Localization of Heart Vectors Produced by Epicardial Burns and Ectopic Stimuli

VALIDATION OF A DIPOLE RANGING METHOD

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ABSTRACT

Location of the equivalent cardiac dipole has been estimated but not fully verified in several laboratories. To test the accuracy of such a procedure, injury vectors were produced in 14 isolated, perfused rabbit hearts by epicardial searing. Strongly dipolar excitation fronts were produced in 6 additional hearts by left ventricular pacing. Twenty computer-processed signals, derived from surface electrodes on a spherical electrolyte-filled tank containing the test preparation, were optimally fitted with a locatable cardiac dipole that accounted for over 99% of the root-mean-square surface potential. For the 14 burns (mean radius 5.0 mm), the S-T injury dipole was located 3.4 ± 0.7 (SD) mm from the burn center. For the 6 paced hearts, the dipole early in the ectopic beat was located 3.7 mm (range 2.6 to 4.6 mm) from the stimulating electrode. Phase inhomogeneities within the chamber appeared to have a small but predictable effect on dipole site determination. The study demonstrates that equivalent dipole location can be determined with acceptable accuracy from potential measurements of the external cardiac field.

KEY WORDS isolated rabbit hearts electromotive surfaces inverse electrocardiographic problem cardiac electrophysiology equivalent cardiac dipole cardiac generator injury current

The concept that the electrical activity of the heart can be represented by a dipole, the heart vector, was formulated at least 60 years ago (1). The magnitude and the orientation of this equivalent cardiac dipole can be directly measured from a properly constructed lead system and have therefore been the subject of intensive vectorcardiographic study. In contrast, the dipole location cannot be determined in such a straightforward manner and has thus received relatively little attention. However, in the last 20 years mathematical techniques have been developed to find the location of the equivalent cardiac dipole (2-5), and computing machinery has been constructed which is capable of performing these mathematical manipulations. Consequently, reports are beginning to appear (6-10) in which the location of the heart vector is estimated as it changes throughout the cardiac cycle.

The purpose of the present study was to test the accuracy with which currently available dipole ranging techniques can locate the heart vector. We created well-localized sources of electrical activity in isolated rabbit hearts by one of two interventions: (1) epicardial cauterization or (2) subepicardial pacing. Each heart was suspended in an “artificial thorax” that consisted of an electrolyte-filled spherical chamber fabricated of polished epoxy to allow visual localization of the intervention site. Potentials created by the intervention were recorded from the chamber surface, and the equivalent cardiac dipole was calculated from these potentials. The computed location of this dipole was then compared with the actual site of the intervention on the heart.

Methods

EPICARDIAL CAUTERIZATION

Fourteen adult male New Zealand white rabbits weighing approximately 3 kg were killed by a
heavy blow to the occiput after receiving heparin intravenously. The heart was quickly excised, and the aortic stump was tied on an electrically insulated perfusion cannula which passed vertically through the top of the spherical chamber. The chamber, which had a radius of 3.175 cm, consisted of two separable hemispherical portions so that it could contain relatively large hearts (11). A typical heart had a maximum eccentricity of 0.74 and was 3.9 × 2.7 × 2.9 cm. The hearts were perfused at a pressure of 70 cm H₂O with Krebs-Henseleit solution which was modified by the addition of 2 g/liter of glucose and preheated to 37.5°C. The perfusate entering the cannula contained O₂ at a partial pressure of 525 mm Hg and CO₂ at a partial pressure of 39 mm Hg.

The mitral valve was disabled, the lower half of the tank was bolted in place, and the entrapped air within the chamber was displaced by warmed, modified Krebs-Henseleit solution. The level of the outflow standpipe was adjusted to the same height as the center of the tank. The partial pressures of the effluent leaving the chamber were determined for one heart; these values were 139 mm Hg for O₂ and 55 mm Hg for CO₂. The excised hearts beat spontaneously during these preliminary steps and continued to do so throughout the remainder of the experiment.

Potentials were recorded throughout the P-T interval from 20 differential electrocardiographic leads which were derived from 20 silver-silver chloride electrodes evenly spaced on the surface of the chamber. These leads were chained to form a closed Kirchoff’s loop. A twenty-first grounded lead. Several steps of signal conditioning followed the real-time data acquisition (11). Repeatability of the wave forms recorded from the 20 leads was checked by autocorrelation and generally found to be excellent. A sequence of QRST complexes (usually 16) was selected from the most stable portion of the record and averaged to reduce asynchronous noise. The averaged signals were converted to lead potentials by means of calibrated gain factors for the preamplifiers. Since the 20 leads formed a closed Kirchoff’s loop, the precision of this technique could be tested by computing closure error. Closure error (CE) was determined from the formula

\[
CE = \frac{1}{N} \sum_{i=1}^{N} \left| v_i \right|,
\]

where \( v_i \) is the potential in the ith lead at the jth msec of sampling and \( N \) is the number of samples in the given QRST sequence (8). Closure errors of less than 0.5% were obtained in a typical experiment. Next, three-point parabolic interpolation was employed to compensate for the time skew between leads which was introduced by the analog-to-digital converter. Finally, the QRST complexes were numerically reduced to unipolar form by referencing the potential of each electrode against a central terminal which represented the average potential of all 20 electrodes. This averaging of the 20 potentials was accomplished using a previously published formulation (9).

By an iterative mathematical procedure which has been described elsewhere (11), the equivalent cardiac dipole was calculated for every millisecond of the QRS complex and the early S-T interval. This mathematical method optimized dipole location, orientation, and strength so that the

SUBEPICARDIAL PACING

Six additional rabbit hearts were suspended in the spherical chamber by the same procedure described for the cauterized hearts. At the time when the mitral valve was disabled, the region of the right atrium containing the sinoatrial node was excised, and a subepicardial bipolar electrode was embedded in the basal portion of the left ventricular free wall. When the hearts were not being driven by the subepicardial electrode, they continued to beat spontaneously from a supraventricular site.

The chamber was reassembled, and potentials of cardiac origin were recorded as previously described both while the hearts were being paced and while they were beating spontaneously. The lower hemisphere of the chamber was replaced by the photographic accessory section, and photographs were taken as described earlier while the hearts were paced and while they beat spontaneously.

Several steps of signal conditioning followed the

Localizing heart vectors could best reproduce, in a least-squares sense, the 20 electrode potentials recorded on the surface of the spherical chamber.

No correction was made during these calculations for the difference in conductivity between the heart and the electrolyte solution. Instead, the resistivity within the entire volume of the chamber, including that space occupied by the heart, was assumed to be 57 ohm cm, which is the resistivity of the electrolyte solution.

Anatomic and electrocardiographic referencing

"Injury current" produced by epicardial searing would be expected to cause base-line depression in electrocardiograms recorded from overlying tank electrode positions (13). However, true base-line level is not actually known in ordinary electrocardiograms because of either unknown amounts of d-c offset in direct-coupled amplifiers or the d-c-blocking property of capacitor-coupled amplifiers. Faced with this problem, we opted to follow the electrocardiographic convention of selecting the most stable portion of the signal, namely the T-P segment, as the base line. Because of this arbitrary but effective choice of reference level, the effects of injury current were identified as deviations of the S-T segment rather than as base-line depression. As will be shown, treating the signals in this manner led to the determination of "injury vectors" that were directed outward from the epicardial surface with approximately normal orientation, with lumped-dipole source equivalents located somewhat subepicardially near the center of the burned area.

The purpose of the photographic system was to provide independently determined heart data against which the validity of the electrocardiographic dipole ranging technique could be checked. To this end we treated the injured area produced by epicardial searing as a uniform electromotive surface. In principle the generator properties of such a surface would be completely determined by the dipole density per unit area and the configuration of the rim that bounds the surface (14). In the case of a burn with an approximately circular plane rim, such as we sought to produce, we would expect that (1) the equivalent generator properties would be strongly dipolar, (2) there would be minimum quadrupolar content (none whatsoever in an ideal situation), (3) octapolar content would be quite small because of relatively small area, (4) the electrical center or lumped-dipole equivalent would be located at the center of the rim, and (5) the axis of the lumped-dipole equivalent would be oriented normal to the plane of the rim.

We believed that the rim of the electromotive surface probably extended somewhat beyond the visible margin of the seared area but was concentric with it. Therefore, the margin of the burn was taken as an identifiable anatomic landmark from which the location and the orientation of the lumped-dipole equivalent generator could be estimated.

![Figure 1](image-url)

Two views of an isolated rabbit heart in the chamber showing the cauterized region. View B was photographed after rotating the heart 72°. Arrows point to the seared region, and the intersection of the cross hairs indicates the center of the chamber.

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Results

EPICARDIAL CAUTERIZATION

Figure 1 shows two photographic views of the cauterized region of one of the hearts. The centroid of the grossly visible border of the burn was estimated from such photographs in the following manner. From five to nine points were selected on the perimeter of the burn. The criterion for choosing each point was that it clearly be visible in at least two different photographic views of the cauterized region. The location of the point was determined from the two views by triangulation. A circle, which was fit to these points by a least-squares method, was employed to approximate the visible border of each seared region. The radius of these circles averaged 5.0 mm with a range of 3.4 to 7.5 mm. The center of the circle was used as an estimate of the centroid of the grossly visible border of the burn.

After cauterization, those surface electrodes located over the seared region recorded S-T segment elevations which were not present before the heart was burned. A representative recording from one such electrode is seen in Figure 2; this recording was taken from the same heart shown in Figure 1. The position of the recording electrode in relation to the seared myocardium is demonstrated in Figure 3, which also shows the distribution of potentials on the surface of the chamber 7 msec after the beginning of the S-T segment. These isopotential surface maps were obtained from the 20 electrode potentials by a centripole-multipole series which was used as an interpolating function. The maps in Figure 3 correspond to the two photographic views of the heart in Figure 1. The dipolar nature of the potential distribution is suggested by the single maximum and minimum with smooth progression of potentials between these extremes.

The computed locus of the equivalent cardiac dipole moved very little during the early portion of the S-T segment. The mean distance from the computed dipole location to the center of the visibly seared epicardium 7 msec after the beginning of the S-T segment is shown in Figure 4. For 13 of the 14 preparations, this distance was less than the radius of the visible border of the burn, and for all 14 cases it averaged less than two-thirds of the burn radius.

The computed dipole locations were not randomly distributed to either side of the plane of the burn margin ($P < 0.001$). In 12 of the 14 preparations the dipole was within the wall of the ventricle, internal to the plane of the burn margin. It can be seen in Figure 4 that this inward displacement of the dipole contributed significantly to the disparity between the computed dipole location and the burn center. A mathematical simulation described in the Appendix demonstrates that lack of compensation for phase inhomogeneities by the dipole ranging technique caused the computed location of the dipole to be shifted inward from its actual location.

The root-mean-square potential residual for the 14 cases averaged 11.9% with a standard deviation of 5.0%. The root-mean-square potential residual indicates the potentials remaining at the 20 surface electrode sites after that portion of the potentials contributed by the equivalent cardiac dipole had...
**LOCALIZATION OF HEART VECTORS**

Comparison of electrically and anatomically estimated injury vectors. P = perimeter of grossly seared epicardium, C = centroid of visible perimeter of burn, D = computed location of injury vector 7 msec after the beginning of the S-T segment, D' = projection of computed injury vector location onto the plane of the burn border, M_D = dipole moment of the computed injury vector, M_D' = dipole moment of the computed injury vector moved to the centroid of the seared epicardium, N_C = line perpendicular to the plane of the burn border, and S.D. = standard deviation. Means and S.D. are for all 14 burns.

The position of the equivalent cardiac dipole throughout the stimulated QRS complex is shown for one of the hearts in Figure 5. It can be seen that the dipole locus began in the vicinity of the pacing electrode and then moved steadily from left to right across the ventricles. All six preparations demonstrated this strong left-to-right movement of the heart vector during the stimulated QRS complex.

**Discussion**

We define dipole ranging as the determination of location, as well as orientation and magnitude, of the equivalent cardiac dipole from external measurements of electrocardiographic potential (10). The underlying mathematical principles of dipole ranging were first enunciated by Gabor and Nelson (2) and have since been refined and extended (3–5). Determination of dipole location from electrocardiographic lead systems (15) has been applied, apparently successfully, to the isolated frog gastrocnemius muscle (16).

In this laboratory, dipole ranging has been applied to isolated turtle (8) and rabbit hearts (1, 10) contained within an “artificial torso.” Comparison of the dipole locus before and after right bundle branch block in the isolated rabbit heart has demonstrated that after block the location of the heart vector is shifted to the right side of the heart during the last half of myocardial depolarization (10).

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**TABLE**

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<tr>
<th></th>
<th>MEAN (mm.)</th>
<th>S.D. (mm.)</th>
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<tbody>
<tr>
<td>BURN RADIUS</td>
<td>5.0</td>
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<tr>
<td>LINE CD</td>
<td>3.2</td>
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<td>LINE CD'</td>
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<td>LINE D'D</td>
<td>2.0</td>
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<tr>
<td>ANGLE M_DN_C</td>
<td>13.5°</td>
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Two recent reports dealing with dipole ranging in humans (6, 7) present examples showing the locus of the equivalent cardiac generator within the ventricles during myocardial depolarization. One of these reports also illustrates the dipole locus within the atria during the P wave and again within the ventricles during the T wave (6).

Although these results reported for human and isolated animal hearts are plausible, they cannot be fully verified, since the actual site of the heart vector as it moves throughout depolarization is not known for these hearts. By searing the epicardium and pacing the left ventricle, we intended to create highly dipolar sites of electrical activity. The known locations of these sites could then serve as bench marks by which to judge the accuracy of the computation of dipole location. The strongly dipolar character of the potentials generated by these two myocardial interventions was confirmed by the fact that the equivalent cardiac dipole accounted for over 99% of the root-mean-square surface potential occurring both in the early S-T segment after cauterization and in the early portion of the QRS complex during pacing.

The reference points with which the computed dipole locations were compared, i.e., the site of the pacing electrode and the center of the circular approximation of the burn border, were themselves only estimates of the electrical center of activity. For the cauterized hearts, some error was probably introduced by assuming that the rim of electrical activity was concentric with the visible border of the seared region and by approximating the burn border with a planar circular rim. For the stimulated hearts, some error could have been introduced by assuming that the stimulating electrode site was the center of electrical activity early in the ectopic QRS complex. At the onset of the stimulated beat, no surface potentials were recorded, because the wave of excitation was a completely closed, uniform wave front moving away from the stimulating electrode in all directions (17). It was only when the wave front broke open at the epicardial surface overlying the stimulating electrode that the onset of the QRS complex was detected on the chamber surface. Therefore, early in the ectopically stimulated QRS complex the center of electrical activity should have been determined by the rim of the activation front on the epicardium (14), not necessarily by the exact location of the stimulating electrode itself.

Notwithstanding these possible errors in the determination of the reference points and even though the dipole ranging technique did not compensate for phase inhomogeneities, the distance from the computed dipole location to the reference point averaged only 3.4 mm for all 20 hearts. In the case of the cauterized hearts, projecting the dipole onto the plane of the burn margin reduced its mean displacement from the center of the seared region to 1.7 mm, which is about one-third of the average burn radius. This projection was made because the 14 computed dipole locations were not randomly distributed to either side of the plane of the burn margin but were displaced inward from the plane an average of 2.0 mm. There appear to be at least two factors which can alter the apparent location of the heart vector. The first of these is failure to compensate for phase inhomogeneities, which causes the computed location of the heart vector to be more centric than its actual location (18). Second, nondipolar characteristics of the cardiac generator probably have an opposite effect, causing the computed location of the heart vector to be more eccentric than its actual location. Indeed, this latter effect, which is suggested by theoretical considerations (4), was confirmed by several numerical simulations.

Because of the strongly dipolar nature of the potentials created by cauterization, phase inhomogeneities probably exerted a greater influence on the computed eccentricity of the injury vector than did the nondipolar components of the injury potentials. The highly idealized mathematical simulation presented in the Appendix was performed in an attempt to gauge the consequences of not compensating for the difference in conductivity between the heart and the perfusate. This simulation indicated that the computed location of the injury vector should have been 3.0 mm nearer the center of the chamber than the actual injury vector location, a distance comparable to the 2.0 mm determined experimentally. Even though conductivity differences within the spherical chamber did not have a large effect on computed heart vector location, this welcome result should not be uncritically extrapolated to dipole ranging in vivo because phase inhomogeneities in that situation are considerably

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more complex than those found in our experimental preparation.

Epicardial cauterization and subepicardial pacing are procedures confined to a discrete region of the heart, and for this reason the concept of heart vector location has obvious physical significance when it is applied to these two interventions. In addition, during appropriate portions of the cardiac cycle both procedures probably create one electro motive surface with a single rim abutting the epicardial surface. Such a generator configuration should be well approximated by a single, locatable dipole. The results reported in this paper demonstrate that in our experimental preparations dipole ranging can be employed successfully to locate (1) a region of myocardial injury produced by cauterization and (2) the site of origin of an ectopic beat produced by left ventricular pacing. Finally, these results illustrate the usefulness of the isolated heart preparation in a spherical chamber as an experimental model that bridges the gap between epicardial and intramyocardial electrode recordings on the one hand and body surface mapping on the other.

Appendix

The algorithm for calculating the heart vector treats the contents of the spherical tank as though they are electrically homogeneous, when in reality the conductivities of the heart and the electrolyte solution are not the same. The effect of this phase inhomogeneity on computed heart vector location and moment was estimated by mathematical simulation. As shown in Figure 6, the heart was idealized as a spherical shell and centered in the spherical chamber which had a radius of 3.175 cm. The distance from the center of the chamber to the endocardial surface of the heart shell was 1.00 cm, and that to the epicardial surface was 1.62 cm. The heart shell was treated as though it were electrically isotropic with a resistivity of 377 ohm cm, which is the geometric mean of the high and the low values found for the canine heart (19). The resistivity internal and external to the heart shell was taken to be 57 ohm cm, which is the resistivity of the modified Krebs-Henseleit solution.

A radially oriented current dipole was located just under the epicardial surface, 1.56 cm from the center of the chamber. This location represents an inward displacement of 0.30 cm from the actual dipole location. The computed dipole was radially oriented with a calculated strength 3.7 times greater than that of the actual dipole magnitude. The root-mean-square potential residual for this simulation was 2.9%. These results agree qualitatively with the findings of Arthur and Geselowitz (18), who performed a series of similar simulations in which the potentials were calculated from multipole coefficients rather than by the method of Barr et al. (20).

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