

Late QRS Activity in Signal-Averaged Magnetocardiography, Body Surface Potential Mapping, and Orthogonal ECG in Postinfarction Ventricular Tachycardia Patients

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Background: Delayed electrical activity necessary for re-entrant ventricular tachycardia (VT) is detectable noninvasively with high resolution techniques. We compared high resolution signal-averaged analysis of magnetocardiography (MCG), body surface potential mapping (BSPM), and orthogonal three-lead ECG (SA-ECG) in the identification of patients prone to VT after myocardial infarction (MI).

Methods: Patients with remote myocardial infarction and cardiac dysfunction were studied, 22 with (VT group) and 22 without VT (control group). MCG with seven channels and BSPM with 63 and SA-ECG with three orthogonal leads were registered. After signal-averaging and highpass filtering, three time domain analysis (TDA) parameters describing late electrical activity were computed: QRS duration (QRSd), root mean square amplitude (RMS) of the last 40 ms of QRS, and the duration of the low-amplitude QRS end (LAS).

Results: All parameters by each method were significantly different between the patients' groups. For example, LAS parameter in MCG was 59 (SD 22) ms in the VT group vs. 37 (SD 13) ms in controls ($P < 0.001$), 77 (SD 22) ms vs. 56 (SD 19) ms in BSPM ($P = 0.002$), and 60 (SD 24) ms vs. 39 (SD 22) ms in SA-ECG ($P = 0.005$). The combination of LAS parameter in MCG and SA-ECG resulted in improved performance in comparison to any single parameter with 95% sensitivity and 68% specificity.

Conclusions: All three high resolution methods identified VT propensity among post-MI patients with cardiac dysfunction and between-method differences were small. Information in MCG and SA-ECG may be complementary and their combination could be of value in postinfarction arrhythmia risk assessment.

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magnetocardiography; body surface potential mapping; orthogonal ECG; ventricular tachycardia; myocardial infarction

Although the risk of malignant ventricular arrhythmias and sudden cardiac death after myocardial infarction (MI) has decreased in the thrombolysis era,¹ the identification of high risk patients remains

important in the face of the new effective therapies including implantable defibrillators.^{2,3} Late potentials recorded with high resolution, signal-averaged orthogonal ECG (SA-ECG) serve as indirect mark-

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ers of the arrhythmia substrate and have shown association with the propensity to ventricular tachycardia (VT) in the chronic phase of MI.⁴⁻⁵

Recently, highly sensitive signal-averaged magnetocardiographic (MCG) mapping has shown promise in the detection of the small amplitude abnormal electrical activity referred to as *late fields*.⁶ There is suggestive evidence that MCG is more sensitive than the orthogonal three-lead SA-ECG in the identification of post-MI VT patients.⁷

Body surface potential mapping (BSPM) provides a comprehensive representation of the potential distribution on the body surface. Both animal and clinical studies suggest that, in comparison to SA-ECG with three orthogonal leads, multilead signal-averaged BSPM may better identify late potentials in postMI patients.⁸ The aim of the present study was to investigate the discriminative ability of MCG late fields and late potentials in both BSPM and SA-ECG in postMI patients with a significant left ventricular dysfunction.

METHODS

Study Patients

The study population comprised 44 patients with a history of MI and left ventricular dysfunction defined as left ventricular ejection fraction (LVEF) \leq 45%. Coronary arteriography was performed and LVEF was obtained from cineangiograms in right anterior oblique projection. A significant coronary artery stenosis was defined as \geq 50% narrowing of the vessel diameter. Left ventricular aneurysm was defined as a left ventricular wall segment with paradoxical systolic motion. Patients with a bundle branch block in 12-lead ECG were excluded from the study. The patients were

divided into two groups based on a history of sustained VT.

Control Group

The control group consisted of 22 consecutive patients with a MI more than 6 months ago, LVEF \leq 45%, and with no history of sustained ventricular arrhythmias. They had been admitted for diagnostic coronary arteriography. In a follow-up of 31 (SD 12) months, 20 of 22 (91%) of the control patients remained free of sustained ventricular arrhythmias and sudden death. The clinical characteristics of the patient groups are given in Table 1.

VT Group

The VT group consisted of 22 patients with a remote MI and referred to electrophysiological study. Seventeen patients had a history of documented sustained (over 30 sec) monomorphic VT and five patients had been resuscitated from ventricular fibrillation (VF) not related to acute MI. Any antiarrhythmic medication was discontinued for at least five half lives before the electrophysiological study. Programmed ventricular stimulation was performed using 600 and 400 ms driving cycle lengths and up to three extrastimuli in two right ventricular sites. Sustained monomorphic VT was inducible in all patients including the patients with VF as the presenting arrhythmia.

MCG Recording and Data Analysis

MCG recordings were performed in a magnetically shielded room (Euroshield Ltd., Eura, Finland) using a 67-channel cardiomagnetometer

Table 1. Patient Characteristics

Characteristics	VT Group (n = 22)	Control Group (n = 22)	P Value
Age (years)	64 (SD 7)	61 (SD 9)	NS.
Female/male	1/21	4/18	NS.
Infarct location:			
Anterior/inferior/both	9/10/3	10/10/2	NS.
Arteriographic finding:			
(1/2/3 vessel disease)	2/7/13	3/7/12	NS.
LVEF (%)	31 (SD 6)	34 (SD 5)	NS.
Left ventricular aneurysm	8 (36%)	1 (5%)	0.021

LVEF = left ventricular ejection fraction; VT = ventricular tachycardia.

(Neuromag Ltd., Helsinki, Finland). The cardiomagnetometer is equipped with seven coaxial (perpendicular to the chest plane) dc-SQUID (Superconducting Quantum Interference Device) gradiometers, which record the component of the magnetic field perpendicular to the chest. The patient lay on a nonmagnetic bed and the cardiomagnetometer was placed close to chest on the left side to record MCG data for 5 minutes (Fig. 1).

Recordings were band-pass filtered at 0.03-300 Hz and digitized with a sampling frequency of 1 kHz. Automatic signal averaging, 40 Hz high pass filtering, and signal processing including the definitions of QRS onset and offset were performed as described elsewhere.⁷ Only channels with an average residual noise ≤ 35 fT (fT = 10^{-15} Tesla, unit of the magnetic field strength) in the 40 ms noise interval in the ST segment were used in the analysis. There were 6 (SD 1) accepted leads in both groups (P = NS.). The mean noise level was 7 (SD 2) fT. The following time domain analysis (TDA) late field parameters were computed: QRS duration (QRSd), root mean square amplitude of the magnetic field strength during the last 40 ms of the QRS complex (RMS_{40}), and duration of the low amplitude signal (LAS) below 300 fT (LAS_{300}). In the final analysis, the mean values of all the seven channels were computed. In order to investigate whether our MCG mapping system would allow enhanced

late field detection with a limited channel selection, the mean values of the three channels with the most abnormal values (in QRSd and LAS the longest and in RMS the smallest values) were computed as well.

BSPM Recording

BSPM with 63 unipolar leads covering the anterior thorax was performed. Wilson's central terminal was used as a reference. The Ag/AgCl electrodes with a vertical interelectrode distance of 5 cm were used. The electrodes were attached to 9 flexible plastic strips each containing 7 electrodes. The strips were attached to anterior torso vertically with the highest electrode density on the left (Fig. 1). The horizontal distances between the electrode strips were determined individually according to the dimensions of the thorax. BSPM was recorded in supine position at rest for 5 min.

SA-ECG Recording

For a conventional SA-ECG recording, an orthogonal bipolar X, Y, and Z lead system was used. The X lead was derived as the difference between two unipolar electrodes positioned at the fourth intercostal space in both midaxillary lines, the Y lead as the difference between the unipolar BSPM elec-

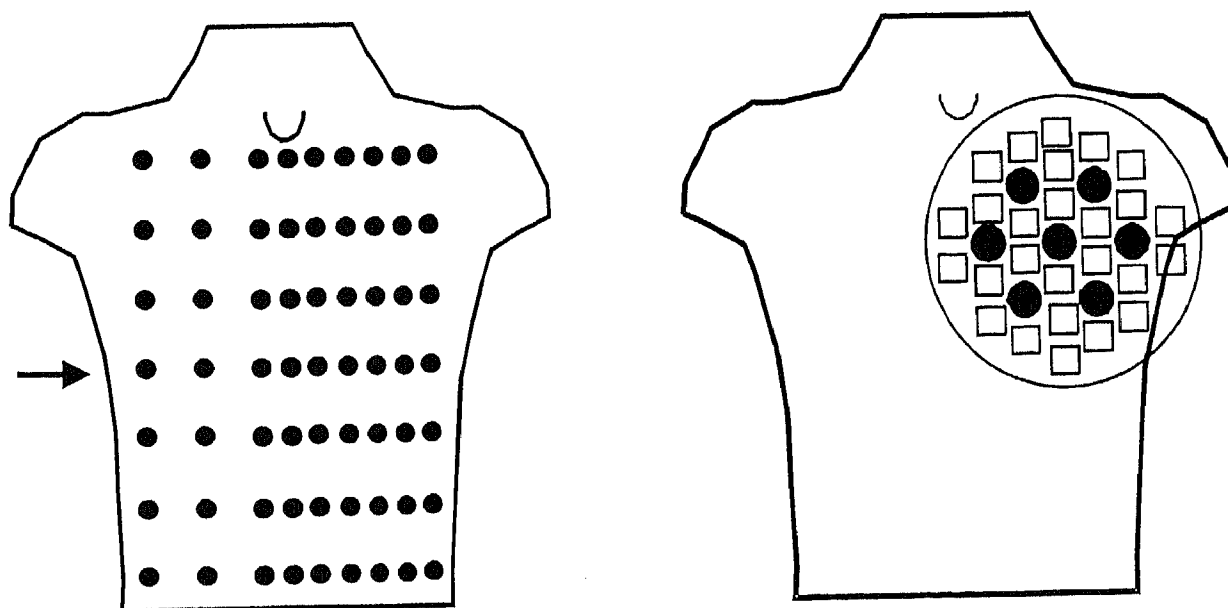


Figure 1. The body surface sites of the 63 BSPM electrodes (left) and the seven co-axial channels in MCG (right, black dots). The arrow indicates fourth intercostal space.

trodes on the superior part of the sternum and at the left iliac crest. The Z lead was derived as the difference between the unipolar BSPM electrode at the fourth intercostal space (V_2 position) and an additional unipolar electrode directly posteriorly on the left side of the vertebral column.

BSPM and SA-ECG Data Analysis

Recordings were band-pass filtered at 0.16-300 Hz and digitized with a sampling frequency of 1 kHz. Signal averaging, time-domain analyses, and determination of QRS onset and offset were performed analogous to the MCG data. For SA-ECG, the filtered X, Y, and Z leads were combined into a vector magnitude $(X^2 + Y^2 + Z^2)^{1/2}$. In BSPM, only channels with an average residual noise $\leq 1.0 \mu\text{V}$ in the 40 ms noise interval in the ST segment were used in the analysis. There were 52 (SD 7) accepted leads in the VT group and 48 (SD 7) in the control group ($P = \text{NS.}$). In SA-ECG, the average residual noise in the 40 ms noise interval of the composite complex was $\leq 1.0 \mu\text{V}$ in all patients. The mean noise level in signal-averaged BSPM was 0.6 (SD 0.2) μV and 0.7 (SD 0.2) μV in SA-ECG.

The following TDA parameters for BSPM and orthogonal SA-ECG were computed: QRS duration (QRSd), root mean square amplitude during the last 40 ms of the QRS complex (RMS_{40}), and duration of the low amplitude signal below 40 μV (LAS). Analogous to the MCG data, in BSPM both the mean of five and ten channels with the most abnormal values and the mean of all the 63 channels were computed.

Statistical Analysis

Continuous variables are presented as mean values and their standard deviations (SD) and discrete variables as frequencies and percentages. Comparisons between the groups were made using the Student *t* test for continuous variables and the Chi-square test for discrete variables. Spearman's rank correlation test was used to study the correlations between the variables.

A backward stepwise logistic regression analysis was performed to study whether the TDA parameters show discriminative value independently of clinical variables. Each parameter was entered in the model separately together with the clinical parameters; a *P* value of 0.05 was used as a limit to enter the equation and a *P* value of 0.10 as a limit to be removed from the equation.

Receiver operating characteristic (ROC) curves were created for individual parameters to assess their performances in VT identification. The areas under the curves together with their standard errors are given in fractions of the maximum value 1, which would be the result of a test yielding a 100% sensitivity and specificity.

Statistical significance was defined as a *P* value < 0.05 . Sensitivity was defined as a percentage of abnormal test results in patients with VT, and specificity as a percentage of normal test results in control patients. Positive predictive value was defined as the percentage of patients with abnormal test results who were correctly diagnosed as VT patients, and negative predictive value as the percentage of patients with normal test results who were correctly diagnosed as nonVT controls. The SPSS for Windows (version 10.0) biostatistic software was used.

The institutional ethical review board approved the study protocol, and the study patients gave an informed consent.

RESULTS

In signal-averaged MCG, the average of the three channels with the most abnormal values discriminated VT and control patients better than the average values of all seven channels. For example, the average over three channels in QRSd was 153 (SD 39) ms in the VT group and 124 (SD 16) ms in controls ($P = 0.003$), and the corresponding average values over all seven channels were 145 (SD 36) ms and 121 (SD 18) ms ($P = 0.008$). An example of the spatial distribution of the parameter values in MCG is shown in Figure 2. In contrast, in BSPM the average of all the channels showed a slightly better VT identification in comparison to average of either five or ten channels. The average of the ten channels in QRSd was 182 (SD 28) ms in the VT group and 157 (SD 31) ms in the control group ($P = 0.008$), and the corresponding averages of all the 63 channels were 149 (SD 22) ms and 128 (SD 18) ms ($P = 0.006$). For the remaining part of the paper, the MCG data will be given as the averages of the three most abnormal channels and the BSPM data as the averages of all the channels.

TDA parameter values in MCG, BSPM, and orthogonal SA-ECG were significantly different between VT and control groups (Table 2). The most significantly different parameter in MCG was LAS_{300} (159 (SD 22) ms in the VT group and 37 (SD

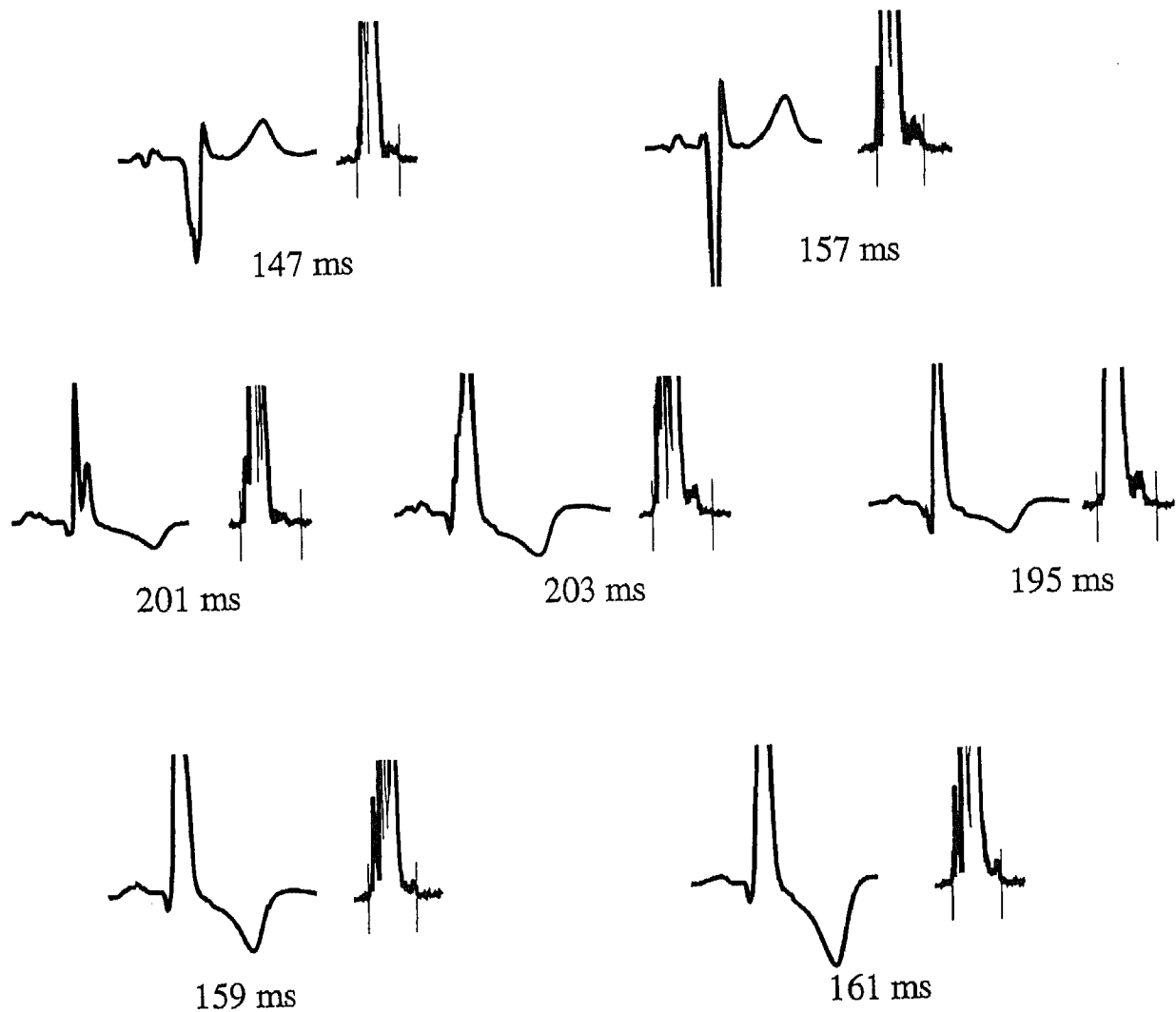


Figure 2. The seven MCG channels in one of the VT patients with the signal-averaged, unfiltered QRS complex before (left) and after (right) 40Hz highpass filtering. The vertical bars indicate QRS onset and offset and the numbers indicate QRS duration in each channel. The average of the three channels in the middle is 200 ms and the average of all channels is 175 ms.

13) ms in controls, $P < 0.001$). Also in BSPM ((77 (SD 22) ms vs. 56 (SD 19) ms, $P = 0.002$) and SA-ECG ((60 (SD 24) ms vs. 39 (SD 22) ms, $P = 0.005$)) LAS_{40} was highly significant. By all three methods, QRS_d and RMS were significantly different between the two groups, as well.

ROC Curves

The ROC curves showed that the differences between the three signal recording methods in VT identification were small (Fig. 3). The areas under the ROC curves ranged between 0.72 and 0.81.

Logistic Regression Analysis

Using the history of VT as the dependent variable, each TDA parameter was entered in the model separately together with age, gender, infarct location, LVEF, the presence of left ventricular aneurysm, and the number of stenosed coronary arteries. All TDA parameters except RMS_{40} in MCG remained in the model, thus contributing significantly to VT identification (Table 3). In contrast, the patient groups were very similar as regards the clinical variables and only the presence

Table 2. Parameter Values in Signal-Averaged MCG, BSPM, and SA-ECG

	VT Group	Control Group	P Value
MCG			
QRS duration (ms)	153 (SD 39)	124 (SD 16)	0.003
RMS ₄₀ (fT)	127 (SD 144)	226 (SD 162)	0.038
LAS ₃₀₀ (ms)	59 (SD 22)	37 (SD 13)	< 0.001
BSPM			
QRS duration (ms)	149 (SD 22)	128 (SD 18)	0.006
RMS ₄₀ (μV)	9 (SD 6)	17 (SD 10)	0.002
LAS ₄₀ (ms)	77 (SD 22)	56 (SD 19)	0.002
SA-ECG			
QRS duration (ms)	149 (SD 27)	127 (SD 26)	0.009
RMS ₄₀ (μV)	11 (SD 8)	25 (SD 19)	0.004
LAS ₄₀ (ms)	60 (SD 24)	39 (SD 22)	0.005

fT = 10⁻¹⁵ Tesla; LAS = low amplitude signal duration; RMS = root mean square amplitude; VT = ventricular tachycardia; MCG = magnetocardiography; BSPM = body surface potential mapping; SA-ECG = orthogonal three-lead ECG.

of left ventricular aneurysm provided independent discriminative value in logistic regression analysis.

Correlations Between the Methods

All the parameters correlated markedly between MCG and BSPM. Correlation coefficient was 0.86

for QRSd (P < 0.001), 0.67 for RMS₄₀ (P < 0.001), and 0.69 for LAS (P < 0.001) (Fig. 4). On the other hand, the correlations between MCG and orthogonal SA-ECG parameters were weaker; correlation coefficient for QRSd was 0.57 (P < 0.001), 0.24 for RMS₄₀ (P = 0.114), and 0.28 for LAS (P = 0.065).

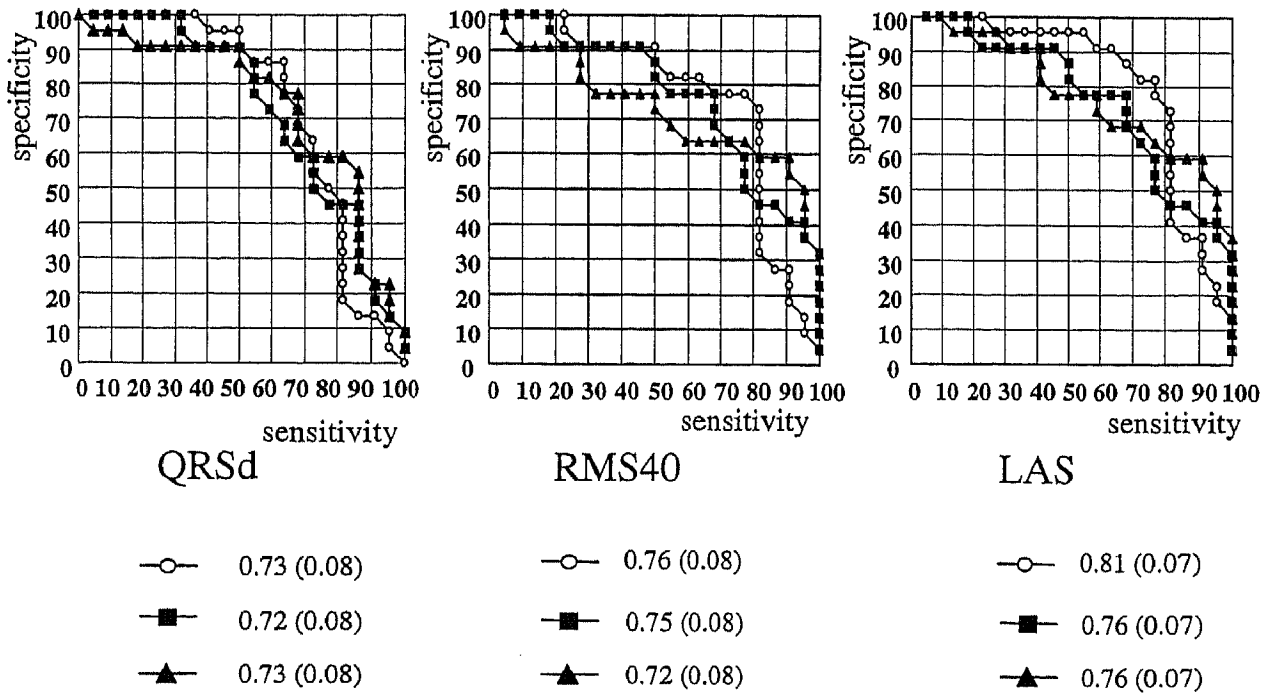


Figure 3. Receiver operating characteristic curves illustrating the discriminative powers of all the time-domain parameters in signal-averaged MCG (○), -BSPM (■), and orthogonal three-lead ECG (▲). The areas under the curves with their standard errors are given under each chart.

Table 3. Results of Stepwise Logistic Regression Analysis with VT as the Dependent Variable

Parameter	RR	P Value
MCG		
QRS duration	1.04 (1.01–1.07)	0.008
*RMS ₄₀	—	—
LAS ₃₀₀	1.08 (1.02–1.13)	0.003
BSPM		
QRS duration	1.04 (1.00–1.07)	0.024
RMS ₄₀	0.89 (0.82–0.98)	0.016
LAS ₄₀	1.05 (1.01–1.09)	0.011
SA-ECG		
QRS duration	1.04 (1.00–1.07)	0.011
RMS ₄₀	0.92 (0.86–0.98)	0.015
LAS ₄₀	1.05 (1.02–1.09)	0.004

Each TDA parameter in MCG, BSPM, and SA-ECG was entered separately into the model together with the clinical variables. RR = Risk ratio (95% confidence interval in brackets); * RMS₄₀ in MCG did not enter the model.

The correlation coefficient values for BSPM and SA-ECG parameters were intermediate to those above.

Combination of TDA Parameters in VT Identification

We also studied the performance of the combinations of the TDA parameters in each method. The best performing cut points resulting in the maximum sum of sensitivity and specificity were obtained from the ROC curves and for each

method the criteria for abnormality was defined as ≥ 2 of 3 parameters displaying abnormal values. Using this criterion the sensitivity and specificity were 77% and 82% in MCG, 68% and 73% in BSPM, and 91% and 59% in SA-ECG. The corresponding positive and negative predictive values were 81% and 78% in MCG, 71% and 70% in BSPM, and 69% and 87% in SA-ECG.

Since LAS parameters in MCG and SA-ECG did not show mutual correlation and both contributed independently to VT identification, we investigated the value of the combination of these parameters. Using a criteria of LAS₃₀₀ in MCG > 47 ms or LAS₄₀ in SA-ECG > 42 ms yielded a sensitivity and specificity of 95% and 68% in classification to VT group.

DISCUSSION

This study investigated delayed ventricular conduction associated with postinfarction VT propensity using signal-averaged, high resolution MCG, BSPM, and SA-ECG based on orthogonal three-lead recordings. To the best of our knowledge, this is the first study comparing these three signal-recording methods in arrhythmia risk stratification. The results show that late fields in MCG as well as late potentials in both BSPM and orthogonal SA-ECG identify patients with a propensity to VT after large MI. The differences between different TDA parameters and between the three recording methods in VT identification were small.

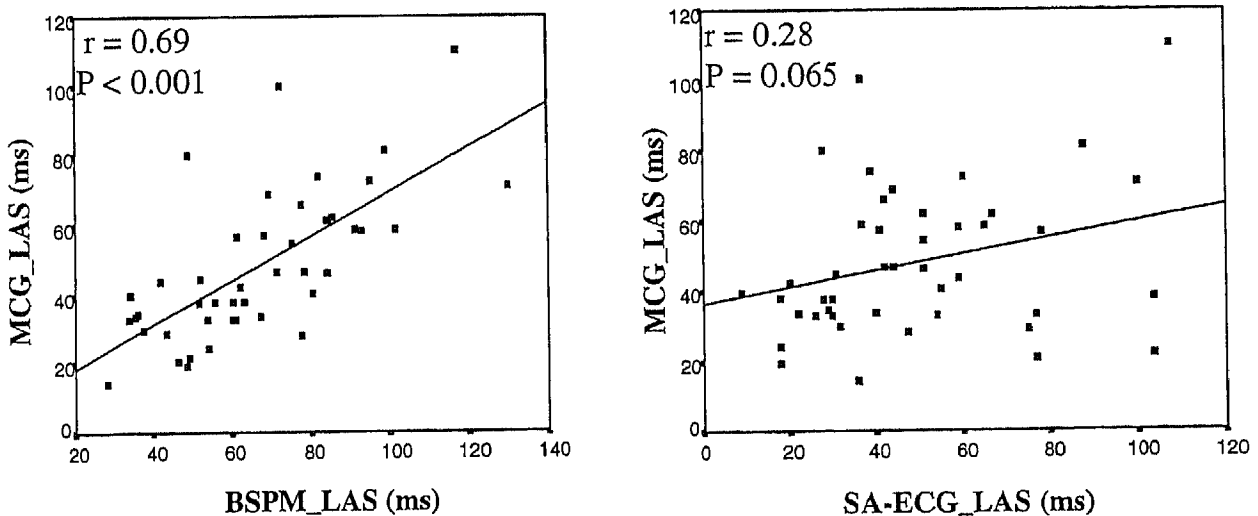


Figure 4. The correlations between LAS parameters in MCG and BSPM (left), and between LAS parameters in MCG and SA-ECG (right).

The parameters in MCG and BSPM correlated strongly whereas the correlations with MCG and orthogonal SA-ECG parameters were small. The combination of LAS parameters of MCG and SA-ECG improved VT identification in comparison to either method alone. This implies that MCG and SA-ECG may have additional value in VT identification. This might in part be due to MCG and ECG being sensitive to different components of the cardiac electric activity. MCG is more sensitive to currents that are tangential to body surface, whereas ECG is more sensitive to currents radial to it.¹¹

Late potentials in SA-ECG, originally presented in clinical VT risk stratification by Simson,⁵ are indirect markers of the arrhythmia substrate in the surviving myocardium. Prospective studies have shown them to be sensitive markers of the increased risk of ventricular arrhythmias in the chronic phase of MI especially in combination with other noninvasive risk parameters.^{9,10} Although the sensitivity and negative predictive accuracy of SA-ECG with three orthogonal leads are good, low specificity and positive predictive accuracy have prompted testing of other noninvasive recording methods for detection of the arrhythmia substrate. The results from a recent study suggested that, in comparison to late potentials, the late fields in high resolution signal-averaged MCG might better identify VT patients especially in the presence of a large infarction and a significant myocardial dysfunction.⁷ MCG has some advantages over SA-ECG, including the lack of skin-electrode contact susceptible to disturbing noise and less influence from the intervening tissues on the recorded signal.¹¹

Multilead BSPM providing a superior spatial resolution in comparison to 12-lead ECG has many potential applications such as localization of accessory pathways and site of origin of VT, enhanced detection of myocardial ischemia, and assessment of abnormal repolarization patterns connected to life-threatening ventricular arrhythmias.¹²⁻¹⁵ The present study on postMI patients with a marked myocardial dysfunction showed late potential parameters in BSPM to have equal discriminative ability in comparison to SA-ECG and MCG.

Previously, Freedman, et al. in animal studies and Sasaki, et al. in patients with ischemic heart disease, showed that late potential parameters in multilead BSPM more strongly correlated with fragmented intracardiac electrograms in comparison to three-lead SA-ECG.^{8,16} On the other hand,

they did not try to correlate these findings to the spontaneous occurrence or inducibility of ventricular arrhythmias and therefore the implications of the results in VT prediction are not clear. In another study by Sasaki, et al, 48-lead BSPM had increased sensitivity but decreased specificity compared to three-lead orthogonal ECG.¹⁷ Although sensitivity and specificity are dependent on the cut-point values chosen, some of the findings in our study lend support to their findings. For example, LAS parameter was markedly longer in BSPM than in SA-ECG indicating better detection of late potentials. However, LAS was much longer in controls as well resulting in false positive findings and the discrimination remained equal to SA-ECG. Ho, et al. found increased sensitivity without loss of specificity using a 28-lead BSPM in comparison to SA-ECG.¹⁸ In contrast to the present study the control patients had only slightly impaired left ventricular function (mean LVEF was 47% compared to 34% in our study) which could have decreased the number of false-positive findings. The results of our study indicate that with a markedly impaired LVEF the late potential parameters exhibit abnormal values in the controls as well.

In MCG using the average of three most abnormal channels was superior compared to averaging all channels in VT prediction. This may imply that high resolution, signal-averaged MCG is capable of sensitive detection of localized areas with delayed conduction in the presence of left ventricular dysfunction. This is also suggested by a previous study, which showed better detection of late fields when MCG was registered over the left side compared to a more central position.¹⁹

In comparison to a recently published study, orthogonal ECG performed better concerning RMS and LAS parameters.⁷ This difference may be explained by different instrumentation. The earlier study utilized a commercial registering device and signal-averaging software whereas this study utilized a custom-made data collection and analysis system.²⁰

Study Limitations

The criteria used in the assessment of sensitivity and specificity were created afterwards on the basis of the ROC curves and therefore their values should be understood as illustrative only. The criteria for abnormality are not necessarily transferable to recordings performed early after MI, or

utilized prospectively in a patient cohort. The figures of positive and negative predictive values of the present study should neither be utilized in prospective postMI patient cohorts due to different prevalences of VT.

The number of the patients studied was relatively small and therefore the results need confirmation in larger patient cohorts. The low correlation between LAS parameters in MCG and SA-ECG does not automatically mean that they provide independent predictive information and factors such as large interindividual variation in parameters could decrease the correlation between them.

Classifying patients to those having or lacking propensity to ventricular arrhythmias was based on history of sustained ventricular arrhythmias. Although the control group remained not completely free of arrhythmias in follow-up, the relative long observation period confirmed that the risk of ventricular arrhythmias was indeed low.

The present study did not utilize any MCG channels and BSPM electrodes covering the back. Although the abnormal delayed conduction is probably best exhibited anteriorly, closest to myocardium, registering on the back might have yielded additional information on posterior part of the heart.

This study did not attempt to utilize the spatial distribution of late potentials in signal-averaged BSPM. With a larger number of patients it could be possible to investigate how infarct location affects late potential distribution over chest.

Conclusions

In comparison to orthogonal SA-ECG the new high resolution methods, MCG and BSPM, performed equally well in the assessment of VT propensity among post-MI patients with a significant left ventricular dysfunction. Combining MCG and SA-ECG information may result in improved detection of late QRS activity indicative of postinfarction arrhythmia propensity. Further studies investigating whether the spatial distribution of late QRS activity could be used in postinfarction risk stratification are warranted.

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