Resolution of Pace Mapping Stimulus Site Separation Using Body Surface Potentials

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Background Several studies have related 12-lead ECG waveform during ventricular tachycardia to ECG waveform during ventricular pacing to identify ablation sites for therapy of ventricular tachycardia. QRS isopotential maps and QRS isointegral maps derived from body surface isopotential maps have also been correlated with left ventricular pacing sites with the same objective. The comparison process used is subjective and only semiquantitative. Improved accuracy of catheter placement may improve success rates of ablation therapy.

Methods and Results This animal study was performed to determine the spatial resolution with which left ventricular pacing sites could be distinguished by body surface isopotential mapping. Potentials were recorded from 64 evenly spaced thoracic leads. Hexapolar or octapolar pacing catheters with 2-mm interelectrode spacing were placed percutaneously in the left ventricle in each of six dogs, and bipolar endocardial pacing was performed using each pair of adjacent electrodes.

A number of experimental and clinical studies have attempted to relate left ventricular pacing site in normal and abnormal hearts to QRS morphology and frontal plane axis of the 12-lead ECG. The stimulation site in these studies has been determined by multiplane fluoroscopy in the case of endocardial pacing and by direct observation with epicardial pacing. The discrimination capability of these studies has been limited to QRS pattern identification associated with stimulation of "regions" of the left or right ventricles. A patient study by Kadish et al. with the most rigorous criteria for visual comparison of ECG waveform, suggested that spatial resolution of the technique of using the 12-lead ECG to discriminate between pacing sites is "generally" about 5 mm.

Body surface potential mapping has also been used to identify sites of ectopic ventricular stimulation. Spach et al. used body surface potential mapping to distinguish between seven epicardial pacing sites in the chimpanzee. Several investigators have used similar techniques in patients to locate accessory pathways in preexcitation syndromes. A body surface mapping study by Hayashi et al. used isopotential maps to correlate a limited number of endocardial pacing sites in both ventricles with map patterns. Detailed patient studies by Sippens-Groenewegen et al. provided map patterns from left and right endocardial ventricular pacing sites in normal hearts and postinfarction hearts using QRS isointegral maps constructed from 62-body surface recordings. Their data suggest that QRS integral map patterns during left ventricular pacing cluster in relation to specific paced segments of the structurally normal left ventricle. They estimate that, on average, resolution of paced regions of the left ventricle using QRS integral maps is about 3.5 cm². Taken together, body surface potential mapping studies suggest that the technique supplies more regionally selective information than the 12-lead ECG. However, none of the cited studies provide information about the precise distance over which maps from different pacing sites can be differentiated. The methods of map comparison depend primarily on visual comparison of map features.

Radiofrequency ablation is increasingly being used as therapy for ventricular tachycardia but with modest success compared with treatment of other types of arrhythmias. Identifying sites suitable for catheter ablation of ventricular tachycardia involves pacing from a precise location that is part of the ventricular reentry circuit. Several factors are involved in determination of an appropriate ablation site. These may include characteristics and timing of the ventricular electrogram and
time interval from the pacing stimulus to ventricular response during entrainment of the ventricular tachycardia. The usual method to identify an appropriate site also involves comparison of a 12-lead ECG during ventricular pacing with a 12-lead ECG of the patient's clinical ventricular tachycardia or induced ventricular tachycardia. Precision of this comparison process involves visual concordance of QRS waveform of varying numbers of leads. Precision and reproducibility of this comparison process is probably limited by subjectivity and by the number of leads used.

The purpose of this study was to determine over what distance different left ventricular endocardial pacing sites could be distinguished by body surface potential mapping in an animal model with a normal heart. The work is viewed as an initial step in development of better techniques to place an ablative catheter as precisely as possible in the ventricular cavity in relation to a ventricular tachycardia reentry circuit. The potential precision of the method described does not depend on radiographic or anatomic markers. The study used a computer-based method of potential map comparison that is quantitative, rapid, and potentially useful in patient studies involving pace mapping.

Methods

Data Recording

The study protocol conformed to the guiding principles of the American Physiological Society for studies involving experimental animals and was approved by the Institutional Animal Care and Use Committee of the University of Utah. Studies were performed in six dogs weighing 18 to 25 kg anesthetized with pentobarbital (20 mg/kg). Corneal reflex was monitored and anesthesia supplemented as needed. Sixty-four recording electrodes were placed on the shaved thorax in eight evenly spaced rows and columns. The top row was at the level of the sternal notch, and the bottom row was at the level of the xiphoid. A bipolar pacing catheter was placed percutaneously in the right atrium. Biplane fluoroscopy was used to place a percutaneously inserted multielectrode catheter sequentially in three different regions of the left ventricle: apical, left posterolateral, and midseptal. Left ventricular catheters had either six or eight electrodes with 2-mm spacing. In one of the six experiments, the eight-electrode catheter was also placed in the right ventricle in two positions. PACing was done at twice diastolic threshold at each site at a cycle length just shorter than sinus rhythm, either 375 or 400 milliseconds. The same rate was used for all pacing sites during any one experiment. For each catheter placement, maps were recorded for 3 to 5 seconds after pacing from each pair of adjacent electrodes for 1 minute, the distal electrode always serving as the cathode. Amplification varied from 500 to 2000, depending on the preparation. All signals were filtered from 0.03 to 500 Hz, sampled and held, digitized to 12 bits at a rate of 1000 Hz per channel, and stored in computer memory. If, after review, data had no evidence of artifact and all beats exhibited capture, the data were stored on disk for later processing. For each catheter placement, the sequence of pacing from each electrode pair was repeated twice. Beat-to-beat variability at each pacing site was analyzed, as well as variability of pacing the same site during two different pacing sequences. The latter comparison was performed to verify stability of catheter placement. Right atrial pacing was delayed as late as possible with respect to ventricular pacing so that P waves occurred during the early ST segment, and they were not included in QRS waveform analysis.

Analysis

Each recording of 64 leads was processed in the same manner. Briefly, three to six QRS complexes from each recording were ensemble averaged to improve signal-to-noise ratio and reduce effects of baseline drift. Potentials at each site were calibrated to a prerecorded signal, and linear baselines defined between adjacent TP segments were subtracted from each lead. Isointegral maps of QRS and ST-T intervals were displayed to ensure that no data were missing or noisy. If such was the case, the data were interpolated, but typically there were no defective recordings. In addition, root-mean-square (RMS) voltage curves were plotted, from which baseline determination was assessed and modified if necessary and from which onset and offset of QRS and offset of T were manually determined.

The two map sequences were cross-correlated in time using all 64 leads and time shifts of ±n milliseconds, where \(-20 < n < 20\). The maximum correlation was noted and used as an index of map similarity. In addition, a difference map was obtained by subtracting the time-aligned maps lead by lead and instant by instant throughout the QRS. RMS voltage of the difference maps was calculated for each instant in the QRS, and an average RMS voltage throughout the QRS was calculated. Maximum correlation, average RMS error, and pacing site separation were tabulated for statistical analysis.

The ability of maximum correlation and average RMS voltage to discriminate stimulus site separation from the maps was assessed by the nonparametric, upaired, Kolmogorov-Smirnov test. Comparisons were made for each catheter placement and not between catheter placements. Because we had no accurate means to precisely measure distance between catheter placements, no attempt was made to differentiate between sites existing in different placement sequences. If the repeat measurements for a given catheter placement were not in agreement (differences of the same pacing site measured at two different times greater than the differences of sites separated by 2 mm), then data from the entire placement were excluded, with the presumption that the catheter had moved sometime during the study. This occurred in 10% of instances, and the data were not included in the final analyses.

For illustration purposes and to approximate subjective pacing site distance discrimination capability of the standard ECG during ventricular pacing, we used 8 leads derived from the 64 evenly spaced body surface leads (3 limb leads closely approximating I, II, and III and 5 precordial leads). ECGs generated by pacing at sites separated by 2 mm and by 8 mm were produced for visual comparison.

Results

An example of plots of RMS voltages and difference voltages as well as plots of extrema voltages (maximum above and minimum below) for each instant in the QRS from one catheter placement in one experiment is shown in Fig 1. RMS voltage differences are shown in the first row and plots of extrema voltages in the second row. In this example, the complexes compared were initiated by pacing sites that were separated by 2, 4, and 8 mm at a cycle length of 400 milliseconds. These plots resulted from catheter placement in the apical region of the left ventricle. RMS voltage from the index site is shown as a solid line and RMS voltage from the comparison pacing site as a dotted line. Visual analysis of the RMS curves shows obvious increasing differences between the curves as pacing site separation increased. The lower dotted line is the numerical difference between the two voltage curves. This difference line provided a visual index of the relative difference between the RMS curves for the sites being compared. Similar plots were obtained from all catheter place-
RMS & Extrema Voltage Comparison

Site Separation: 2 mm  4 mm  8 mm

RMS Voltage

Extrema Voltages

Fig 1. Graphs showing a comparison of root-mean-square (RMS) voltage curves (upper row) and extrema voltage curves (maxima and minima) for pacing sites separated by 2, 4, and 8 mm. Data are from one catheter placement. Solid and dotted lines closely superimposed represent curves from the two pacing sites being compared for RMS voltage curves; the lower dotted curve is the difference between the two upper curves.

ments in all experiments in all three regions of the left ventricle. The difference between extrema voltage curves with increasing pacing site separation was less apparent, but in general, the difference in amplitude and timing of positive and negative extrema increased as pacing site separation increased.

A graph of the RMS differences between maps as a function of pacing site separation is shown in Fig 2. Comparison indexes between all pacing site pairs were stratified according to distance between pacing sites, tabulated, and assessed for significance. Beat-to-beat variation of paced complexes was assessed for all stimulation

Fig 2. Graphs showing root-mean-square (RMS) voltage curve differences as a function of pacing site separation. Each numbered graph is an average of all pacing sites in that experiment. Bars represent SD. See text for discussion of variability of SD. "0 mm" pacing site separation refers to comparison of maps pacing the same site at two different times. Nonparametric statistical comparison showed pacing site separation discernible at 2-mm distance in some instances but at 4-mm distance in all comparisons at the level of \( P < .002 \).
sites in all experiments by comparing six sequential paced complexes from each pacing site in all possible pair combinations. The average and SD of RMS voltage differences between maps from all left ventricular pacing sites as a function of pacing site separation in each of six experiments is shown. The Roman numerals above each graph refer to the number of each experiment. As already noted, each pacing site was used twice during each catheter placement, and each recording was separated by 3 to 5 minutes. "0" separation in this figure refers to pacing from the same site at the two different times. SD of the RMS voltage difference tended to increase with increasing separation of pacing sites. As can be noted, SD for any length of pacing site separation varied from experiment to experiment. This probably was due to variations of pacing site in relation to Purkinje fibers, cardiac movement, phase of respiratory cycle, etc. This variation of SD emphasizes that each preparation must serve as its own control for comparison analyses.

Application of the nonparametric, unpaired Kolmogorov-Smirnov test to these data showed that RMS voltage difference could resolve pacing site separation of 4 mm or more at the $P<.002$ level of significance.

Fig 3 diagrams correlation coefficients of potential maps over the entire duration of ventricular activation generated from each pacing site as a function of pacing site separation for maps from all left ventricular catheter placements in each experiment. Again, SD tends to increase with increasing pacing site separation but is variable from experiment to experiment for the same reasons as noted above with regard to RMS voltage differences.

Results of applying nonparametric statistical testing documented that the correlation coefficient comparison between isopotential maps during the QRS was able to resolve pacing site separation of $\geq 4$ mm at the $P<.01$ level of significance. Importantly, in three of the five experiments, it was possible to resolve separations as small as 2 mm with the same level of significance.

Results of comparing maps from one of the two catheter placement sites in the right ventricle in one experiment are shown in Fig 4. Comparisons were made for all electrode sites as described above for the left ventricular sites. RMS voltage differences and QRS correlation coefficients as a function of pacing site separation are similar to data for left ventricular placements. Application of nonparametric statistical testing to these data again documented that maps could be used to resolve pacing site separation of $\geq 4$ mm at a significance level of $P<.01$.

To simulate difficulties of the currently used technique of visual comparison of standard ECG leads, we constructed 8-lead ECGs from the 64-lead array. The leads included the standard limb leads I, II, and III and 5 precordial leads as used in canine electrocardiography. A pacing sequence from a catheter placement in one experiment was chosen as an example of the difficulty of using only visual comparison of recorded potentials in too few leads. Fig 5, left column, shows the 8-lead ECG of an index pacing site, and the middle and right columns show the same 8 leads recorded from pacing at sites 2 mm and 8 mm distant from the index site. Pacing cycle length was 400 milliseconds. Visual concordance of each ECG lead is high. Currently used criteria for similarity of complexes would probably conclude that there was no separation of pacing sites.

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**Fig 3.** Graphs showing correlation coefficients of QRS isopotential maps compared at 1-millisecond intervals as a function of pacing site separation for all pacing sites and all three left ventricular catheter placements for each of six experiments. Each numbered graph is an average of all pacing sites in that experiment. Bars represent SD. Nonparametric statistical comparison showed pacing site separation discernible at a 4-mm distance at the level of $P<.04$. 

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Body surface isopotential maps from one left ventricular catheter placement are shown in Fig 6. Maps are shown with the canine torso displayed as a cylinder unrolled from the midvertebral line. The top middle point of each map corresponds to the midsternum. Each row is labeled as to the number of milliseconds from the onset of the QRS, and each column is labeled as the reference pacing site and the distance of the comparison pacing site from the reference. Visual comparison of these maps clearly indicates that the most distinctive map was recorded at 20 milliseconds after QRS onset at the reference site. The map recorded at 20 milliseconds using a pacing electrode 2 mm from the reference electrode is distinctly different, whereas maps recorded at 20 milliseconds that resulted from pacing sites 4 mm and 8 mm from the reference site share more visual similarities than differences. The similarity of maps recorded at 40, 60, and 80 milliseconds after QRS onset at all pacing sites is apparent.

Discussion

This study demonstrates that in a canine model, pacing sites separated by as little as 4 mm can be distinguished by analysis of the body surface distribution of cardiac potentials during ventricular activation. In the normal hearts used in this study, the ability to distinguish between ventricular pacing sites separated by 4 mm or more was independent of the region of left ventricular pacing. Although not all regions of the left ventricular cavity were paced, the minimum 4-mm resolution distance was consistent across all experiments, including two catheter placements in the right ventricle in one experiment. Use of these methods in a diseased human ventricle presents differences of anatomy, and intraventricular conduction and precision of the technique under these conditions must be confirmed in actual patient studies.

Use of catheter ablation techniques in therapy of ventricular tachycardia requires precise catheter placement. The degree of precision required is uncertain, but inexact catheter placement probably accounts for some of the failures to prevent recurrent tachycardia. Mean dimensions of the catheter ablation lesion in the canine left ventricle by radiofrequency energy of 300 J are reported to be 7.1±2.8 mm long × 4.8±2.0 mm wide × 4.2±2.4 mm deep.15 This lesion size is smaller than the resolution of published methods, which use correlations of pacing sites with 12-lead ECG waveforms or QRS isointegrals from body surface maps. It is probable that several radiofrequency-induced lesions could fit within the boundaries defined by published resolutions, since these have been reported to enclose average areas of 3.3 cm² or greater.11 The 4-mm distance discrimination of techniques reported in this study approximates the dimensions of radiofrequency ablation lesions.

Potential Clinical Utility

The quantitative techniques used for map comparison in this study can be automated and done on line in the electrophysiology laboratory. Regional localization of the tachycardia circuit could be approximated from the body surface potential map recorded during tachycardia. Location of the minimum during the early QRS of
isopotential maps recorded during ventricular tachycardia or use of QRS isointegral maps such as reported in the study by SippensGroenewegen et al.\(^{11,12}\) should provide an accurate starting point for pace mapping. Maps recorded during pacing from different sites within that region could then be compared in an iterative way with a body surface map of induced or spontaneously occurring ventricular tachycardia to move progressively closer to an appropriate site within the reentry circuit. Additional factors such as morphology of recorded electrograms and time from stimulus to ventricular response may be necessary to select an effective ablation site. Similar techniques using body surface potential pace mapping have recently been described by Dubuc and coworkers\(^{16}\) to guide catheter ablation of accessory pathways in patients with Wolff-Parkinson-White syndrome. In this study, these authors paced from multielectrode catheters in the left ventricles of two patients and reported detectable differences in body surface maps recorded from pacing sites separated by 5 mm with some catheter placements, a result in line with findings of this study.

**Limitations of the Study**

Bipolar stimulation was used in this study. It is impossible to be certain that stimulation always occurred at the cathode of each pair, although this is most likely. In any event, electrode pairs were separated by only 2 mm, and the discrimination distance of the methods used was 4 mm. It is unlikely that variation in stimulation electrode site in each pair had a bearing on results of the study, since differences in maps were always significant when pacing sites were known to be separated by 4 mm or more. It also seems unlikely that discrimination of distances less than 4 mm is possible with the methods described here.

Although this study was performed in dogs with normal hearts, the methods can be adapted to patients. The precision of distance discrimination using the methods described in this study in patients with diseased hearts and localized areas of conduction delay are unknown. This study does suggest that an evaluation in coronary artery disease patients of the utility of body surface potential mapping to discriminate pacing sites may be useful. Recording electrodes are available that are invisible on fluoroscopy and do not interfere with catheter visualization.\(^{17}\) It is also possible but not documented that limited lead arrays\(^{18}\) such as the 32-lead array currently used in recording body surface maps from patients at our institution and others would provide adequate discrimination of different pacing sites without the inconvenience of more extensive arrays.

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**References**


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