size and the median and span of the SSV value was found to follow a similar profile for Frank leads X, Y and Z. An example of this relationship is, for Frank VCG lead X depicted in Figure 1.

From Figure 1 it can be seen, that both median and span of the SSV decrease with increasing training set size. However, after an initial phase of improvement, median and span of the SSV can be seen to only marginally decrease with additional increases in the size of the training dataset. Based upon the relationship depicted in Figure 1 one can speculate that this marginal improvement continues for training set sizes larger than 370.

The size N_*, after which a further increase in the training set size is associated with only marginally improvements in the median and the span of the SSV was assessed and is provided in Table 2. For Frank VCG lead X the size N_* was found to be 180 subjects. The span of the SSV was, at this training set size, found to be low (0.7 µV) when compared to the median SSV value (17.4 µV). This indicates that any particular training set of size 180 will lead to a LELT matrix with a similar SSV. In addition, the findings in Table 2 indicate for Frank VCG lead X that no notable reduction in the median SSV value can be achieved by increasing the training set size from N_* = 180 to 370 subjects. Based on the findings for the median and the span of the SSV at training set sizes of 180 and 370 we conclude that an increase in the training set size beyond N_* = 180 subjects has no notable effect on the SSV of a LELT that derives Frank VCG lead X from the standard 12-lead ECG. Similar findings can be made for training set sizes N_*=160 for Frank VCG lead Y and N_*=200 for Frank VCG lead Z.

The heart-vector model [13] of the cardiac electrical activity postulates that any ECG lead can be expressed as a weighted sum of the orthogonal Frank VCG leads. We therefore speculate that a training set size of N_*=200 (largest training set size N_* of all Frank VCG leads in Table 2) should be sufficient for reducing the SSV of any LELT matrix that is used to derive any given ECG lead from the standard 12-lead ECG.

A limitation of this research is that the assessed LELT matrices were developed and tested on ECG data that was obtained from two equally represented cohorts (normal subjects and subjects with myocardial infarction). Whether the presence of different additional cardiac disorders in the training and testing datasets would have an influence on the training set size N_* has not been assessed in this research.

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