The cellular electrophysiologic changes induced by ablation: comparison between argon laser photoablation and high-energy electrical ablation

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ABSTRACT The cellular electrophysiologic effects of myocardial ablation performed in vitro with argon laser energy were compared with those of high-energy electrical shocks. A border zone of injured but nonnecrotic tissue surrounding the site of energy delivery was present after tissue ablation by both energy modalities. A decrease in resting membrane potential, action potential amplitude, and maximum rate of upstroke velocity was noted in each tissue sample, was greatest nearest the site of energy delivery, and was of graded severity at increasing distances from the crater edge. The extent of injury, as indexed by changes in action potential variables and necrosis, histologically determined, was greater for tissues exposed to high-energy shocks. The relatively focal injury after argon laser photoablation may explain the lower incidence of arrhythmias and hemodynamic dysfunction noted with the use of this method of ablation in vivo.


TRANSVENOUS CATHETER ablation has evolved as an alternative to surgery in management of clinical tachyarrhythmias. High-energy electrical ablation has been successfully applied to the atrium, atrioventricular node, and accessory pathways for control of automatic and reentrant supraventricular tachycardias. More recently, foci of sustained, refractory ventricular tachycardia have been ablated with the use of high-energy electrical shocks.

Although electrical ablation has been associated with successful control of refractory tachycardias, transient life-threatening proarrhythmic and hemodynamic complications have been reported. A potential explanation for these complications has been suggested. Recent work in isolated tissues has demonstrated that, after a catheter-delivered high-energy shock, a large border zone of injured but nonnecrotic myocardium develops around the ablation site. Depressed action potentials, abnormal conduction and refactoriness, and abnormal membrane phenomena have been demonstrated in this surrounding injured border zone.

The use of laser energy has been suggested as an alternative to ablation, since it offers better control of energy delivery. Although tissue injury may spread beyond the target site when laser exposure time surpasses the thermal relaxation time of the target tissue, the distribution of spread follows a Gaussian relationship and is expected to be focal. Thus, a smaller border zone of injured myocardium should be present after laser photoablation. This in turn may explain the lower incidence of arrhythmic and hemodynamic complications noted in animal studies during laser photoablation.

The present series of experiments was performed to study the consequences of argon laser photoablation in normal canine myocardium. After exposure to laser energy, action potential characteristics, variables sensitive to tissue injury, were recorded at varying distances from the crater to document the extent of cellular injury. The pattern of injury was compared with that after high-energy electrical shocks of sufficient energy to yield craters of comparable size to document

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the more focal nature of laser-mediated injury. Finally, the distribution of cellular electrophysiologic changes noted after argon laser or electrical ablation was compared with that of the resulting tissue temperatures and electric field strengths to document the potential mechanisms of the pattern of resultant tissue injury in each case.

Methods

Experiments were performed on 18 ventricular epicardial tissue samples removed from 17 adult dogs of both sexes weighing between 8 and 30 kg. The animals were anesthetized with intravenous sodium pentobarbital (30 mg/kg body weight). The chest of each was opened via a left lateral thoracotomy and the heart was removed. Epicardial strips 1 to 4 mm thick, 2 to 3 cm wide, and 2 to 4 cm long were removed so that their longitudinal axes were parallel to the superficial fiber orientation. The tissue samples were placed in a 100 ml tissue support bath, superfused with standard oxygenated Tyrode’s solution, and paced at a basic cycle length of 1000 msec via bipolar stimulating electrodes consisting of two Teflon-coated silver wires applied at the margin of the tissue. Constant-current rectangular wave pulses of 2 msec duration and twice diastolic threshold intensity were used. With these methods, described in detail previously, action potential variables remain near control values for 4 to 6 hr.

Intracellular action potentials were recorded from cells in the most superficial layer of the epicardial preparations with the use of standard 3M potassium-filled microelectrodes. Before data acquisition, a stable resting potential (>45 sec) was confirmed for each impalement. The action potentials were amplified (WPI), displayed on an oscilloscope (Tektronix), and photographed (Polaroid or 35 mm film). The maximum rate of depolarization was determined graphically and/or with an electronic differentiator (Bloom) (minimum resolution 5 V/sec). Action potential variables were measured to the nearest millivolt and millisecond. A GTCO 1117 manual digitizer interfaced with a Hewlett-Packard 9836 computer was used. Action potential variables with magnitudes less than the minimum resolution of the analyzing systems were assigned a zero value.

Technique of laser ablation in vitro. All ablative lesions were induced after the tissue samples were placed in the tissue bath and after five to 10 control microelectrode impalpements were made over a 10 mm range of distance from the target site. An argon laser was used for these experiments. After acquisition of the control recordings, the tissue bath was drained of its solution and argon laser energy (3.5 W delivered over 5 sec producing a crater 1 to 3 mm in diameter and 1 mm in depth) was directed at the target site via a quartz fiber tube (200 μm diameter). Craters of 1 mm diameter were produced in 10 tissue strips, while craters of 3 mm diameter were produced in three additional tissue strips. Immediately after exposure to the laser, the tissue perfusion bath was again filled with standard oxygenated Tyrode’s solution and the tissues were allowed to reequilibrate for 30 min. Five to 10 action potentials were then recorded at distances up to 10 mm from the edge of the crater. The location of each impalement was determined with an optical micrometer by observing the dimple midpoint produced at the site of impalement (resolution 0.08 mm). Control recordings obtained before ablation were compared with those obtained in the same locations (±0.1 mm) after laser photoablation.

Technique of high-energy electrical ablation in vitro. The cathode used was 1.5 mm in diameter, made of silver, and insulated except at the contact surface. The anode used was a platinum plate 25 mm in diameter centered beneath the tissue. Delivered shocks (5 to 20 J) were damped sinusoidal waveforms of 5 to 10 msec in duration (Hewlett-Packard 78670A). Control recordings were made from microelectrode impalpements 0 to 10 mm from the target site. Immediately after the shock, the tissue perfusion bath was flushed with oxygenated Tyrode’s solution, the anode and cathode were removed, and the tissue samples were allowed to reequilibrate for 30 min. Five to 10 action potentials were then recorded 0 to 10 mm from the edge of the crater, and these results were compared with those obtained during control recordings from the same tissue samples in the same locations (±0.1 mm).

In these experiments there was a tendency for slow improvement of the action potential variables with time after ablation. In the first tissue strips studied, the action potential variables remained fairly constant over a 4 to 5 hr period. This was much longer than the time needed to complete our data acquisition (usually less than 1 hr). Nevertheless, in those experiments requiring longer acquisition times due to the fact that a greater number of recordings were made, impalpements at different distances were made in a random sequence.

Technique of thermography. To quantify the degree of tissue heating during argon laser photoablation, a close-up infrared microthermography system (Hughes Aircraft) having a spatial resolution of 100 μm or better was used. This unit had a time resolution of 100 msec, a temperature range of 30° to 160° C, and a temperature resolution of ±5°. The camera was focused on the tissue surface during laser photoablation. The data were acquired on a videocassette recorder and displayed on a color monitor. Thermoclines were color coded and were traced onto data sheets; distances between thermoclines were measured manually. Thermography was performed in five tissue samples in which action potentials were also recorded.

Histologic methods. Specimens that had undergone laser photoablation or high-energy electrical ablation were studied. The tissues were fixed in a 4% formalin solution for at least 24 hr, embedded in paraffin, and sliced in 5 μm sections that were then stained with hematoxylin-eosin. Crater size and the extent of necrosis were measured with a grid reticle eyepiece (precision at 400× magnification = 10 μm). The extent of necrosis after laser photoablation in seven tissue samples was evaluated by examining serial sections at 250 μm increments from the center of the crater. In four tissue strips, serial sections at 1, 5, and 10 mm from the crater induced with electrical shocks were also examined and the results of the two methods of ablation were compared.

Prediction of the distribution of the electric field strength. Myocardial damage from electrical ablation may occur by three potential physical mechanisms: (1) direct injury by the electric field or current density, (2) thermal injury by the heat deposited by the current dissipation due to tissue resistance, and (3) blast injury by the explosive arc discharge created at the small electrode. Since previous studies in this preparation in vitro have shown that the injury caused by electrical ablation is localized along the current path between cathode and anode and is related to current density, we assumed that blast injury was not an important mechanism for distal injury in this preparation. The electric field strength and current density in the tissue during electrical ablation are difficult to measure. We therefore obtained estimates of these quantities by theoretical modeling.

Our preparation for the electrical ablation experiment assumes that current is passed from a flat disk electrode (radius a) at the end of an insulated cylinder (“catheter”) abutting the surface of the tissue (thickness L) to an effectively infinite ground plane beneath the tissue. The entire system is immersed in conducting buffer, and the tissue conductivity is taken to be isotropic and identical to that of the buffer.
For the frequencies involved in a defibrillator discharge, the determination of the electric field strength is essentially an electrostatic problem. The field in the tissue (E) is the gradient of the electrostatic potential (V), which obeys Laplace’s equation within the tissue, where there are no fixed charges.

The form of the potential is determined by the boundary conditions imposed by the electrode geometry. In the preparation described above, these conditions are as follows: (1) the potential must be finite everywhere and vanish at infinity, (2) the potential must vanish on the ground plate, (3) the potential must be equal to \( V_0 \), the applied voltage on the disk electrode, and (4) the normal electric field must vanish at the surface of the insulated cylinder. These conditions completely determine the potential, and therefore the electric field. The current density follows from the field by its multiplication by conductivity.

The potential was expanded in terms of solutions of Laplace’s equation obtained by separation of variables in cylindrical coordinates. The resulting expansions, obtained separately for the regions \( r<a \) and \( r>a \), were found to be:

\[
V_1(r,z) = \sum_{n=1}^{\infty} \frac{1}{n \pi} \sin \left( \frac{n \pi r}{L} \right) I_n \left( \frac{n \pi r}{L} \right) A_n \left( \frac{n \pi L}{L} \right) + V_0 z; \quad 0 < z < L \quad (1a)
\]

and

\[
V_2(r,z) = \int_0^\infty B(k) \sin (kz) K_0(kr) \, dk; \quad r > a \quad (1b)
\]

where \( I_n \) and \( K_n \) are modified Bessel functions of the 0th order.

To determine the expansion coefficients \( A_n \) and \( B(k) \), we required that the potential and its radial derivative be continuous across the cylindrical boundary \( r=a \), \( 0 < z < L \) between the regions of applicability of equations 1a and 1b:

\[
V_1(r,a) = V_2(r,a); \quad 0 < z < L \quad (2a)
\]

\[
\frac{\partial V_1(r,a)}{\partial r} = \frac{\partial V_2(r,a)}{\partial r}; \quad 0 < z < L \quad (2b)
\]

Equation 2b, together with the boundary condition 4, determines the radial derivative of \( V_2 \) at \( r=a \) for all values of \( z \). This permits solving for the coefficient \( B(k) \) by inverting the Fourier transform implicit in equation 1b. This gives \( B(k) \) in terms of the (as yet unknown) coefficients \( A_n \). By inserting the result into equation 2a and inverting the resulting Fourier series, we obtained an infinite set of linear simultaneous equations for \( A_n \).

The coefficients of these equations are compounded integrals involving ratios of Bessel and trigonometric functions and were computed numerically.

The simultaneous equations for \( A_n \) were solved by truncating to finite order and numerically inverting the resulting matrix. The resistance of the electrode configuration was determined by assuming an applied voltage \( V_0 \) of 1 V and integrating the vertical component of the current density over an infinite horizontal plane within the tissue. The actual applied voltage was then calculated from the resistance and the peak current, which was measured in some experiments.

The instantaneous temperature rise of the tissue due to ohmic dissipation of the current pulse was found from:

\[
T = \frac{\sigma E t \ell}{C} \quad (3)
\]

where \( \sigma \) is the electrical conductivity, \( C \) is the specific heat, and \( t \) is the effective duration of the pulse (i.e., the duration of a rectangular pulse with the same peak current and total energy). For the numerical calculations shown, we used the following values: peak current = 15 amperes; delivered energy = 17.5 J; conductivity = 14 mmhos/cm (equal to normal saline); specific heat = 1° C/calorie; catheter radius (a) = 0.75 mm; tissue thickness (L) = 3 mm. The resultant distribution of electric field strength is described more completely in the Results section.

**Statistical methods.** All tabular data are expressed as the mean and SD. Comparisons of means were by analysis of variance. Because of the confounding effect of distance on the cellular electrophysiologic effects of ablation, action potential characteristics from paired samples equidistant from the site of energy delivery were used. A p value less than or equal to .05 was considered indicative of a significant difference. The correlation between variables was determined by linear regression techniques. A p value less than or equal to .05 and an r value greater than or equal to .70 were assumed to indicate a significant correlation.

**Results**

Nature and extent of action potential abnormalities after argon laser photoablation. Analog recordings of action potentials from one tissue sample after laser photoablation (1 mm crater) are shown in figure 1. Also shown is a typical control recording. Before laser photoablation, the action potentials in the isolated epicardial strips were of normal amplitude and configuration. After laser photoablation, decreases in resting membrane potential, action potential amplitude, and upstroke velocity were present in some of the recorded action potentials. The action potential abnormalities were limited to implemated sites relatively close to the site of delivery of laser energy. Action potential variables were reduced at sites closer than 2 to 3 mm from the craters’ edge. In addition, as shown in the example in figure 1, at sites closer than 1 mm from the craters’ edge, a marked reduction in resting potential was noted. In these implemamentals, only subthreshold electrotonic potentials or no electrical activity were recorded.

A similar pattern of injury was present in each of the experiments. In addition, this pattern of relatively focal injury was also seen in the three tissues in which craters of 3 mm diameter were produced with laser energy. The summary data are presented in table 1. Impalements at 2, 5, and 10 mm for each tissue within each group were compared with control action potentials recorded at the same locations before photoablation. Resting membrane potential was minimally reduced at a distance of 2 mm from the crater site (for both 1 mm and 3 mm craters), but these changes did not reach statistical significance. Significant reductions in action potential amplitude and the maximum rate of upstroke velocity were, however, present in action potentials recorded at a distance of 2 mm from the craters’ edge. In contrast, no significant reduction in any of these variables was noted in action potentials recorded 5 and 10 mm from the site of laser photoablation. Thus, although the area of injured myocardium bordering the crater was larger than that to which the
FIGURE 1. Analog recording of action potentials at varying distances from the edge of the crater after delivery of laser energy. At distances of 5 to 10 mm from the crater, the action potentials were relatively normal. However, there was a progressive loss of resting potential, action potential amplitude, and maximum rate of upstroke velocity (dV/dT) as the distance between the crater and impalement site decreased.

laser energy was directly applied, it was relatively focal and not significantly altered by the size of the crater itself.

**Comparison of changes in action potential induced with argon laser photoablation and those induced with high-energy electrical shocks.** High-energy electrical ablation was also associated with significant changes in action potential variables (table 1). A reduction was seen in resting membrane potential (21.2 ± 11.6 mV at 2 mm and 51.6 ± 8.9 mV at 5 mm after shock vs 80.6 ± 3.8 mV on control recordings; p<.005), action potential amplitude (4.6 ± 10.3 mV at 2 mm and 22.6 ± 18.7 mV at 5 mm after shock vs 90.8 ± 5.6 mV on control recordings; p<.001), and the maximum rate of upstroke velocity (0.8 ± 1.8 V/sec at 2 mm and 7.4 ± 9.8 V/sec at 5 mm after shock vs 142.7 ± 15.6 V/sec in control recordings; p<.001). These changes were extensive relative to cathode size; in all cases, the

<table>
<thead>
<tr>
<th>Condition</th>
<th>Resting membrane potential (mV)</th>
<th>Action potential amplitude (mV)</th>
<th>dV/dT (V/sec)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2 mm</td>
<td>5 mm</td>
<td>10 mm</td>
</tr>
<tr>
<td>Control</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(n = 18)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Laser</td>
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<tr>
<td>(1 mm; n = 10)</td>
<td></td>
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<tr>
<td>Laser</td>
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<td></td>
<td></td>
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<tr>
<td>(3 mm; n = 3)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Electrical</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>(1-1.5 mm; n = 5)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>80.9±5.3</td>
<td>81.9±7.2</td>
<td>79.4±5.0</td>
</tr>
<tr>
<td>Laser</td>
<td>72.2±13.9</td>
<td>85.2±7.6</td>
<td>80.0±6.6</td>
</tr>
<tr>
<td>Laser</td>
<td>76.7±7.6</td>
<td>80.0±2.0</td>
<td>78.0±2.0</td>
</tr>
<tr>
<td>Electrical</td>
<td>21.2±11.6^</td>
<td>51.6±8.9^</td>
<td>69.0±9.3^</td>
</tr>
</tbody>
</table>

The measures 2 mm, 5 mm, and 10 mm represent the distance of the impalement from the edge of the crater. The appropriate crater size is listed in parentheses for each mode of ablation.

dV/dt = maximum rate of upstroke velocity.

^p ≤ .05 compared to control values within each tissue.
cathode was 1.5 mm in diameter, yet depressed action potentials were typically recorded 5 to 10 mm away from the shock site.

The extent of the border zone of injury after electrical ablation was significantly greater than that seen after laser photoablation. In table 1 summary data for impalements made 2 mm from the crater after electrical or laser photoablation are presented. The reduction in resting potential and action potential amplitude after a high-energy electrical shock was significantly greater than that after laser photoablation (1 or 3 mm crater). The mean resting potential at a distance of 2 mm from the crater after a high-energy electrical shock was 21.1 ± 11.6 mV compared with 72.2 ± 13.9 mV (1 mm crater) and 76.7 ± 7.6 mV (3 mm crater) after laser photoablation (p < .05). The mean action potential amplitude after the high-energy shocks was 4.6 ± 10.3 mV compared with 72.3 ± 30.3 mV (1 mm crater) and 79.3 ± 1.2 mV (3 mm crater) after laser photoablation (p < .05). The decrement in the maximum rate of upstroke velocity after a high-energy electrical shock differed only from the laser (1 mm) group. The mean maximum rate of upstroke velocity after the high-energy shock was 0.8 ± 1.8 V/ sec compared with 70.6 ± 37.9 V/sec (1 mm crater) and 48.7 ± 44.7 V/sec (3 mm crater) after laser photoablation (p < .05). There were no significant differences in resting potential, action potential amplitude, or the maximum rate of depolarization noted in the 1 mm laser and 3 mm laser groups.

Similar findings were noted at a distance of 5 mm from the crater (table 1). Resting membrane potential, action potential amplitude, and the maximum rate of upstroke velocity were more depressed after a high-energy shock as compared with after laser photoablation (1 or 3 mm craters). The mean resting membrane potential at a distance of 5 mm from the crater after a high-energy shock was 51.6 ± 8.9 mV compared with 85.2 ± 7.6 mV (1 mm crater) and 80.0 ± 2.0 mV (3 mm crater) after laser photoablation (p < .05). The mean action potential amplitude at a distance of 5 mm from the crater after a high-energy shock was 22.6 ± 18.7 mV compared with 98.1 ± 10.7 mV (1 mm crater) and 91.0 ± 3.6 mV (3 mm crater) after laser photoablation (p < .05). The maximum rate of upstroke velocity of the action potential at a distance of 5 mm from the crater after a high-energy electrical shock was 7.4 ± 9.8 V/ sec compared with 107.0 ± 42.2 V/sec (1 mm crater) and 119.3 ± 32.2 V/sec (3 mm crater) after laser photoablation (p < .05). The differences in resting potential, action potential amplitude, and the maximum rate of depolarization at a distance of 5 mm from craters of 1 mm diameter after laser photoablation were not significantly different from those values noted at 5 mm from the craters of 3 mm diameter.

The resting membrane potentials of impalements 10 mm from the crater after high-energy electrical shocks differed only from those in the 1 mm crater laser group (table 1). The mean resting potential at a distance of 10 mm from the crater after a high-energy shock was 69.0 ± 9.3 mV compared with 80.0 ± 6.6 mV (1 mm crater) after laser photoablation (p < .05). No significant difference in resting potential was present between the 1 mm crater laser and 3 mm crater laser groups, or between the 3 mm crater laser and the high-energy electrical shock groups. In contrast, action potential amplitude at a distance of 10 mm from the crater after a high-energy electrical shock differed significantly from that noted 10 mm from the crater after laser photoablation (1 mm or 3 mm craters). Mean action potential amplitude 10 mm from the crater after a high-energy electrical shock was 74.0 ± 9.4 mV compared with 94.4 ± 3.8 mV (1 mm crater) and 95.0 ± 0.0 mV (3 mm crater) after laser photoablation (p < .05). The maximum rate of upstroke velocity at a distance 10 mm from the crater did not differ significantly among the three groups.

Changes in action potential variables: relation to mechanisms of injury. The extent of cellular injury, as indexed by changes in action potential variables, after ablation was related to the mechanism of injury of the particular ablative procedure used. Thermal mechanisms likely underlie cellular necrosis and injury after argon laser photoablation. In five tissue samples, the extent and distribution of temperature elevation during laser photoablation were compared with the changes in action potential variables that developed. Figure 2, A, is an example of the relationship of peak surface temperature to distance in one tissue during laser photoablation. The falloff of temperature with distance was quite rapid and followed a Gaussian distribution. There was only a mild elevation of surface temperature noted 3 mm from the crater, while no appreciable temperature elevation was present 5 mm from the crater. These findings were present in each tissue strip. The distribution of temperature change with distance from the crater and site of laser energy delivery was related to the change in resting membrane potential. Figure 2, B, is a plot of resting potential change (control minus postablation values) versus distance from the site of laser photoablation in the same tissue. It is apparent that this plot parallels that of temperature versus distance (figure 2, A). There was a relationship between

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The extent of temperature elevation and the decrement in resting potential for 21 impalements in five tissue samples with 1 mm craters in which both thermography and determination of action potential variables were performed. These values were strongly correlated (r = 0.88; p < 0.001), suggesting that the thermal gradient is in part responsible for the injury gradient seen after laser photoablation.

The mechanisms of electrical ablation, however, are less well understood. Recent data suggest that current density or electric field strength may be important determinants of cellular injury. \(^{17}\) These variables could not be directly measured in our experiments, but rather were modeled (see Methods). In figure 3 the predicted relationship of electric field strength, temperature, and distance from the site of energy delivery is shown as the semilogarithmic plot of distance from the site of energy delivery (abscissa) and the electric field strength (ordinate). The solid horizontal line depicts the electrical injury threshold of 80 V/cm. \(^{22-24}\) The intersection of the dashed horizontal lines with the plot depict the distance at which a 5° and 100° C rise in temperature are predicted. Note that the thermal changes are quite focal relative to the changes in electric field strength after a high-energy electrical shock. In fact, the extent of thermal change is very much similar to that seen after laser photoablation (figure 2, A). In contrast, the model predicts that the electric field strength will exceed the threshold for electrical injury at a much greater distance from the shock site. The distribution of electric field strength with distance was similar to the distribution of cellular injury with distance as indexed by resting membrane potential. Figure 4 is a plot of resting potential change versus distance for a tissue sample in which the delivered energy was 20 J and the measured current was 15 amperes. That the distribution in change in resting potential par-

![Figure 2](image2.png)

**FIGURE 2.** A. Plot of peak surface temperature (measured with a custom optical system) and distance from the site of laser photoablation. The falloff of temperature with distance was quite rapid. B, Plot of change in resting membrane potential vs distance from the site of laser photoablation. Note that changes in resting potential occurred in a limited distribution around the site of laser energy delivery.

![Figure 3](image3.png)

**FIGURE 3.** The predicted relationship of electric field strength to distance after a high-energy shock of 17.5 J yielding a peak current of 15 amperes delivered via a cathode 1.5 mm in diameter into a tissue strip 3 mm thick with a conductivity of 14 mhos/cm and a specific heat of 1°C/C/cal. Shown is the semilogarithmic plot of electric field strength (ordinate) vs distance from the site of energy delivery (abscissa). Because of the logarithmic scale, the same curve (with a differing logarithmic scale factor) represents temperature rise due to ohmic heating. The points of intersection of the dashed line with the plot depict the distance at which 5° and 100° C temperature rises are predicted. The solid horizontal line depicts the theoretical electrical injury threshold. \(^{22-24}\) Note that the predicted electric field strength exceeds the threshold for injury at a relatively large distance from the site of energy delivery. In contrast, temperature rise is quite focal.

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allels that of the electric field strength suggests that the electric field strength is in part responsible for the extent of injury seen after a high-energy electrical shock.

Pathologic changes after laser photoablation and high-energy electrical ablation. All of the specimens examined histologically exhibited necrosis. The extent and type of necrosis noted was dependent in part on the type and dose of delivered energy. After laser photoablation, craters were present that consisted of depressions filled with necrotic debris. Evidence of cellular injury was present beyond the boundaries of the crater. Craters were surrounded by islands of hyperbasophilic necrotic myocytes characterized by an amorphous basophilic cytoplasm. Nuclei were pyknotic or absent. Scattered islands of contraction band necrosis were also evident in five of the seven samples. The histologic injury extended beyond the crater in each case. The maximum breadth of histologic changes at the epicardial surface ranged from 1.25 to 3.0 mm (mean ± SD = 1.78 ± 0.53 mm) and the depth of histologic changes ranged from 0.5 to 1.9 mm (mean ± SD = 1.16 ± 0.44 mm).

All of the specimens subjected to high-energy shocks exhibited contraction band necrosis. Injury extended in a radial pattern from the site of energy delivery and typically showed a three-layered pattern. A crater developed in each case and was filled with necrotic debris. Immediately beneath the crater was a zone of myocytes exhibiting pyknotic nuclei but free of contraction bands. Still deeper into this layer was tissue consisting of cells with typical contraction bands and foci of fiber disruption and hemorrhage. The extent of injury away from the crater was dose dependent. The distribution of necrosis was radial in each case, but was most extensive in the two tissue samples receiving 20 J shocks. In these two specimens, necrosis extended at least 5 mm beyond the outer border of the crater (i.e., >10 mm breadth of injury). Thus, the pattern of necrosis seen histologically was similar to the electrophysiologic pattern of injury; that is, necrosis was more extensive after high-energy shocks. In both cases, however, the action potential abnormalities were more extensive than the histologic changes, implying that a border zone of injured but viable myocardium is present after ablation.

Discussion

The major finding of this study is that laser photoablation leads to more focal myocardial injury, as indexed by changes in action potential characteristic and histology, than does high-energy electrical ablation. In both cases action potential changes were noted in a border zone of injured but nonnecrotic myocardium, but the border zone was more extensive after high-energy electrical shocks. Suggested mechanisms for tissue injury were presented in an attempt to explain the differences noted.

A depression in action potential amplitude, resting membrane potential, and the maximum rate of upstroke velocity was noted after both laser and high-energy electrical ablation (figure 1; table 1). The abnormalities after laser photoablation were not limited to the crater itself, but rather extended to a border zone 2 to 3 mm from the edge of the necrotic myocardium. Of interest is that the extent of this border zone was independent of the size of the crater; that is, there were no significant differences noted in action potential variables at any given distance in tissues with craters 1 mm or 3 mm in diameter (table 1). In contrast, after a high-energy shock, the border zone of injured but nonnecrotic myocardium was larger and extended 5 to 10 mm from the edge of the crater (table 1). After both laser and high-energy electrical ablation, changes in action potential characteristics were most significant close to the shock site and were of graded severity at increasing distances from the crater.

The differences in extent of action potential changes may be explained by differences in the mechanisms of cellular injury resulting from the two techniques. Laser photoablation leads to cellular necrosis via thermal mechanisms.\textsuperscript{19, 20} Tissue injury may extend beyond the site of energy delivery when laser exposure time exceeds the thermal relaxation time of the tissue.\textsuperscript{20} In
these experiments, rapid pulsed delivery was not used and the distribution of the temperature rise with distance from the ablation site followed a Gaussian relationship (figure 2, A). Temperatures approaching 100°C were noted near the site of energy delivery. At increasing distances from this site, a rapid falloff of temperature with distance was noted. The changes in action potential variables with distance closely paralleled and were strongly correlated with the temperature changes, suggesting that the thermal gradient and injury gradient were related (figure 2). Thus, the limited extent of the border zone of injured but nonnecrotic myocardium after laser photoablation may be explained by the steep temperature gradients with distance that were noted.

The mechanisms of cellular injury resulting from high-energy electrical shocks are less well understood. Thermal injury, barotrauma, and the effects of electrical current on the myocardium have all been proposed. Indeed, it is likely that multiple mechanisms may lead to myocardial necrosis and injury close to the site of energy delivery. The finding that transseptal shocks give rise to symmetric lesions at the anode and cathode positions, even though the measured shock waves differ for anodal and cathodal shocks, strongly suggests that barotrauma is not a major factor. We and others have noted an increase in temperature after a high-energy electrical shock. This, however, has been quite focal (figure 3) relative to the extent of tissue injury noted, as indexed by action potential characteristic changes (figure 4). In addition, the finding that postshock dysfunction is independent of total energy in cultured myocytes subjected to electric field stimulation of differing waveforms suggests that the effects of high-energy shocks are not mediated via thermal mechanisms. In fact, the latter studies suggest that the dysfunction is due to a current voltage–related phenomena. The authors provide evidence for functional microlesions that develop in the sarcolemma and suggest that they are produced because of compression of the cell membrane by the electric field. The “membrane breakdown” hypothesis was supported by previous work from our laboratory. In those studies, altering cathode characteristics, maximizing current density, or optimizing the cathode-anode configuration allowed us to maximize tissue injury. In addition, our finding of polarization of cell nuclei in border zone tissues after high-energy shocks is also consistent with current-induced injury. The results of our present experiments lend further support to a role of electric field strength in determining myocardial injury after high-energy electrical ablation. The predicted electric field strength exceeded that level shown to cause cellular injury in myocytes at a distance of 7 to 10 mm from the ablation site (figure 3). The extent of tissue injury, as indexed by changes action potential characteristics, closely paralleled the predicted distribution of electric field strength (figures 3 and 4), supporting the notion that current voltage–related phenomena are relevant to tissue injury.

The findings of this study provide insight into possible mechanisms of complications inherent in ablation of arrhythmic foci. Arrhythmias and hemodynamic changes occur in animals and man after ablation by either laser or electrical energy. The presence and complexity of the arrhythmias, however, have been more evident after high-energy electrical ablation. Similarly, regional wall motion abnormalities have been more prevalent and extensive after electrical shocks than after laser photoablation. Our data demonstrate that a border zone of injured but nonnecrotic myocardium develops after both laser and electrical energy delivery to the myocardium. The extent of the border zone of injury, however, was far greater after high-energy electrical shocks. In addition, laser energy led to a more focal region of myocardium devoid of action potentials. Thus, the size of the area demonstrating depressed, heterogeneous cellular electrophysiologic characteristics, which may provide the substrate for arrhythmogenesis and may lead to a depression in regional function after ablation, is larger after high-energy electrical ablation than after laser photoablation. Our data therefore suggest that the use of laser energy may allow for controlled, selective injury to targeted areas, while causing minimal damage to surrounding normal tissues.

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LABORATORY INVESTIGATION—ARRHYTHMIA
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