Uncertainty Principle of Signal-Averaged Electrocardiography

Jeffrey J. Goldberger, MD; Sridevi Challapalli, MD; Michael Waligora, MD; Alan H. Kadish, MD; David A. Johnson, BS; Mirza W. Ahmed, MD; Shmuel Inbar, MD

Background—Signal-averaged ECG (SAECG) reproducibility is reported to have a component that is independent of residual noise.

Methods and Results—In group 1, multiple paired SAECGs were obtained to noise levels of 0.3±0.1 and 0.5±0.2 μV. For the 0.5- and 0.3-μV noise recordings, QRS duration (QRSd) was 101.2±11.3 and 104.6±9.6 ms, respectively (P<0.0001), and the differences in paired QRSd (ΔQRSd) were normally distributed, with variances of 11.4 and 26.2 ms² (P<0.0001). Paired SAECGs were obtained in group 2 patients without and with late potentials; ΔQRSd variance was 3.3 and 217.9 ms² (P<0.0001). In group 3, ≥10 SAECGs were acquired at noise levels of 0.2 to 0.8 μV, in 0.1-μV increments. QRSd increased as noise level decreased. The variance was greater in low-noise (0.2 to 0.4 μV) versus higher-noise (0.5 to 0.8 μV) recordings. In group 4, SAECGs were analyzed with bidirectional and Bispec filters, with no difference in QRSd between the 2 filters and a normally distributed ΔQRSd. A computer simulation demonstrated that alterations in the phase relationship of noise to signal results in a normal distribution of signal end points.

Conclusions—Within the acceptable noise range for SAECG, lower noise results in longer QRSd and larger variance, suggesting that more accurate recordings may have less reproducibility. The random timing of noise relative to signal results in the distribution/variance of repeated measurements. Statistical strategies may be used to reduce some of this variance and may enhance the diagnostic utility of SAECG. (Circulation. 2000;101:2909-2915.)

Key Words: electrocardiography ■ diagnosis ■ tests ■ statistics ■ arrhythmia

Signal averaging is used to expose (low-amplitude) portions of the signal that would otherwise be obscured by underlying noise. In the presence of random electrical and/or myopotential-generated noise, signal averaging reduces noise while maintaining the integrity of the intrinsic signal. This technique has been applied to the QRS complex to detect late potentials that may identify patients at risk for ventricular arrhythmias.

Although signal averaging reduces residual noise, some noise remains. Commercial signal-averaged ECG (SAECG) systems allow the user to set a predefined noise level; averaging continues until this level is reached. Computer algorithms for identification of QRS end points (separating signal from baseline noise) are used that depend on the residual noise level. In the absence of noise, one could precisely determine QRS duration (QRSd). Because noise cannot be eliminated, algorithms are used to set QRS end points at a point at which signal amplitude is larger than the noise. Because the true end points are not identified, this results in less accurate QRSd determinations. Moreover, with increasing noise, measured QRS end points need to be set at higher thresholds, resulting in progressively shorter (and less accurate) QRSd. However, there is also variability in SAECG parameters that is reported to be independent of absolute noise level. The source of this variability is not understood.

Methods

We hypothesized that the phase relationship of noise to signal affects SAECG reproducibility. Although noise is random, it has peaks and troughs; on 1 SAECG, the peak of the noise may sum with the terminal signal, and on another occasion, the trough of the noise may sum with the signal, yielding different results (Figure 1). To confirm this hypothesis, the following studies were performed. In study 1, results of paired SAECGs at 2 different noise levels in the same subjects were compared: the distribution of observed differences in paired QRSd at each noise level was hypothesized to reflect a normal distribution centered around zero; at a given noise level, there should be no systematic bias in QRSd when the SAECG is repeated. In study 2, the distribution of the differences in paired QRSd was assessed in patients with and without late potentials, hypothesizing that there is a wider distribution in patients with low-amplitude terminal signals. In study 3, the effect of residual noise on SAECG reproducibility was defined over the 0.2- to 0.8-μV range. We hypothesized that as noise level was reduced, lower-amplitude portions of the QRS would be exposed, resulting in increasingly accurate QRSd but accompanied by a decrease in reproducibility. In study 4, we evaluated all SAECGs in our database with 2 different filters. Filters have both magnitude and phase responses. Filters are designed to have as close to a flat-magnitude response in the
Figure 1. Schematic of effect of phase relationship of noise to signal in determining QRS duration. Left, True signal with low-amplitude terminal portion (L). Noise is depicted for demonstration purposes only as a repetitive signal. When signal and noise are summed so that L and noise are in phase (peak of L with peak of noise), there is no appreciable effect on major portion of signal; however, L is accentuated and is therefore detectable above residual noise. When signal and noise are summed so that L and noise are out of phase (peak of L with trough of noise), there is still no appreciable effect on major portion of signal; however, L is now no longer detectable above residual noise.

bandpass as possible; thus, the magnitude responses of the 2 filters are expected to be similar. Because the phase responses may be quite different and may affect the relative timing of signal to noise, we hypothesized that the distribution of the differences in the results with the 2 filters would be a normal distribution. Finally, a computer model verified the hypothesis.

Subjects

Study 1: Low Versus High Noise
Group 1 comprised 14 normal volunteers (8 men, 6 women, mean age 28±5 years) in whom the effects of autonomic stimulation and blockade on the SAECG were evaluated.9

Study 2: Low- Versus High-Amplitude Terminal Signal
Group 2 comprised 30 subjects with coronary artery disease (standard QRSd≤110 ms) who underwent electrophysiological testing. Group 2A included 7 men and 3 women (age 56±13 years) in whom late potentials were absent. Group 2B included 15 men and 5 women (age 66±8 years) in whom late potentials were present.

Study 3: Accuracy Versus Reproducibility With Noise Reduction
In group 3, 22 subjects with coronary artery disease were enrolled; 3 were excluded because adequate recordings were not obtained. Thus, there were 16 men and 3 women (age 60±14 years). SAECG was positive in 12 and negative in 7 subjects.

Study 4: Effect of Different Filters
In group 4, 125 subjects (89 men, 36 women, age 56±16 years) with no structural heart disease (n=40), coronary artery disease (n=67), nonischemic dilated cardiomyopathy (n=9), hypertrophic cardiomyopathy (n=5), or other disease (n=4) were evaluated. SAECG was positive in 25 and negative in 100 subjects.

SAECG Recordings

All ECG data were recorded with Ag/AgCl electrodes positioned in standard X, Y, and Z lead positions9 on a Predictor 1 (series 6.0, Arrhythmia Research Technology) and averaged with Predictor software; normal QRS complexes were averaged to the designated noise levels. Noise was measured in an isoelectric window of 100 points as the SD of voltage in that segment.

In group 1, ECG data were acquired at 1 kHz in 5-minute segments and stored on optical disk for subsequent analysis; signal averaging was performed offline on the stored data. In groups 2 and 4, SAECGs were acquired either online or offline, as for group 1 subjects. In group 3, a series of fifteen 3-minute recordings were sequentially acquired at 1 kHz. Thus, 45 minutes of data were available from which to perform SAECGs. Because multiple SAECGs were required at each residual noise level, these recordings could be combined (by splicing individual 3-minute recordings together) to provide an adequate number of complexes to achieve the desired noise reduction. Initially, each of the fifteen 3-minute files was used to generate SAECGs with a 0.8-μV noise end point. If possible, each of the files was then used to generate SAECGs for each of the lower noise end points. At some noise level, the number of complexes in an individual recording was no longer adequate to achieve the desired noise reduction. To obtain additional QRS complexes for averaging, initially 2 recordings were spliced together. For the lowest residual noise SAECGs, multiple files needed to be spliced together. The choice and order of files spliced together were random. To ensure an independent relationship between the noise and the QRS, for each noise level, there were no 2 SAECGs in which >67% of the QRS complexes overlapped.

The Predictor has a 12-bit analog-to-digital converter with the least significant bit representing 0.09765 μV at the patient cable. All calculations are done in 16 bits, with the 4 least significant bits set to zero in the conversion from 12 to 16 bits. To test Predictor performance, SAECGs were acquired at 2 kHz with an ECG simulator. Ten recordings were made using 5000 complexes to reduce environmental noise to a minimum (0.018 to 0.023 μV). Measured QRSd was 88.5 to 89.0 ms for all recordings. This is within the 0.5-ms accuracy expected at a 2-kHz sampling rate, thereby validating the fidelity of the Predictor acquisition and processing functions.

SAECG Analysis

X, Y, and Z recordings were combined into a vector sum. In groups 1 and 3, a Bispec filter was used (high-pass, 40 Hz). In group 2, a bidirectional filter was used (high-pass, 40 Hz). Automated analysis calculated QRSd, root-mean-square voltage in the terminal 40 ms of the QRS (RMS), and low-amplitude (<40 μV) signal duration (LAS).

SAECGs were visually inspected to confirm QRS end points. Reproducibility analysis focused on QRSd, because RMS and LAS are derived from the QRS end points and are correlated with it.9 Late potentials were present if 2 of 3 parameters were abnormal: QRSd≥120 ms, LAS≥38 ms, RMS≤20 μV.

Study 1

Because autonomic tone affects both QRSd and residual noise level,10 SAECG reproducibility was assessed by evaluating paired SAECG acquisitions under the variety of autonomic conditions tested and then evaluating the distribution of the differences in results. Two SAECGs were generated for each condition evaluated from the digitally stored data to achieve low residual noise (0.3±0.1 μV), and another pair was generated to achieve relatively higher noise (0.5±0.2 μV).

Subjects underwent a study evaluating autonomic effects on the SAECG.9 Briefly, on day 1, recordings were made at baseline and during epinephrine and isoproterenol infusions (50 ng · kg·min⁻¹), β-blockade (propranolol 0.2 mg/kg), and double blockade (atropine 0.04 mg/kg after β-blockade). On day 2, recordings were made at baseline and during phenylephrine infusion titrated to increase blood pressure 20 to 30 mm Hg, parasympathetic blockade (atropine 0.04 mg/kg), and phenylephrine infusion after atropine. During each condition, three 5-minute recordings were made.

From each 5-minute recording, 2 SAECGs were obtained. The first used only 100 beats, resulting in relatively high but acceptable noise levels (0.5±0.2 μV). The second SAECG was averaged to a noise end point of 0.2 μV or until all complexes in each recording

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were used, achieving lower noise levels (0.3±0.1 μV). For each set of 3 SAECGs (per condition per patient) at each noise level, the 2 SAECGs with the lowest residual noise were used for analysis. The change in QRSd (ΔQRSd) for each pair was calculated. For each set of duplicate recordings, SAECGs were randomly assigned to be recording 1 or 2, to remove any effect of acquisition order.

**Study 2**

The effect of low-amplitude signals on immediate SAECG reproducibility was assessed by acquisition of duplicate SAECGs under basal conditions in subjects with and without late potentials. Duplicate SAECGs were obtained to identical noise end points (target 0.3 μV; range 0.3 to 0.4 μV). ΔQRSd for each pair was calculated. For each set of duplicate recordings, SAECGs were randomly assigned to be recording 1 or 2.

**TABLE 1. Results of SAECG Analysis in Group II**

<table>
<thead>
<tr>
<th></th>
<th>QRSd, ms</th>
<th>RMS, μV</th>
<th>LAS, ms</th>
<th>Noise, μV</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Negative SAECG</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recording 1</td>
<td>108.4±14.1</td>
<td>41.9±19.2</td>
<td>26.3±7.6</td>
<td>0.31±0.04</td>
</tr>
<tr>
<td>Recording 2*</td>
<td>108.4±14.0</td>
<td>42.4±20.0</td>
<td>27.2±8.0</td>
<td>0.31±0.03</td>
</tr>
<tr>
<td><strong>Positive SAECG†</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recording 1</td>
<td>121.0±14.5</td>
<td>11.8±6.2</td>
<td>49.0±12.8</td>
<td>0.32±0.04</td>
</tr>
<tr>
<td>Recording 2*</td>
<td>126.4±16.6</td>
<td>10.8±12.2</td>
<td>54.3±15.1</td>
<td>0.31±0.03</td>
</tr>
</tbody>
</table>

*Recording 2 parameters did not differ from those of recording 1.
†QRSd, RMS, and LAS were significantly (P<0.0001) different in patients with positive vs negative SAECG. Residual noise levels were not different.

**Study 3**

SAECG accuracy and reproducibility were evaluated by obtaining 10 to 15 SAECGs in each subject at noise levels of 0.2, 0.3, 0.4, 0.5, 0.6, 0.7, and 0.8 μV. QRSd variance was calculated for each subject for each noise level as the index of reproducibility. In 1 subject, multiple SAECGs could not be obtained at 0.2 μV, so the value at 0.3 μV was used for analysis.

**Study 4**

Each SAECG was analyzed with Bispec and bidirectional filters (bandpass 40 to 250 Hz). ΔQRSd for each pair was calculated.

**Study 5: Phase Relationship of Signal to Noise**

A computer model (Mathematica, Wolfram Research) was used to test whether the phase relationship of noise to signal explains the observed normal distributions for repeated QRSd measurements. A test signal with no noise and a known end point is defined. To create a real signal, computer-generated noise is summed with the test signal. The end point of the summed signal (test signal plus noise) is then calculated. The summed signal is modified by time-shifting the noise signal and creating a new summed signal whose end point is then calculated. This process of shifting the noise signal and summing it with the test signal is repeated many times to evaluate the effect of the phase relationship of noise to signal on the determination of signal end points.

Test signals were defined (2-kHz sampling rate): S1(t) = 4−0.1×t for 0≤t≤40 ms and S2(t) = 5−0.25×t for 0≤t≤20 ms and S(t) = 0 for 20≤t≤160 ms.

S1 and S2 have end points at 40 and 20 ms; S1 is steeper than S2. The noise signal was generated by a random-number generator (>10⁶ points). An 8-point moving average filter was applied to limit the noise bandwidth to ~250 Hz. The mean of this signal was subtracted, and it was scaled so that the noise signal [N(t)] would have a zero mean and an SD of 0.2. A 160-ms segment of N(t) was added to each of the signals (S1, S2). To maintain the parallel with SAECG (in which the vector sum is performed), the absolute value of S1(t)+N(t) and S2(t)+N(t) was calculated. The end point of these signals was measured with a threshold of 0.8. Next, N(t) was shifted by 100 points and added to each of the signals (S1, S2). The absolute value was calculated, and end points were measured. This process was repeated 10 000 times. Thus, for each of the modified (by addition of noise) versions of S1 and S2, there were 10 000 measurements of their end points in which each measurement was made on signals that differed only in the phase relationship of noise to signal. The distribution created by the phase relationship of noise to signal should occur at the signal onset and end. Because these distributions are independent (relative timing of noise to signal at signal onset does not predict relative timing of noise to signal at its end), the variance of the duration measurement (end point minus onset) should equal the sum of the variances of the distributions for the onset and end point. Another simulation was performed to assess the effect of the phase relationship of noise to signal at its onset and termination.

**Figure 2.** Histogram of ΔQRSd between paired SAECG recordings in study 1. Top, Histogram for 100-beat SAECGs (mean noise 0.5±0.2 μV); bottom, histogram for 5-minute, lower-noise SAECGs (mean noise 0.3±0.1 μV). On each histogram is superimposed fitted normal distribution (100-beat SAECGs: variance 11.4 ms², R²=0.95; low-noise SAECGs: variance 26.2 ms², R²=0.73).
S₃ was defined as a triangle wave with onset at 40 ms and end point at 120 ms: $S_3(t)$ for $0 \leq t \leq 40$ ms; $0.1 \times t$ for $40 < t \leq 80$ ms; $12 - 0.1 \times t$ for $80 < t \leq 120$ ms; and 0 for $120 < t \leq 160$ ms.

The noise signal was generated and summed with $S_3$ as noted above; signal onset and end point were determined and duration was calculated, resulting in 10,000 measurements of signal onset, end point, and duration.

**Data Analysis**

$\Delta$QRSd between pairs of SAECG recordings was calculated to assess reproducibility. If SAECG reproducibility is high, the distribution of $\Delta$QRSd should be tightly centered around zero. As $\Delta$QRSd distribution widens, this indicates less reproducibility. Histograms of $\Delta$QRSd were plotted and fitted to normal distributions. Variances of these distributions (a measurement of their width) were compared with an equality-of-variance F test (Statview4.5, Abacus Concepts). Repeated-measures ANOVA was used to evaluate SAECG reproducibility over the 0.2- to 0.8-mV noise range. Post hoc comparisons were performed with paired $t$ tests. Values of $P<0.05$ were considered statistically significant.

**Results**

**Study 1**

We recorded 109 SAECG pairs under the various conditions. For the 100-beat SAECGs, in each set of recordings, noise level was $0.48 \pm 0.17 \mu$V, with no significant differences in mean QRSd between recordings ($101.1 \pm 11.5$ ms, $101.2 \pm 11.3$ ms). For the 5-minute recordings, noise levels were $0.29 \pm 0.10 \mu$V for the first and $0.28 \pm 0.10 \mu$V for the second, with no significant differences in QRSd between recordings ($103.9 \pm 10.6$ ms, $104.9 \pm 9.5$ ms). Thus, group means were reproducible at each noise level. Average noise in the 100-beat SAECGs was greater ($P<0.0001$) and mean QRSd was shorter ($101.2 \pm 11.3$ ms) than in the 5-minute recording SAECGs ($104.6 \pm 9.6$ ms; $P<0.0001$).

Figure 2 shows $\Delta$QRSd distributions for the 100-beat and 5-minute SAECGs. Each distribution was fitted to a normal distribution with $R^2$ values of 0.95 and 0.73, respectively. $\Delta$QRSd variance was $11.4 \text{ ms}^2$ for the 100-beat SAECGs and $26.2 \text{ ms}^2$ ($P<0.0001$) for the 5-minute (lower-noise) recordings; thus, the $\Delta$QRSd distribution for duplicate recordings is wider for lower-noise recordings. Lower-noise recordings are therefore less reproducible.

**Study 2**

SAECG parameters with either positive or negative SAECGs did not differ between duplicate recordings (Table 1). Positive SAECG parameters were significantly different from those of negative SAECGs ($P<0.0001$), whereas noise level was the same. $\Delta$QRSd variance was $3.3 \text{ ms}^2$ in negative SAECGs and $217.9 \text{ ms}^2$ ($P<0.0001$) in positive SAECGs. This variance is an order of magnitude larger than that observed in the normal subjects, demonstrating that SAECG reproducibility is reduced in the presence of low-amplitude terminal signals. Figures 3 and 4 provide examples of duplicate SAECG tracings.

Twenty-seven patients had concordant results on repeated SAECGs. When the 3 patients with discordant results were removed from analysis (to remove potential bias of including them in the positive group), $\Delta$QRSd variance in patients with positive SAECGs ($n=17$) was $158.4 \text{ ms}^2$ ($P<0.0001$ compared with the variance in patients with negative SAECGs). Of the 3 excluded patients, 1 had and 2 did not have inducible monomorphic ventricular tachycardia at electrophysiological
testing. Of the 10 patients with negative SAECGs, only 1 had inducible ventricular tachycardia. Of the 17 patients with 2 positive SAECGs, 10 had inducible ventricular tachycardia.

Study 3
To more carefully define the relationship of accuracy to reproducibility as residual noise level is lowered, multiple SAECGs were acquired at noise levels of 0.2 to 0.8 μV in 0.1-μV increments in each subject. For each subject, a mean QRSd and variance were calculated at each noise level. Figure 5 shows the group mean QRSd and variances obtained for the multiple recordings in each subject. There was progressive QRSd lengthening as noise level was reduced ($P<0.0001$; all pairwise comparisons were significant). The variability in QRSd measurement (variance) was significantly larger at lower noise levels than at higher noise levels ($P<0.0003$). The variance at noise levels of 0.2 to 0.4 μV varied from 26.0 to 31.0 ms$^2$ and did not differ significantly in this noise range; the variance at noise levels of 0.5 to 0.8 μV varied from 7.8 to 15.7 ms$^2$ and did not differ significantly in this noise range (Table 2).

Study 4
QRSd did not differ between the bidirectional (107.5±14.9 ms) and Bispec (106.2±13.0 ms) filters. Figure 6 shows the normal distribution ($R^2=0.92$) for ΔQRSd between the 2 filters with a variance of 61.1 ms$^2$.

Study 5
Figure 7 shows the distributions of the measured end points for the signals tested. With multiple measurements of signal end point when there is noise, there is a normal distribution of results. Furthermore, the distribution for the steeper signal (S$_2$) is narrower than the distribution for S$_1$ ($P<0.0001$ for the differences in variances). For S$_1$ and S$_2$, the mean (±SD) measured end points were 32.7±1.8 and 17.1±1.3 ms, respectively. With the lower-amplitude signal (S$_1$), end-point measurements were less accurate.

For S$_2$, there were normal distributions for the onset, end point, and duration of the signal. The variances were 3.82, 3.59, and 7.42 ms$^2$, respectively. As predicted, the variance of the duration was equal to the sum of the variances of the onset and end point, confirming that the phase relationship of noise to signal at the signal onset is independent of the phase relationship of noise to signal at the end of the signal.

**TABLE 2. QRSd and Its Variance for Repeated SAECGs Performed With Multiple Residual Noise Levels**

<table>
<thead>
<tr>
<th>Noise Level, μV</th>
<th>QRSd, ms</th>
<th>Variance, ms$^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.2</td>
<td>123.3±21.9</td>
<td>31.0±39.7</td>
</tr>
<tr>
<td>0.3</td>
<td>120.1±21.9</td>
<td>26.0±32.3</td>
</tr>
<tr>
<td>0.4</td>
<td>116.6±22.3</td>
<td>27.5±34.5</td>
</tr>
<tr>
<td>0.5</td>
<td>114.2±23.1</td>
<td>15.7±18.8</td>
</tr>
<tr>
<td>0.6</td>
<td>112.3±23.2</td>
<td>10.8±10.4</td>
</tr>
<tr>
<td>0.7</td>
<td>111.6±23.4</td>
<td>8.9±6.5</td>
</tr>
<tr>
<td>0.8</td>
<td>110.2±23.2</td>
<td>7.8±6.5</td>
</tr>
</tbody>
</table>

**Figure 5.** Plots of QRSd (circles) and variance for repeated QRSd determinations (bars) at each noise level in study 3.

**Figure 6.** Histogram of difference in QRS duration (ΔQRSd) observed between SAECG results using bidirectional and Bispec filters in study 4.

**Figure 7.** Histograms of QRS end points measured in study 5. Each histogram is based on 10 000 measurements (top, S$_1$; bottom, S$_2$).
The longer QRSd represents closer approximation of the true conditions used in this study.

To expect systematic differences in these factors under the no filtering. Although there are other externalities that may be identical. In addition, in the computer model, there was confirmed by testing the performance of the Predictor with an SAECG simulator. Furthermore, in study 4, 2 different filters were applied to the same averaged QRS complex after selection of complexes, aligning of complexes, and averaging. Because these processes were identical for both analyses, they could not have contributed to the observed normal distribution. Signal processing is also most likely not an important factor contributing to the observed variability in SAECG results, because for studies 1, 2, and 3, processing was identical. In addition, in the computer model, there was no filtering. Although there are other externalities that may affect the SAECG, such as autonomic tone, there is no reason to expect systematic differences in these factors under the conditions used in this study.

Lower noise levels result in increased QRSd, even within the “acceptable” noise range for SAECG recording. The longer QRSd represents closer approximation of the true QRSd because the lowest-amplitude portions of the QRS become manifest as noise decreases. Although the effects of the magnitude of residual noise on QRSd have been well studied, several investigators have reported variability that is independent of absolute noise level.2,7,8 Engel et al8 studied immediate SAECG reproducibility in 18 normal subjects. Although they noted that the percent difference in paired measurements was normally distributed (actual data not shown), they concluded that “noise did not influence the variation in measurements in the time domain in a systematic way.” However, they did not consider the possibility of the phase relationship of signal to noise to explain their findings. Christiansen et al5 evaluated immediate SAECG reproducibility at noise levels of 0.2 and 0.4 μV. At the lower noise level, there appeared to be less variability. However, there was some systematic difference in the 2 SAECGs as the second QRSd was significantly prolonged compared with the first for both noise levels. Thus, their findings may be affected by some external factor that altered the average QRSd between the 2 recordings.

Our finding that, at a given noise level, the QRSd is normally distributed suggests that there is intrinsic statistical variability to the SAECG. If one recorded multiple SAECGs to the same noise end point in an individual, one would obtain a normal distribution of QRSd. The distribution would be wider in the presence of low-amplitude signals, such as late potentials. This variability is due in large part to the phase relationship of noise to signal, as shown schematically in Figure 1. The computer simulation confirmed this hypothesis. The only variable that changed among the 10 000 repeated determinations was the phase relationship between noise and signal; this resulted in a normal distribution of end point and duration measurements.

This reciprocal relationship between accuracy (increases with noise reduction) and reproducibility (decreases with noise reduction) has significant implications. As noise was reduced from 0.5 to 0.3 μV, QRSd increased by 3.4 to 6 ms, presumably because of improved accuracy. At the same time, 95% CIs for a single QRSd estimate also increased by 3.4 ms (±6.6 ms at 0.5 μV and ±10.0 ms at 0.3 μV in study 1); this increase in 95% CIs for a single QRSd estimate results in decreased reproducibility, which may offset the improved accuracy achieved by noise reduction in this range. Because SAECG reproducibility is even less with late potentials, it is possible that the improved accuracy associated with noise reduction from 0.5 to 0.3 μV might be associated with an even greater loss in reproducibility. SAECG analysis in clinical practice must take this tradeoff into account.

Considerable variation in SAECG parameters in patients with late potentials has been described. With late potentials, the phase relationship of noise to the low-amplitude signal has more dramatic effects on determination of QRS offset, accounting for the diminished reproducibility. This was nicely demonstrated by the wider distribution for S1 in the computer simulation.

Implications
In an individual, multiple QRSd measurements at the same noise end point results in a normal distribution centered at the mean QRSd for that noise level. A single measurement may
arise from anywhere in this distribution and may therefore differ from the expected QRSd at that noise level. Whenever sampling from a normal distribution, the reliability of the sample as an estimator of the mean can be improved by multiple versus single sampling. The 95% CI with multiple sampling decreases inversely with the square root of the number of samples (50% reduction with 4 samples). Berbari et al. provided an example of the utility of using repeated SAECGs to identify low-amplitude late potentials. Although acquiring multiple SAECGs may be impractical because of time constraints, Lander et al. reported a modified form of filtering that can acquire high-quality, low-noise SAECGs averaging only 64 beats. This technical advance makes it more practical to acquire multiple SAECGs. The average QRSd obtained from multiple recordings is a better estimate of the QRSd for that noise level than any single determination. Importantly, the strategy of multiple sampling at a given residual noise level can be generalized to any process that assesses low-amplitude signals.

An alternative strategy is to evaluate SAECG clinical utility at different noise levels. It is possible that an optimal residual noise level is identifiable that achieves an ideal balance between accuracy and reproducibility; signal averaging can then be adjusted to target this level rather than trying to achieve minimum noise levels.

The importance of the phase relationship between signal and noise as a determinant of reproducibility can be generalized. For example, the reproducibility of low calcium scores on electron-beam CT of the heart is lower than that of high scores. Although there are clearly many technical factors that may affect the immediate reproducibility of this test, it is possible that the phase relationship of noise to signal plays an important role in subjects with low signal levels.

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References
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