Locally Propagated Activation Immediately After Internal Defibrillation

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Background—Electrical mapping studies indicate an interval of 40 to 100 ms between a defibrillation shock and the earliest activation that propagates globally over the ventricles (globally propagated activation, GPA). This study determined whether activation occurs during this interval but propagates only locally before being blocked (locally propagated activation, LPA).

Methods and Results—In five anesthetized pigs, the heart was exposed and a 504-electrode sock with 4-mm interelectrode spacing was pulled over the ventricles. Ten biphasic shocks of a strength near the defibrillation threshold (DFT) were delivered via intracardiac catheter electrodes, and epicardial activation sequences were mapped before and after attempted defibrillation. Local activation was defined as dV/dt  0.5 V/s. Postshock activation times and wave-front interaction patterns were determined with an animated display of dV/dt at each electrode in a computer representation of the ventricular epicardium. LPAs were observed after 40 of the 50 shocks. A total of 173 LPA regions were observed, each of which involved 2 6 2 (mean 6 SD) electrodes. LPAs were observed after both successful and failed shocks but occurred earlier (P<.0001) after failed (35 6 8 ms) than successful (41 6 16 ms) shocks, although the times at which the GPA appeared were not significantly different. On reaching the LPA region, the GPA front either propagated through it (n=135) or was blocked (n=38). The time from the onset of the LPA until the GPA front propagated to reach the LPA region was shorter (P=.01) when the GPA front was blocked (32 6 12 ms) than when it propagated through the LPA region (63 6 20 ms).

Conclusions—LPAs exist after successful and failed shocks near the DFT. Thus, the time from the shock to the GPA is not totally electrically silent. (Circulation. 1998;97:1401-1410.)

Key Words: defibrillation  ■  mapping  ■  waves

Electrical mapping studies of defibrillation shocks slightly lower than the DFT have established the presence of an interval of 40 to 100 ms between the shock and the earliest GPA.1-4 Because it was assumed that electrical activity was absent during this postshock interval at the GPA origin, the interval was described as the isoelectric window.4 Using optical mapping techniques, Kwaku and Dillon5 found that an isoelectric window does not exist but that activation immediately begins to propagate away from the borders of regions that are excited directly by the shock field. Both findings can be accommodated if activation occurs during the isoelectric window, but this activation can propagate only locally within a small region before being blocked because of postshock tissue refractoriness. To test this hypothesis, we mapped the activation sequences on the epicardium of both ventricles after shocks of a strength near the DFT to determine whether locally propagated activation (LPA) occurs.

The results demonstrate that the so-called isoelectric window is not truly electrically silent. LPAs, which occur on the epicardium soon after the shocks, propagate locally and then block before another activation, the GPA, appears and propagates across the entire heart.

Methods

Animal Preparation
Five healthy pigs (30 to 35 kg) were tranquilized with acepromazine (1.1 mg/kg) and ketamine (22 mg/kg), anesthetized with sodium pentobarbital (30 mg/kg initially; 0.05 mg  kg 1 1  min 1 maintenance dose), intubated, mechanically ventilated with supplemental oxygen, and given intravenous fluids. The ECG and arterial blood pressure were monitored continuously. Core body temperature, arterial blood gas values, and electrolyte levels were maintained within the normal range throughout the experiment. The chest was opened through a median sternotomy, and the heart was suspended in a pericardial cradle.
Electrode Placement
Catheter-mounted, platinum-coated titanium coil electrodes (CPI-Guidant Corp) were used for defibrillation. A 34-mm catheter (surface area, 390 mm²) was inserted into the right external jugular vein and advanced to the RV apex and served as cathode for the first phase of the biphasic shock. A 68-mm catheter (surface area, 780 mm²) was inserted into the left external jugular vein, and its distal tip was positioned at the junction of the SVC and right atrium. The position of the catheters was verified with fluoroscopy (Fig 1A), and then the catheters were secured with a ligature at the venotomy site to stabilize their positions. Bipolar pacing electrodes (Ag/AgCl, 1 mm in diameter, with 2-to-3-mm interpolar spacing) sutured to the SVC was superior vena cava and the catheters were secured with a ligature at the venotomy site to stabilize their positions. Bipolar pacing electrodes (Ag/AgCl, 1 mm in diameter, with 2-to-3-mm interpolar spacing) sutured to the RV apex and anterobasal LV free wall were used to pace the heart so that the mapping array could be oriented. The bipolar electrode at the RV outflow tract also was used as the fibrillating electrode.

A 504-electrode array constructed from an elastic sock was used to record unipolar epicardial electrograms. There were 14 rows of electrodes with 6, 14, 22, 26, 32, 34, 38, 40, 44, 46, 48, 50, 50, and 54 Ag/AgCl, 1-mm-diameter electrodes per row from apex to base of the ventricles. Electrodes were spaced ~4 mm from center to center. For data analysis, the sock was divided conceptually into apical (7 rows), middle (4 rows), and basal (3 rows) regions (Fig 1B and 1C). The sock was pulled until its center contacted the LV apex and its base extended above the atrioventricular groove (Fig 1B). Two 3-mm-diameter Ag/AgCl disk reference electrodes were sutured to the aortic root 5 mm apart. One served as the reference for unipolar recordings and one as the ground electrode for the mapping system.

Data Acquisition
The 504 epicardial unipolar electrogram signals referenced to the aortic root were simultaneously band-pass filtered between 0.5 and 500 Hz and recorded digitally with a 528-channel computer-assisted cardiac mapping system.6,7 The procedure of recording events before, during, and after attempted defibrillation via electrical shock was as follows. At 10 ms before the beginning of the shock, an external timing device signaled the mapping system microprocessor8 to switch the attenuators on, change the amplifier coupling from AC to DC, and decrease the gain of each channel. Approximately 5 ms after the end of the shock, the external timing device signaled the microprocessor to switch the attenuators off. During the next 4 ms, the attenuators finished switching, the amplifier coupling was changed to AC, and the gain of each channel was increased to the preshock value. The signals were recorded digitally at a rate of 2000 samples per second per channel, together with real-time information indicating the sequence of events during the recording.9 Positioning of the return and ground electrodes to the aortic root allowed electrograms to be observed quickly after the shock.10

Defibrillation Protocol
Brief runs of normal sinus rhythm and of pacing from each of the three bipolar pacing electrodes and from the tip of the defibrillation catheter at the RV apex were recorded at the beginning of each experiment to determine the orientation of the mapping array. VF was then electrically induced by a 60-Hz alternating current delivered via the bipolar pacing electrode at the RV outflow tract. After 10 seconds of VF, defibrillation was attempted with 10-ms biphasic truncated exponential shocks generated by a 150-μF defibrillator (Ventritex HVS-02). Biphasic shocks were 6 ms in duration for the first phase and 4 ms in duration for the second phase, with a 0.2-ms interphase delay. A single-capacitor discharge was emulated by adjustment of the leading-edge voltage of phase 2 to approximately the same level as the trailing-edge voltage of phase 1; the overall tilt varied with system impedance11 (Fig 1D). The delivered voltage and current were displayed on the monitor of a waveform analyzer (DATA 6100, Analogic Inc). Total delivered energy was calculated by the waveform analyzer.12

To obtain an approximately equal number of successes and failures at the same shock energy, DFTs were determined with a modified three-reversal up/down protocol.13,14 The initial shock strength, 400 V, was chosen because it was near the expected 50% probability of success. The leading-edge voltage was then decreased or increased in 80-V steps after a successful or failed defibrillation attempt, respectively, until a first reversal in defibrillation outcome was achieved. At each reversal point, the sign of the voltage change of the algorithm was reversed; after the first reversal, the voltage step was changed to 40 V, and after the second reversal, it was changed to 20 V. The successful shock strength that was part of the pair of shocks forming the third reversal was defined as the DFT.

VF was induced for 6±2 episodes (mean±SD) in each animal to determine the DFT. Next, shocks of the DFT strength were given after 10 seconds of VF during 10 different VF episodes in each animal. After unsuccessful shocks, defibrillation was obtained within

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**Figure 1.** Diagram representing defibrillation electrode configuration, mapping array, and shock waveform. A, Defibrillation electrodes were positioned at SVC and RV apex. Electrode at RV apex was cathode and electrode at SVC was anode for first phase of the biphasic shock. B, A 504-electrode elastic sock was pulled over heart. For data analysis, ventricles were conceptually divided into (I) apical, (II) middle, and (III) basal thirds. C, Polar projection of sock was used in animated computer display of dV/dt at each electrode site (squares). D, Biphasic waveform had interphase delay of 0.2 ms. Ao indicates aorta; LAD, left anterior descending coronary artery; PA, pulmonary artery; RA, right atrium; and RVOT, right ventricular outflow tract.
10 seconds with a higher-energy shock delivered through the same electrode pair. Only the 10 shocks at the DFT strength were used for analysis. A minimum of 4 minutes was allowed to elapse between VF episodes. At the end of the study, the anesthetized animal was euthanized by fibrillation.

**Terminology**

Earliest GPA is the first activation (dV/dt ≤ −0.5 V/s) after the shock that gives rise to an activation front that propagates across almost the entire epicardium. The GPA was determined from the dV/dt animation as described previously. The GPA epicardial site of origin (GPA origin) is the epicardial site at which the GPA is first detected.

LPAs are activations (dV/dt ≤ −0.5 V/s) that occur before activation occurs at the GPA origin. They do not spread to activate the entire epicardium but rather propagate only locally before blocking and becoming extinguished. An LPA region is a group of spatially adjacent electrode sites at which LPAs are recorded. LPA sites are the individual recording electrode sites within the LPA region that record LPAs.

The postshock interval is the interval between the beginning of the shock and the first postshock activation at an electrode site. The postshock interval at the GPA origin has been called the isoelectric window in previous studies. The preshock interval is the interval between the time of activation at the LPA site closest to the shock and the beginning of the shock at an electrode site.

**Data Analysis**

The mapping data were transferred to a computer workstation (Sun Microsystems, Inc), where all activations were analyzed by visualization of an animation of the first derivative (dV/dt) of the unipolar electrograms. The dV/dt was determined over a 2-ms sliding window spanning five data points. Any electrode with a dV/dt ≤ −0.5 V/s was defined as active. This method of analysis has several advantages over isochronal mapping and has been used previously to observe wave-front propagation and the presence of collision or reentry. Beginning 20 ms after the leading edge of the shock, ie, 10 ms after the end of the shock, activations were determined in 0.5-ms steps until the GPA front had traversed the epicardium. The first 10 ms after the end of the shock was not examined because of the restrictions of the switched mapping system hardware.

**Determination of LPA**

For an event to be described as an LPA, it was required that the activation at the site be dV/dt ≤ −0.5 V/s, that it occur at least 20 ms after the leading edge of the shock but before the GPA arose, and that it be excluded from noise by comparison of the display of the unipolar electrogram to its derivative (dV/dt). The numbers of LPA sites and LPA regions and the minimum dV/dt at each LPA site and at the GPA origin were determined for all defibrillation episodes.

**Determination of Preshock and Postshock Interval and VF Cycle Length**

The preshock and postshock intervals were determined at all LPA sites and GPA origins for each defibrillation episode from the animated computer display. Mean VF cycle length was determined at all LPA sites and GPA origins in all episodes. At each LPA site and GPA origin, the time of each activation, identified as the time at which dV/dt was a minimum and was also ≤ −0.5 V/s, was determined for 10 VF cycles before the shock. The average of the 10 activation intervals was used to define the mean VF cycle length at that site.

**Determination of the Wave-Front Interaction Time**

Wave-front interaction time at an LPA region was defined as the interval between the time of activation at the LPA site closest to the approaching GPA wave front in each region and the time at which the GPA wave front propagated to an electrode adjacent to that LPA site. Wave-front interaction time was determined for all LPA regions for each defibrillation episode. In some cases, an interaction between the LPA and the GPA front could be observed: propagation of the GPA wave front blocked in the LPA region. Block was considered to be present if the interval between the activation criteria being first met at adjacent electrodes was >40 ms, implying a conduction velocity of <0.1 m/s, which is thought to be unphysiological.

**Statistical Analysis**

Comparison of data between successful and unsuccessful defibrillation episodes was performed with Student’s t test for paired and unpaired data. Spatial distributions of LPA sites and GPA origins were analyzed by one-way ANOVA. When statistical significance was found, individual comparisons were carried out with Fisher’s post hoc test. Values are shown as the mean ± SD. Differences were considered to be significant for P ≤ 0.05.

**Results**

Of the 50 defibrillation attempts in the five pigs, 23 were successful and 27 were not. The DFT was 424 ± 132 V (range, 280 to 640 V). Heart weight was 220 ± 30 g.

**Existence of LPAs**

LPAs were seen in 40 of the 50 defibrillation attempts and were associated with successful defibrillation in 18 episodes. A total of 173 LPA regions (65 for successful episodes and 108 for failed episodes) and 339 GPA sites (155 for successful episodes and 184 for failed episodes) were observed in the five animals.

Recordings from one electrode in one animal after two different shocks are shown in Fig 2. In Fig 2A, an LPA is seen with a GPA. The mean minimum dV/dts for the LVFA, the LPA, and the GPA for this event were −1.1, −1.7, and −0.9 V/s, respectively. No LPA occurs in Fig 2B, with the mean minimum dV/dt for the LVFA and the GPA being −1.2 and −1.9 V/s, respectively. Fig 3 shows propagation of LPAs. The four regions seen in frame 2 all become blocked and extinguished by frame 8. Examples of recordings in and around the LPA region from Fig 3 at which the GPA front blocked are given in Fig 4. Tracings a through e are from LPA sites (arrows), and tracings 1 through 5 are from electrodes surrounding but just outside the LPA region. The minimum dV/dts for the LPAs in electrograms a through e and for the GPA in electrograms 1 through 5 were −1.24 ± 0.47 and −3.32 ± 0.68 V/s, respectively. The GPA in tracings 1 through 5 does not activate the LPA region at which electrograms a through e were recorded, although it does cause a small (possibly electronic) deflection. The minimum dV/dt for the small deflections after LPAs in electrograms a through e was −0.39 ± 0.08 V/s.

LPAs were significantly more common in the apical and middle thirds of both ventricles (Table 1A and Fig 5A), whereas GPa were significantly more common in the apical third, and mostly in the LV (Table 1A and Fig 5B). The minimum dV/dt for the GPA origins was −3.2 ± 2.0 V/s, significantly less than the minimum dV/dt for the LPAs (−1.60 ± 1.64 V/s).

**Interaction of the GPA Front With the LPA Region**

The GPA front blocked when it reached 38 of the 173 LPA regions. The GPA front did not pass through this area that...
Successful and Unsuccessful Defibrillation

Relationship Between LPA and GPA for Successful and Unsuccessful Defibrillation

Figure 2. Unipolar epicardial electrograms from two episodes of unsuccessful defibrillation. A, Recording at one LPA site (top) showsVF (left), defibrillation shock (multiple vertical lines), and signals after shock (right). Derivative of electrogram (bottom) is also shown. Arrow labeled S indicates beginning of shock. LPA was detected 50 ms after shock (arrow labeled LPA); GPA origin was first detected 67 ms after leading edge of shock at a different electrode. GPA wave front reached this LPA site 80 ms after shock (arrow labeled GPA), 30 ms after LPA at this site. LVFA at this recording was detected 70 ms before shock (arrow labeled LVFA). B, Recording (top) and its derivative (bottom) at same electrode as in A but during a different defibrillation episode in same animal. In this episode, no LPA was detected. Only GPA (arrow) was detected when GPA front reached this site.

Relationship Between LPA and GPA for Successful and Unsuccessful Defibrillation

On average, LPAs occurred significantly earlier than GPAs for both successful and failed shocks (Table 2A). The number of LPAs sites and regions was not significantly different between successful and unsuccessful shocks. However, the mean time until the LPAs occurred was longer for successful than for failed shocks (Table 2A). The time from earliest activation within an LPA region and the activation time at the GPA origin was 26±11 ms for the 65 LPA regions during successful defibrillation episodes and was 29±9 ms for the 108 LPA regions during unsuccessful episodes (P≤.05). This interval for successful and failed episodes combined was 27±10 ms. Because there was no significant difference for the postshock interval at the GPA origin between successful and failed shocks (Table 2A), the time interval between the LPA and the GPA origin was longer for unsuccessful than for successful episodes. Thus, the time at which GPA wave fronts encountered the LPA region was usually later for failed shocks. The incidence of block of the GPA front in the LPA region was not significantly different for successful and failed shocks (Table 2B). In about one half of all episodes with LPAs, the GPA front propagated through one or more LPA regions but blocked in one or more other LPA regions.

Comparison of Preshock Intervals at the LPA Sites and the GPA Origins

The preshock interval at LPA sites and GPA origins was normalized by dividing by the mean VF cycle length at that site. Preshock intervals at LPA sites were longer (P<.01) than at GPA origins (Tables 2A and 1B). Minimum dV/dt for activation during VF immediately preceding the shock at the GPA origins (−2.1±1.1 V/s) was less than at the LPA sites (−1.7±1.2 V/s) (P<.01).

Discussion

This study shows that after shocks near the DFT, small activation fronts (LPAs) quickly appeared that propagated for only a short distance before blocking and becoming extinguished. These LPAs appeared 27±10 ms before the epicardial appearance of the first activation front that propagated across almost the entire epicardium after the shock, ie, the GPA front. Thus, the time interval between the shock and the appearance of the GPA front, which previously has been called the isoelectric window,3,4 was not electrically silent. LPAs were observed after most (80%) defibrillation shocks of near DFT strength, irrespective of their outcome. Both the incidence and distribution of LPAs differed from those of GPAs. LPAs were registered at only ~2% of electrode sites during a shock episode. LPA sites were more generally distributed, appearing frequently in the apical and middle thirds of both ventricles, whereas GPA activation fronts arose primarily from the apical third of the left ventricle. Approximately 20% of GPA fronts blocked when they reached an LPA region. When GPA block occurred, the time from the onset of the LPA until the GPA front reached the LPA region was significantly shorter (32±12 ms) than when GPA block did not occur (63±20 ms).

Presence of LPAs

Several lines of evidence differentiate LPAs from shock artifacts in the recordings. LPAs were observed only occasionally and were not observed repeatedly at the same
electrode (Fig 2). After different shocks, LPAs appeared in many different electrodes dispersed over most of the ventricular epicardium and frequently occurred in clusters. The strongest evidence that the LPAs are not artifactual is that they altered refractoriness of the tissue in the vicinity of the LPA. This is indicated by blocking of the GPA activation front when it encountered an LPA region (Fig 3) in some cases and by slowing of the propagation velocity in others (Fig 6). When GPA block occurred, the time after the LPA at which the GPA activation front reached the LPA region was 32±6±12 ms, which is consistent with this region still being in its absolute refractory period. When the GPA front slowly propagated through the LPA region, however, this time period was 63±20 ms, which is consistent with the region being in its relatively refractory period.25,26

Origin of LPAs
GPA fronts after shocks near the DFT do not represent unaltered continuation of activation fronts present just before the shock.2 The same appears to be true for LPAs in that the sum of the preshock and postshock intervals for LPAs, 114±61 ms (Table 1B), was significantly longer than the mean activation rate at the same electrodes during the previous 10 activations during VF just before the shock (83±12 ms).

Although it cannot be definitely ruled out that LPAs arise from foci triggered by the shock, it is likely that LPAs are part of an activation front that arises and propagates away from the border of a region that is excited directly by the shock, as has been demonstrated for GPA fronts by optical mapping.5 The possibility that early sites of postshock activation could be caused by graded responses that slowly propagate for a distance and then trigger activation from a less refractory site27 may be pertinent to the origin of the GPA, because the preshock interval suggests that tissue at the GPA origins was partially refractory at the time of the shock. Slow propagation of the graded response could have been missed in the extracellular recordings and could account for the postshock interval at GPA or LPA sites.

LPAs were observed 38±13 ms after the shock, which is not as early as would be expected if the LPAs arose from an...
activation front that propagated away from a directly excited region (Table 1B). The conduction velocity may be slowed because the activation fronts are propagating through relatively refractory tissue in which the refractory period has been extended by the shock.28–31 Indeed, some conduction slowing is evident near the boundary of the directly excited region in the figures shown in the study by Kwaku and Dillon,5 in which most shocks were much weaker than the

![Diagram](http://circ.ahajournals.org/)

**Table 1. Spatial Distribution and Preshock and Postshock Intervals of LPA Sites and GPA Origins**

<table>
<thead>
<tr>
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<th>LPA Site, n (%)</th>
<th>GPA Origin, n (%)</th>
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<tr>
<td><strong>A. Spatial distribution of LPA sites and GPA origins</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Apical third</td>
<td>159 (47%)†</td>
<td>24 (60%)†‡</td>
</tr>
<tr>
<td>Middle third</td>
<td>145 (43%)†</td>
<td>12 (30%)</td>
</tr>
<tr>
<td>Basal third</td>
<td>35 (10%)</td>
<td>4 (10%)</td>
</tr>
<tr>
<td>Right ventricle</td>
<td>206 (61%)</td>
<td>4 (10%)</td>
</tr>
<tr>
<td>Left ventricle</td>
<td>133 (39%)</td>
<td>36 (90%)§</td>
</tr>
<tr>
<td><strong>B. Preshock and postshock intervals at LPA sites and GPA origins for all shock episodes</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preshock intervals, ms</td>
<td>76±6</td>
<td>52±20</td>
</tr>
<tr>
<td>Postshock intervals, ms</td>
<td>38±13</td>
<td>61±10</td>
</tr>
<tr>
<td>Preshock + postshock intervals, ms</td>
<td>114±61</td>
<td></td>
</tr>
<tr>
<td>VF cycle length, ms</td>
<td>83±12</td>
<td>81±12</td>
</tr>
<tr>
<td>Preshock intervals, % VF cycle length</td>
<td>92±73</td>
<td>65±25</td>
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</tbody>
</table>

*The sites are classified into apical, middle, and basal thirds (see Fig 1B). The total number of those sites is also divided into the left and right ventricles. Values in parentheses show the percentage of the total number of LPA sites or GPA origins.

†P<.05 vs basal third, ‡P<.05 vs middle third (one-way ANOVA, Fisher’s post hoc analysis), §P<.05 vs right ventricle (Student’s t test); ¶P<.001 vs LPA, ¶¶P<.001 vs VF cycle length.
DFT. Such slowing might have been exacerbated in our study, in which shocks were closer to the DFT, resulting in more tissue being excited directly by the shock and the generation of the boundaries of the directly excited region in more highly refractory tissue. An alternative explanation is that the activation fronts giving rise to LPAs originated from the endocardium or midwall and the postshock interval represents the time required for these activation fronts to reach the epicardium.

The site at which direct excitation occurs and LPAs arise should be determined by the changes in the transmembrane potential caused by the shock, which can be influenced by the

Figure 5. Polar projection maps of LPA sites and GPA origins for all shock episodes in one animal. A, Distribution of LPA sites (stars) for successful defibrillation episodes. Circles represent LPA sites for failed episodes. B, Distribution of GPA origins (stars) for successful defibrillation episodes. Circles represent GPA origins for failed episodes. Abbreviations as in Fig 1.

Figure 6. Example in which GPA front propagates slowly through LPA region. Interval between consecutive maps is 4 ms. First panel is 26 ms after leading edge of shock (280 V). The only LPA region in this unsuccessful episode was detected 30 ms after leading edge of shock. GPA was detected 62 ms after shock (arrow) at LV apex. GPA activation front propagated through LPA region. GPA wave front propagated slowly in LPA region relative to surrounding area, causing wave front to arc around edges of LPA region and converge on other side. Wave-front interaction time is 88 ms (from frame 2 to frame 24).
TABLE 2. Characteristics of LPA Sites and GPA Origins in Relationship to Success or Failure of Defibrillation

<table>
<thead>
<tr>
<th></th>
<th>Successful Shocks</th>
<th>Unsuccessful Shocks</th>
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<tbody>
<tr>
<td>A. No. of LPA sites and regions and postshock and preshock intervals at LPA sites and GPA origins*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of LPA sites for each shock</td>
<td>9±6</td>
<td>8±5</td>
</tr>
<tr>
<td>No. of LPA regions for each shock</td>
<td>4±2</td>
<td>5±3</td>
</tr>
<tr>
<td>Postshock interval at LPA sites, ms</td>
<td>41±16</td>
<td>35±8†</td>
</tr>
<tr>
<td>Postshock interval at GPA origins, ms</td>
<td>64±10‡</td>
<td>62±9‡</td>
</tr>
<tr>
<td>Preshock interval at LPA site, ms§</td>
<td>84±72% (72±63)</td>
<td>99±74% (81±61)</td>
</tr>
<tr>
<td>Preshock interval at GPA origin, ms§</td>
<td>60±23% (49±21)</td>
<td>69±27% (55±20)</td>
</tr>
<tr>
<td>B. No. (%) of defibrillation episodes in which the GPA front did or did not block in an LPA region¶</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Block in all LPA regions</td>
<td>3 (17)</td>
<td>1 (4)</td>
</tr>
<tr>
<td>Block in no LPA region</td>
<td>6 (33)</td>
<td>9 (41)</td>
</tr>
<tr>
<td>Block in some LPA regions but not others</td>
<td>9 (50)</td>
<td>12 (55)</td>
</tr>
</tbody>
</table>

*Data are for the 40 shock episodes with LPA sites.
†P<.0001 vs successful shocks, ‡P<.0001 vs postshock interval at LPA sites, §mean±SD (values in parentheses are the actual [not normalized] preshock interval), ¶P<.01 vs at LPA sites; †P-values in parentheses show the percentage of the total number of successful or unsuccessful defibrillation episodes with LPAs.

The association of the outcome of defibrillation with the length of the so-called isoelectric window is controversial. Although some studies indicate that this interval is longer for transmembrane potential is markedly altered by the shock, direct excitation should occur in some tissue areas but not others, depending on whether depolarization or hyperpolarization is present.

Comparison of GPA and LPA Wave Fronts
As opposed to GPA wave fronts, the pathways of LPA fronts are small, typically traversing an area covered by only a few electrodes, and terminate soon after they appear on the epicardium. LPA fronts are probably extinguished by conduction block when they encounter adjacent tissue that is refractory because of lack of recovery from its last activation before the shock, prolongation of its refractory period by the shock, or direct excitation by the shock.

In contrast, LPAs appear later after the shock, arise primarily in the region exposed to the lowest shock potential gradient, and propagate to activate all of the epicardium except for some LPA regions in which they may be blocked. Because they occur later after the shock than the LPAs, the myocardium has had more time to recover and is less refractory, which may explain why GPA fronts do not also block and become extinguished. In addition, the preshock interval is shorter, so the tissue at the GPA origin is more refractory at the time of the shock and the mean minimum dV/dt is more negative, ie, the downslope is faster. Although the postshock interval was longer at the GPA origin and the tissue had more time to recover from the shock, the sum of the preshock and postshock intervals was not different. Thus, the time from the last activation before the shock to the first activation after the shock was not significantly different for sites of GPA origin and sites of LPAs. The dV/dt for the VF activation just before the shock was also more negative at the sites of GPA origin.

LPAs and Defibrillation
The association of the outcome of defibrillation with the length of the so-called isoelectric window is controversial. Although some studies indicate that this interval is longer for shock potential gradient field, interruptions in the myocardium, and the orientation and curvature of the myofibers. Because LPAs occurred almost anywhere over both ventricles, they appeared in portions of the heart exposed to both high- and medium-strength shock potential gradient fields as well as in regions exposed to the weaker shock potential gradient field (Fig 5A). For the electrode configuration used in this study, the shock potential field is largest in the right ventricle adjacent to the shocking electrode and falls off with distance, being weakest in the lateral apical left ventricular free wall. In contrast, most GPA activation fronts arose in the apical third and mostly from the left ventricle, the region in which the shock field was weakest (Fig 5B).

Recent findings that interruption of the myocardial syncytium gives rise to secondary sources and the orientation and curvature of the myofibers raise the possibility that, even in regions of high potential gradient, the transmembrane potential may not be changed markedly during the shock, especially in regions of high potential gradient, these regions were not excited directly by the shock, even though the cells were in a late stage of their refractory period and hence excitable.

Electrodes, and terminate soon after they appear on the epicardium. LPA fronts are probably extinguished by conduction block when they encounter adjacent tissue that is refractory because of lack of recovery from its last activation before the shock, prolongation of its refractory period by the shock, or direct excitation by the shock.

In contrast, GPAs appear later after the shock, arise primarily in the region exposed to the lowest shock potential gradient, and propagate to activate all of the epicardium except for some LPA regions in which they may be blocked. Because they occur later after the shock than the LPAs, the myocardium has had more time to recover and is less refractory, which may explain why GPA fronts do not also block and become extinguished. In addition, the preshock interval is shorter, so the tissue at the GPA origin is more refractory at the time of the shock and the mean minimum dV/dt is more negative, ie, the downslope is faster. Although the postshock interval was longer at the GPA origin and the tissue had more time to recover from the shock, the sum of the preshock and postshock intervals was not different. Thus, the time from the last activation before the shock to the first activation after the shock was not significantly different for sites of GPA origin and sites of LPAs. The dV/dt for the VF activation just before the shock was also more negative at the sites of GPA origin.

LPAs and Defibrillation
The association of the outcome of defibrillation with the length of the so-called isoelectric window is controversial. Although some studies indicate that this interval is longer for...
successful than for failed shocks\textsuperscript{2,3} and suggest that it may be used to predict the outcome of defibrillation, other studies do not indicate an association.\textsuperscript{2,15} In the present study, we found no difference in the so-called isoelectric interval for successful and failed shocks. This discrepancy may reflect methodological differences. Most studies that showed differences in the isoelectric window between successful and failed shocks used a monophasic waveform in dogs together with shocks of different strengths such that the mean shock strength for the failed shocks was lower than for successful shocks.\textsuperscript{3,4} Zhou et al,\textsuperscript{2} using both monophasic and biphasic shocks in dogs but comparing successful and failed defibrillation shocks of the same strength, found no differences in the so-called isoelectric window. The study by Usui et al,\textsuperscript{15} which also found no difference in the so-called isoelectric interval for successful and failed shocks, was similar to the present study in that they used a biphasic waveform in pigs, an RV-SVC defibrillation electrode configuration, and successful and failed shocks of the same strength. A greater shock strength may be the common cause of two effects that may be independent of each other: an increase in the success rate of defibrillation and an increase in the duration of the so-called isoelectric window. It is possible that LPAs were recorded in previous studies\textsuperscript{1,2,15} but that they were not noted because LPAs are fleeting, occupy small regions, appear close to the shock artifacts, and are quickly overshadowed by the large GPA wave front that passes across most of the epicardium.

Dillon has suggested that shocks defibrillate by causing a uniform degree of refractoriness throughout the ventricles.\textsuperscript{39} However, the results of our study suggest that a uniform degree of refractoriness is not absolutely necessary for successful defibrillation. The LPAs, occurring 38±13 ms after the shock, should have caused the LPA regions to be more refractory than the remainder of the myocardium after the LPAs occurred. Yet defibrillation was still successful even in the presence of LPAs. In fact, the postshock interval at the LPA sites was significantly longer for successful than unsuccessful shock episodes, suggesting that the difference in the time of recovery between LPA regions and the remainder of the ventricles was even greater for successful than for unsuccessful shock episodes.

Although the postshock interval at the GPA origins was not different between successful and failed shocks, LPAs occurred earlier after failed shocks than after successful shocks (Table 2A). However, LPAs alone did not reinitate VF, because LPAs existed immediately after shocks that ultimately succeeded as well as after shocks that failed to defibrillate. It is not known whether the interactions between GPA and LPA fronts play a causative role in the outcome of defibrillation or whether the small but significant differences in mean times of LPAs after successful and unsuccessful shocks is a concomitant effect of some other causative mechanism for defibrillation. The answer to this question will require additional studies in which recording electrodes are spaced more closely than in this study to allow determination of whether activation fronts arise in the LPA region after the GPA front and lead to the reinitiation of VF.

Limitations of the Study
The limitations of the study concern evaluation of the LPAs and are primarily inherent in electrical mapping. Because transmural recording was not performed and the epicardial electrodes were ~4 mm apart, actual postshock windows for the LPAs and GPAs were probably shorter than reported in this study. The potential gradient field was not estimated. We could not observe activations for 10 ms after the end of the shock, nor could we tell which regions were excited directly by the shock or directly visualize the action potentials in the LPA regions or in the surrounding tissue where the LPA is blocked. Conduction velocity was not measured because, unlike for an electrode plaque, the interelectrode spacings within the sock were not constant. Because these limitations can be overcome by optical mapping, such a study is needed to confirm our initial observation of LPAs and to learn more about how and why they occur.

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