Sources of Variability in Normal Body Surface Potential Maps

Gyorgy Kozmann, PhD, Robert L. Lux, PhD, and Larry S. Green, MD

Within-group variability of body surface potential maps was assessed on data from 685 carefully validated normal subjects (348 men and 337 women). Sources of within-group variability were evaluated by subgrouping maps by patient sex, age, height, and weight. Contribution of reproducibility error to total variance was assessed in a separate group of 52 normal subjects in whom multiple maps were recorded. Total variance was significantly lower in women than in men. Total variance tended to decrease with age, and the greatest decrease occurred in men during the 3rd decade. The ratio of total variance to mean signal energy showed a slow decrease with age for each group. Results suggest that the dominant source of within-group variability arises from variability of cardiac electric sources while the influence of volume conductor variability is significantly less. Variability due to measurement reproducibility was approximately half of the total variance. (Circulation 1989;79:1077–1083)

The performance of statistical methods for classifying body surface potential maps ultimately depends on the extent of overlap of the probability distributions representing the classes to be separated. Even if the class distributions overlap, there is a chance of improving diagnostic performance by using additional information, such as geometry, to form tighter probability distribution subgroups within a clinically homogeneous population. In this case, reduction of overlap should result in improved classification accuracy. To find a reasonable, small number of efficient additional parameters, a better understanding of the sources of within-group scattering is needed. If it is assumed that the sources of within-group variability are similar in all clinically homogeneous classes, then the conclusions drawn from the study of one class can be cautiously extended to others.

Considerable experimental and theoretical information has been published about the main sources of within-group variability in electrocardiographic data. Parameters of the heart (geometrical and electrical) and the body (geometrical and conductive) can be considered random variables, which contribute to the resultant scatter of measured potential field parameters. Also, errors in electrode placement (reproducibility errors) contribute to total variance. The different components of variability may have different levels of importance, and the contribution of some components may be negligible, whereas that of others may be dominant. Comprehensive study is further needed to assess and rank the importance of the variability sources so that statistical interpretation of maps may be improved. The principal goals of this study were to rank the importance of heart- and body-related ‘‘inherent’’ components and to estimate the contribution of reproducibility error to the total within-group variability.

Methods

Selection and Representation of Clinically Homogeneous Groups

This study was based on analysis of a large, clinically normal, previously studied group of 685 normal subjects (348 men and 337 women). The sample size is shown as a function of sex and age decade in Figure 1. All subjects had a normal medical history, physical examination, standard 12-lead electrocardiogram (ECG), and serum electrolyte and blood sugar levels. None was taking medication at the time of the study. Height, weight, age, and sex were used to cluster subjects. A different group of 52 subjects (35 men and 17 women) were used to estimate reproducibility error. These subjects were classified as normal based on ECG alone, and they were mapped twice within 1–10 years (mean, 3.33 years). Because there was an insufficient number of carefully validated normal subjects who had repeat mappings done, the 52 subjects were selected from previously recorded maps.

From the Nora Eccles Harrison Cardiovascular Research and Training Institute, University of Utah, School of Medicine, Salt Lake City, Utah.

Supported by awards from the Nora Eccles Treadwell Foundation.

Address for reprints: Dr. Gyorgy Kozmann, Nora Eccles Harrison CVRTI, Building 100, University of Utah, Salt Lake City, UT 84112.
data in which the criterion for normality was a normal ECG. Sixteen of the 35 normal male subjects were in the 3rd decade at the time of the first mapping, and the second mapping occurred within 0.1–5 years (mean, 2.32 years). The rest of the normal male subjects (19) were in the 4th or 5th decade at the time of the first mapping, and the second mapping occurred within 2–10 years (mean, 4.1 years). Similarly, six of the 17 normal women were in the 3rd decade at the time of the first mapping and the between-measurement interval was 2–3 years (mean, 2.3 years). The remaining 11 women were in the 4th–6th decades for the first mapping, and the second mapping occurred within 2–8 years (mean, 4.1 years). The recordings of this group were used to estimate the variance component due to the reproducibility error. In this case, only the changes between subsequent measurements were analyzed. Hence, we assumed that rigorous validation of clinical classification, beyond the 12-lead ECG, was not necessary.

All patients gave informed consent for body surface mapping, and the study protocol had the prior approval of the Institutional Review Board of the University of Utah.

Body surface potential maps in this study were recorded from 32 body surface sites by a statistically designed, optimal, limited lead system.9 Electrode locations were a subset of points on a 12-row by 16-column grid (Figure 2). The rows were equally spaced between the sternal notch and the umbilicus, and the columns were equally spaced in the four quadrants of the thoracic circumference. To minimize electrode placement errors, the grid system was sketched on each subject before application of the electrodes. The Wilson central terminal was used as a recording reference. All data were recorded at a rate of 1,000 Hz. From each subject, several heart cycles were stored. During processing, three to six sinus beats were selected and averaged to reduce random noise and the minor effect on maps due to superficial respiration.2 QRS and ST-T onset and offset were manually selected from the “power curve” (sum of the squared potentials over the chest surface vs. time). Subsequent to baseline and gain adjustment, QRS and ST-T intervals were time normalized. (Time normalization is expected to force comparison of similar electrophysiologic events in the heart.) QRS-T data were represented by spatial and temporal Karhunen-Loeve eigenvector coefficients.10,11

To reduce redundancy, dimensionality, and computation effort, QRS area maps of each subject were represented by a spatial Karhunen-Loeve basis. This resulted in an efficient representation of the mean electrical forces during depolarization.10 The QRS area map of each subject was represented by a point in the 12-dimensional space of the spatial Karhunen-Loeve components.

FIGURE 1. Bar graph of distribution of the normal population studied as a function of gender and age decades.

FIGURE 2. Schematic arrangement of the measuring locations of the 32-lead limited lead system. The midline of the unrolled representation coincides with the sternal line; the left and right vertical borderlines are along the spinal column; the upper horizontal line is at the height of the sternal notch; and the lower horizontal line is at the height of the umbilicus.
where $c_{ij}$ is the $ith$ component of the 12-dimensional spatial Karhunen-Loeve coefficient vector of subject $j$, $m_i$ is the vector of map values in 192 electrode sites of subject $j$, and $v_i$ is the $ith$ normalized eigenvector of the covariance matrix representing the whole population.

The points characterizing a group of normal individuals form a point cloud. The subsequent analysis was performed to rank those parameters that were primarily responsible for the large within-group scatter of points in this cloud.

**Working Hypotheses**

To rank the different sources of variability, the normal population was divided into subgroups under the assumptions that 1) in tight (homogeneous) age- and body geometry-restricted groups of clinically normal men or women, variability in maps is primarily due to source (heart) variability and reproducibility error and is negligibly influenced by body geometry or subject age, and 2) comparison of two different tight age- and body geometry-restricted groups reflects differences of the probability distributions of men or women arising from chest- and heart-geometry differences.

**Statistical Analyses**

The total empirical variance (TV), defined as the sum of the variances of the 12 Karhunen-Loeve coefficients, was used to characterize the scatter of the point clouds:

$$TV = \frac{1}{N-1} \sum_{j=1}^{N} \sum_{i=1}^{12} (c_{ij} - \bar{c}_i)^2$$

where $\bar{c}_i$ is the mean value of the $ith$ spatial Karhunen-Loeve coefficients, and $N$ is the sample size.

The heart-related variability, which includes the variability due to reproducibility error, was computed exactly as total variance, with tight age- and body geometry-restricted groups.

The reproducibility error component of variability (RCV) was calculated as the variance of two measurements of the same subjects for the group of 52 subjects:

$$RCV = \frac{2}{N-1} \sum_{j=1}^{N} \sum_{i=1}^{12} \left( c_{ij}(1) - c_{ij}(2) \right)^2$$

where $c_{ij}(1)$ and $c_{ij}(2)$ are the $ith$ spatial Karhunen-Loeve components of subject $j$ for measurements 1 and 2, respectively.

The group mean signal energy (GMSE) was computed as

$$GMSE = \frac{1}{N} \sum_{j=1}^{N} \sum_{i=1}^{12} c_{ij}^2$$

The empirical variances were compared by the $F$ test, with degrees of freedom equal to the sample size minus one in each group. The $F$ test is valid for Gaussian distributions, an assumption approximately valid for the sum of the uncorrelated random Karhunen-Loeve coefficient variables under the central limit theorem.

To visualize the scattering of QRS area maps of group members, we used the plane of the eigenvectors corresponding to the two largest eigenvalues of the sample covariance matrix of the group considered. Because the highest possible percentage of the total variance is represented by the first two principal components, this plane is the best two-dimensional display to qualitatively visualize the ability of the auxiliary information (sex, age, height, and weight) to make tighter probability distribution subgroups within the population.

**Results**

**Evaluation of Grouping by Sex**

In the first part of this study, all data in decades 3–6 were pooled by sex. Total empirical variance was estimated for both sexes, and variances were compared to the group mean signal energy as shown in Figure 3. Difference in total variance between
men and women was significant by the $F$ test ($p<0.05$). As shown, total variance is approximately half of the group mean signal energy in both sexes. The diagram also shows values of the reproducibility error component of variability, estimated separately from repeated measurements of 35 men and 17 women. Comparison of total variance and the reproducibility error component of variability shows that the "inherent" variability components are significant, $p<0.001$ for men and $p<0.05$ for women. The use of a subset of the repeated measurements to decrease the average between-measurement interval from 3.33 to 1.3 years only slightly affected the reproducibility error component of variability value, indicating that the contribution of age-dependent changes to our initial estimate was not important.

**Evaluation of Grouping by Age and Sex**

Subgrouping by sex was used to reduce body and heart geometry–related differences between men and women. Subgrouping by age decade allowed quantitative study of the importance of age on within-group variability. As shown in Figure 4, variances decreased with age, and the decrease was almost exponential in men. The ratio of male to female variances was significant ($p<0.005$) in the 3rd decade but insignificant for the given sample sizes in other decades. Similarly, a decreasing trend in group mean signal energy occurred as well. The ratio of the two variables is plotted in Figure 5, and the plot shows a decreasing tendency. With increasing age, the point clouds representing the group in the 12-dimensional Karhunen-Loève space are more tightly clustered around the group means than are those of the younger decades. The ratio plotted in Figure 5 shows somewhat higher values for the men than for the women. In Figures 4 and 5, the samples of the 5th and 6th decades were pooled to increase the number of subjects within the group for the sake of more reliable estimation.

The number of subjects within the normal population with multiple measurements was not large enough to permit study of the age dependence of the reproducibility error component of variability.

**Evaluation of Grouping by Age, Sex, and Body Habitus**

Heart-related and body geometry–related effects on variability were assessed by comparing data from subgroups of men and women in the 3rd decade. The large sample size of these groups allowed definition of tight geometry subgroups (weight, mean±10 lb; height, mean±1 in.). The average number of subjects per tight group was 17 for men and 12 for women. In Figure 6, the distributions of 162 men between the age limits of 20 and 29 years are represented in the height-weight parameter space. Tight geometry subgroups within this population are enclosed in boxes on the scatter diagram. Figure 7 shows total variance (solid bar) and average variance of the three (G1–G3) tight
subgroups (open bar) of men and women in the 3rd decade. Differences between arbitrary pairs of tight geometry group variances were insignificant in both male and female groups at a level of $p<0.05$. Furthermore, ratios of total to tight group variances were also insignificant by the $F$ test at a significance level of $p<0.05$ in both genders.

The first of these findings shows that between-group differences were unobservable by simple comparisons of variance for the given sample sizes. The second result indicates that heart-related variability and not variability due to body geometry is responsible for the dominant scatter of within-group point clouds. The same conclusion is further substantiated in Figures 8 and 9. In Figure 8, the Karhunen-Loeve domain scatter of normal men in the 3rd decade is shown. The open circles represent the projection of the cloud points on the plane of the two first principal components, whereas the closed circles distinguish the members of the G2 subgroup (defined in Figure 6). Clearly, tight clustering of geometric factors did not result in similar, tight clustering in the Karhunen-Loeve space. Scatter of QRS area maps corresponding to the subgroup G2 is shown in Figure 9 in which amplitude normalized (root mean square) QRS area distributions are shown. The large pattern differences are clearly recognizable. Considerable interindividual differences are found even in such robust parameters as the relative position of the maxima and minima or the ratio of the positive and negative maximal amplitudes. These and similar results from women in the 3rd decade consistently suggest that the main source of within-group variability is related to the heart, that is, differences in the sequence of activation or geometry or both.

Discussion

Misclassification of body surface maps occurs when there is overlap of the probability density distribution of the variables representing the dif-
ferent classes. Knowledge of those factors responsible for broadening these probability distributions may offer a strategy for controlling within-group variability and result in improved diagnostic performance of statistical classifiers. A limitation of our study is that only simple global parameters of variance were used to characterize scatter within clinically homogeneous groups. Similarly, simple global parameters were used to characterize the influence of body geometry. The available sample size placed a lower limit on bin sizes of the homogeneous groups based on geometry and age. Another limitation was the confinement of the study to a clinically normal group in which only the QRS area distributions were studied. Despite the previously mentioned limits, the main conclusion that source variability dominates total variability can probably be extended to the whole time sequence of maps in normal as well as pathologic groups. This logic follows because the body-geometry differences can be assumed to be the same and because the sources in pathologic conditions can be considered to be the sum of the prepathologic (normal) source distributions plus those representing pathologic alterations. Because the pathologic-related component is also random, the resultant variance will be larger than that of normal subjects; therefore, the dominance of the source component would be expected to remain.

According to our results, there is significant difference in the average, and also the comparable age group-restricted total variance of men and women (Figures 3 and 4). Figure 4 shows that variance decreases with age. After the 3rd decade, the decrease is less steep, and the variances for men and women do not differ significantly. For men, the total decrease during the 3rd–6th decades is about 50% of the initial value measured in the 3rd decade. For women, the decrease in variance is also observed, but both its steepness and total change are lower. The group mean signal energy decreases monotonically as a function of age, and the ratio of the total variance and group mean signal energy slowly decreases. The ratio observed for the male group was higher than that for the female group. The observations on the group mean signal energy are indirectly comparable with data published earlier on age and sex dependence of ECG amplitudes or amplitudes of extrema in body surface potential maps.8,14

In a narrow age range, the ranked importance of inherent within-group variability sources is 1) heart-related variability, and 2) body geometry–related variability. The first component is clearly responsible for most of the point cloud spread of the normal group (Figures 8 and 9). This order of importance is probably valid in pathologic groups too, except the

Figure 9. Example of the manifestation of heart-related variance in the measurement space. In the figure, 15 of the normalized QRS area maps of the right geometry subgroup G2 (see Figure 6) are displayed. The body surface representation is given as an unrolled cylinder cut along the spine. The central line coincides with the midsternal line; the upper horizontal borderline is at the level of the sternal notch; and the lower horizontal borderline is at the umbilicus. Contour lines are drawn with equal root mean square amplitude normalized increments.
heart-related component would be expected to be even more important because of pathologic alteration. Though chest geometry seems to contribute insignificantly to QRS area variance, Green et al suggest that geometric factors do have significant effects on potential distributions. This apparent paradox can be explained by a translation or rotation or both of the point clouds, which would not affect total variance of the tight subgroups.

Heart-related variance is the primary variable that limits the diagnostic performance of statistical body surface potential map interpretation. This theoretical limit can be approached by a mapping technology that decreases reproducibility errors. In this study, the small number of subjects with repeated measurements did not allow a detailed analysis of mechanisms of variance related to reproducibility error, but the estimate of the average value of this component (Figure 4) shows that approximately half of the total variance is due to this type of error. Other investigators have shown that reproducibility error is due mostly to errors of electrode placement and that biologic variability and electronic or computational noise contribute to a lesser extent. To improve statistical classification accuracy, a logical step would be the use of techniques that allow a more consistent placement of electrodes. One may expect that by increasing the number of electrodes the reproducibility error would be reduced. Use of electrodes obviously would increase representation accuracy of the maps; however, in the case of repeated measurements, it is not obvious whether the reproducibility error, originating now from more but presumably smaller components, would increase or decrease the resultant error. Even if resultant reproducibility error decreased, the increased cost of instrumentation and time of electrode application would make the benefit doubtful.

These results suggest that statistical classification of body surface potential maps can be improved by 1) reducing variance related to reproducibility error through techniques that minimize electrode placement errors, 2) subgrouping by sex because significant map differences were observed between male and female groups, 3) subgrouping by age (20–40 years, >40 years) to decrease the influence of age-related variations. Subgrouping by geometry parameters seems to be unnecessary.

References


KEY WORDS • heart-related variability • body geometry-related variability • reproducibility error • rank of variability components
Sources of variability in normal body surface potential maps.
G Kozmann, R L Lux and L S Green

_Circulation_. 1989;79:1077-1083
doi: 10.1161/01.CIR.79.5.1077

_Circulation_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1989 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/79/5/1077