Electrical Properties of Canine Subendocardial Purkinje Fibers Surviving in 1-Day-Old Experimental Myocardial Infarction

Thomas M. Argentieri, Lawrence H. Frame, and Thomas J. Colatsky

The passive electrical properties of subendocardial Purkinje fibers surviving in infarcted regions of canine ventricle 24 hours after coronary ligation were studied by using microelectrode techniques and cable theory. In normal hearts, cells within the subendocardial Purkinje fiber strands were found to be well coupled to each other but electrically isolated from neighboring myocardium. Voltage response to intracellular current injection was consistent with one-dimensional cable behavior and yielded estimates of passive electrical properties in general agreement with previous work on free-running Purkinje fibers (membrane length constant, 1.2±0.1 mm; membrane time constant, 7.3±0.8 msec; input resistance, 67.4±7.4 KΩ; membrane resistance, 8.2±0.7 KΩ·cm; axial resistance, 0.52±0.06 MΩ·cm; membrane capacitance, 960±102 nF/cm (n=21). On the day after coronary ligation, subendocardial Purkinje fiber action potentials were prolonged and slightly depolarized. Significant increases were measured in input resistance (+40.5%), membrane resistance (+43.9%), and axial resistance (+47.5%), whereas membrane capacitance was found to be significantly decreased (−24.3%) (n=19). Conduction velocity, membrane length constant, membrane time constant, and the time constant and capacitance for the foot of the action potential remained unchanged. These results are consistent with electrical uncoupling between adjacent cells, which will increase internal resistivity, accompanied by changes in cellular phospholipid content, which can increase membrane resistance and alter membrane capacitance. Alternatively, the results can be explained by a simple model in which the apparent electrical structure is altered by changes in electrical coupling alone, with specific electrical properties remaining constant. Although the mechanisms underlying the observed changes remain uncertain, the present study indicates that myocardial infarction is associated with alterations in the passive electrical structure of surviving subendocardial Purkinje fibers, which, together with changes in action potential configuration, may provide a substrate for the generation of ventricular arrhythmias 24 hours after coronary ligation. (Circulation Research 1990;66:123–134)

Considerable evidence has been gathered supporting a principal role for subendocardial Purkinje fibers (SPFs) in the generation of ventricular arrhythmias 24 hours after coronary artery ligation in dogs.1–9 Microelectrode studies have established that SPFs remain viable within the region of infarction, although they exhibit abnormal electrical properties, including reduced maximal diastolic membrane potential, action potential overshoot and maximal upstroke velocity (Vmax), and a marked prolongation of action potential duration.1–3,5,6 Most studies suggest that the predominant spontaneous ventricular rhythms observed during this period result from abnormal automaticity in the SPFs.2,6–8 However, more rapid rhythms that may be due to reentry have also been observed in SPFs in vitro,2 and the prolongation of action potential duration and slower phase 3 repolarization in infarcted zones SPFs have been cited as factors contributing to unidirectional block and the slow conduction of premature beats.2,8

The precise mechanism underlying the electrophysiological alterations observed in surviving SPFs remains obscure. Since excitability and the configura-
tion of the action potential depend on membrane current flow, which, in turn, is determined by the interaction between the active and passive properties of the cardiac membrane, the arrhythmias observed in SPFs 24 hours after occlusion could involve 1) specific changes in the gating of the ion channels or 2) changes in the passive electrical properties of the SPFs. For example, slowed conduction and conduction block could result equally well from changes in the gating of the excitative sodium channel as from regional differences in membrane length constant (λ) or membrane time constant (τm). Similarly, automaticity may be enhanced by the more rapid activation of the pacemaker current, as well as by an increase in the resting (background) membrane resistance, which would amplify the voltage change produced by changes in specific ionic currents (Ohm’s law).

Several lines of evidence indicate that alterations in the electrical structure of the myocardium may play a major role in the electrophysiological consequences of ischemia and infarction. It is well known, for example, that acute hypoxia and ischemia can disrupt cell-to-cell coupling in the heart\textsuperscript{9} and slow cardiac conduction by increasing internal resistivity (axial resistance [ri]) and reducing λ.\textsuperscript{10-14} Also, uncoupling of the SPF from adjacent Purkinje fibers or ventricular muscle can remove electrotonic interactions that help to determine the configuration of the cardiac action potential.\textsuperscript{15,16} The accumulation of lysophosphatidylcholine (LPC) found to occur within surviving SPFs\textsuperscript{17,18} may also be involved. Application of exogenous lysophospholipids to normal Purkinje fibers can produce arrhythmias and action potential abnormalities resembling those seen in surviving SPFs\textsuperscript{19} and has been reported to increase both ri and resting membrane resistances, λ, and τm.\textsuperscript{20} On the other hand, recent voltage-clamp studies also indicate that LPC can alter the current-voltage characteristic of the inwardly rectifying background potassium channel\textsuperscript{21} and decrease its single-channel conductance.\textsuperscript{22} Reductions in the delayed rectifier current and the inward current have also been described.\textsuperscript{23,24} No data are available to indicate whether similar changes in either passive electrical properties or channel activity occur in SPFs 24 hours after coronary ligation.

The present study was undertaken to characterize the electrical structure of SPFs by cable analysis and to determine whether changes in passive electrical properties occur in SPFs surviving myocardial infarction. In addition, a careful analysis of the electrical structure of the SPF would also provide a basis for assessing the feasibility and limitations of performing voltage-clamp studies in these preparations that would more directly define possible changes in ionic current. Preliminary reports of this work have been presented.\textsuperscript{25,24}

**Materials and Methods**

**Experimental Preparations**

**Normal dogs.** Male mongrel dogs weighing 11–13 kg were anesthetized with sodium pentobarbital (30 mg/kg i.v.), and a left thoracotomy was performed at the level of the fourth intercostal space. Hearts were quickly removed, placed in cold oxygenated Tyrode’s solution, and rinsed free of any remaining blood. The atria were then removed, and an incision was made through the left ventricular free wall to expose the septum. Sections of endocardium containing visible bands of unbranched discrete SPFs approximately 200 μm in diameter were carefully dissected from the septal region below the tip of the papillary muscle. Each section measured approximately 1 cm×1 cm and was 3 mm in thickness. In initial studies, for purposes of comparison, small free-running Purkinje fibers bridging between adjacent trabeculae were also dissected from the same region of ventricle. Before study, preparations were allowed to equilibrate for 1 hour at 37° C in a Sylgard-lined Plexiglas chamber (4.5 ml total volume) while being superfused with oxygenated Tyrode’s solution of the following composition (mM): NaCl 125, KCl 4, CaCl\textsubscript{2} 1.8, NaHCO\textsubscript{3}, 24, NaHPO\textsubscript{4}, 1, MgCl\textsubscript{2}, 0.5, and dextrose 5.5. The solution was bubbled with a 95% O\textsubscript{2}-5% CO\textsubscript{2} gas mixture to achieve a final bath pH of 7.4. In some experiments, 1 mM BaCl\textsubscript{2} was added to the Tyrode’s solution to increase resting membrane resistance. Temperature was maintained at 37±0.5° C with aCambion peltier device and voltage source.

**Experimental myocardial infarction.** Transmural myocardial infarctions were produced under sterile conditions by a two-stage ligation of the left anterior descending coronary artery by the procedure of Harris.\textsuperscript{22} Male mongrel dogs weighing 11–13 kg were anesthetized with sodium pentobarbital (30 mg/kg i.v.) and ventilated with room air. Hearts were exposed through a small left thoracotomy, the pericardium was opened to expose the left anterior descending coronary artery approximately 1–2 cm from its origin, and a total occlusion of the vessel was produced in two stages. Lidocaine (2 mg/kg i.v.) was administered prophylactically during the occlusion to protect against lethal ventricular arrhythmias. The chest wall was then closed in layers, and the animals were permitted to recover while receiving routine postoperative care, including antibiotics. Twenty-four hours after surgery, the dogs were returned to the laboratory, and the presence of spontaneous ventricular arrhythmias was confirmed by recording a lead II electrocardiogram. The animals were then reanesthetized with sodium pentobarbital (30 mg/kg i.v.), and the chest incisions were reopened. As in the normal dogs, the hearts were quickly removed and rinsed free of blood. The area of infarction was clearly demarcated by its pale appearance and extended over most of the anterior aspect of the left ventricular septum and free wall. Sections of endocardium, which under the dissecting microscope appeared to contain relatively unbranched SPF strands, were dissected from the infarcted region of the left ventricle and superfused with oxygenated Tyrode’s solution in the tissue bath for at least 1 hour.
before study. Impalement of SPFs was confirmed by action potential characteristics.

**Electrophysiological Measurements**

Transmembrane action potentials were recorded by conventional microelectrode techniques. Microelectrodes were pulled from precut fiber-filled glass tubing (1.2 mm o.d., WPI, New Haven, Connecticut) using a vertical puller (model 700D, David Kopf Instruments, Tujunga, California) to yield tip resistances of 8–10 MΩ when filled with 3 M KCl. In some experiments, lower tip resistances (~2 MΩ) were obtained by using thin-walled glass capillary tubing (model 1211-L, Glass Company of America, Bargain-town, New Jersey) or by beveling with an aluminum oxide slurry technique to improve current passing capability.26 Recording of membrane potentials and injection of current were accomplished by using an electrometer (model KS-700, WPI), and the resulting signals were monitored on a storage oscilloscope (model 5111A, Tektronix, Beaverton, Oregon). The oscilloscope display was photographed on Polaroid film to obtain a permanent record (camera model C-5B, Tektronix). In addition, voltage and current signals were digitized at a minimum sampling rate of 1 KHz for storage and later analysis using a DEC 11/03 computer system with A/D interface.

Preparations were paced at a basic cycle length of 500–630 msec with bipolar Teflon-coated silver electrodes placed on the endocardial surface. These cycle lengths were sufficiently short to suppress automaticity in the preparations under study. Constant (5 mA) current stimulus pulses of 2 msec were delivered by a digital stimulator with isolator (model 1800, WPI). The stimulator was also used to set the timing and duration of current pulses delivered during diastole for determination of \( \tau_m \) and \( \lambda \). The pulses were timed to occur early in diastole after complete repolarization. Electrophysiological measurements were begun after equilibration of the preparation in the tissue bath and stabilization of resting potential and action potential configuration.

In addition to the analysis of passive electrical properties (see below), the following basic electrophysiological parameters were measured in each preparation: 1) resting potential and action potential duration at 90% repolarization (APD\(_{90}\)), 2) conduction velocity (\( \theta \)), and 3) time constant of the foot of the action potential (\( \tau_{AP} \)). \( \theta \) was calculated by using the time between upstrokes of two uniformly propagating action potentials recorded at different sites along a continuous SPF strand on the endocardial surface. The distance between recording sites was measured with a stereo dissecting microscope (model M-3, Wild, Heerbrugg, Rockleigh, New Jersey) fitted with a micrometer eyepiece with a resolution of approximately 12 \( \mu \)m at a magnification of \( \times 16 \). The rising phase of the action potential was recorded at a fast sweep speed, digitized, and fitted by an exponential function through its first 20 mV to obtain \( \tau_{AP} \). \( \dot{V}_{max} \) was not determined in these experiments.

The extent of electrical coupling between adjacent layers of SPFs and ventricular muscle was evaluated by passing a 50 nA hyperpolarizing constant current pulse of 100–150 msec through a microelectrode placed in a cell in the most superficial SPF layer and observing the voltage deflections recorded by a second microelectrode positioned less than 50 \( \mu \)m away. The recording electrode was advanced gradually through the successive layers of SPFs until action potentials characteristic of ventricular myocardium were seen. Movement of the electrode from one cell layer to the next was indicated by a sudden return of the voltage output to ground potential (0 mV) immediately before obtaining a more negative resting potential in the next cell layer. Fibers used in this study were not used for cable analysis.

**Cable Analysis**

Passive electrical properties were determined in each preparation by using cable theory. Cable parameters were derived only for those fibers in which all electrical measurements were successfully obtained. Partial experiments were excluded from analysis. In general, analysis was based on the assumption that the SPF strands could be approximated to one-dimensional semi-infinite cables under the conditions of these experiments. This assumption was supported by several lines of experimental evidence, as discussed below. To determine the cable properties of the SPF preparations, a 50 nA hyperpolarizing current pulse (\( I_0 \)) of 100–150 msec was injected during diastole through a microelectrode placed at one end of the SPF strand, and the resulting voltage deflection (\( V_m \)) was measured by a second roving microelectrode inserted at a varying distance (\( x \)) from the site of current injection along the long axis of the SPF strand. The magnitude of the voltage response in these experiments was generally 5 mV or less. \( \lambda \) was calculated by fitting the longitudinal voltage distribution obtained in this fashion to a single exponential function: \( V_m = V_0 \exp(-x/\lambda) \), where \( V_0 \) is the voltage deflection at the site of current injection (\( x=0 \)). This value of \( V_0 \) was then used to calculate the input resistance (\( R_m = V_0/I_0 \)). Since the current electrode was positioned near the cut end of the fiber, current flow was limited to the hemicable, and consequently, \( R_m = (r_m t)^{\frac{3}{5}} \), where \( r_m \) is membrane resistance. \( \tau_m \) was estimated by fitting the time course of the normalized voltage change to an appropriate error function solution.\(^{28}\) A convenient approximation could be used in the special case when voltage transients were analyzed at a distance \( x=\lambda \). At this site, \( V_m \) rises exponentially to approximately 63% of its final value in 1.24 time constants. Therefore, values for \( \tau_m \) could be estimated from an exponential fit of the data that incorporates the propagation delay for the decremental wave.

From the measurements of \( \lambda \), \( \tau_m \), and \( R_m \), values were calculated for \( r_m \) (in ohms times centimeters), \( r_i \)
(in ohms per centimeter), and membrane capacitance ($c_m$) (in farads per centimeter) by using the conventional equations relating these variables.\(^27,28\) In addition, the capacitance charged during the foot of the action potential upstroke ($c_{up}$) was calculated from the measurements of $\tau_{AP}$, $\theta$, and $r_1$.\(^29,30\) For purposes of comparison with other studies, specific resistances and capacitances were calculated by using a right cylindrical radius of 100 $\mu$m with no corrections for infoldings or other hidden membranes. This value for the radius is consistent with the average diameter of the fibers used in the study (200±18 $\mu$m, $n=21$) and, in the absence of more rigorous morphometric data, should provide a reasonable approximation for the purpose of this calculation.

**Validity of Methods**

The use of the one-dimensional cable theory rests on several basic assumptions: 1) $r_m$ and $r_1$ are ohmic (linear). 2) The resistivity of the extracellular space is small relative to the $r_1$ and may be neglected. 3) Axial current flows through an unbranched cylinder of uniform cross-sectional area.\(^28\) Also, to make use of the infinite cable solution of the general cable equation, the preparation must be infinitely long relative to its resting $\lambda$ (i.e., $V_m$$\rightarrow$0 as $x$$\rightarrow$$\infty$). The problems generally inherent in applying one-dimensional cable theory to multicellular preparations have been discussed previously in considerable detail.\(^13,20,28\) Despite its limitations, this approach has yielded useful data, even when applied to such morphologically complex preparations as sheep Purkinje fibers.\(^20,27,30\)

Several lines of evidence exist that suggest that the SPF strands may be treated as one-dimensional cables. Previous histological and electrophysiological evidence suggests that few, if any, intercellular connections exist between Purkinje fibers on the endocardial surface of the heart and the underlying ventricular myocardium,\(^31-33\) except for discrete regions of transition where propagation from Purkinje fibers to muscle can occur.\(^31,34\) The lack of frequent electrical coupling between SPFs and subjacent myocardium would tend to reduce the probability that current flow is multidimensional, except perhaps in the immediate vicinity of the current electrode.\(^35\) In addition, the SPF layer has been reported to be less than four cell layers in thickness in normal hearts and less than two cell layers in infarcted preparations,\(^1,6\) which would help to limit problems of radial current flow.

A major portion of the present study was directed toward evaluating the one-dimensional cable behavior of the SPF preparations. The data in support of this assumption are now briefly summarized. As suggested by previous investigators, cells within the SPFs appeared to be well coupled to each other but electrically isolated from the surrounding ventricular myocardium. The strands selected for study were straight and unbranched, approximately 200 $\mu$m in overall diameter and approximately 1 cm in total length. Because of the small overall diameter of the preparations, radial current flow would be expected to be negligible; thus, $r_1$ would be treated as ohmic. Moreover, since 1 cm is considerably greater than the $\lambda$ of 1–3 mm typically measured for most cardiac Purkinje fiber preparations,\(^20,27,30,36-38\) the use of the infinite cable solution appeared to be justified. One-dimensional cable behavior was further supported by the observation that the longitudinal voltage distribution [$V_m(x)$] remained a smooth, simple exponential function of distance, even when $\lambda$ was increased several times by the addition of 1 mM BaCl$_2$ to the Tyrode’s solution. Under conditions of two-dimensional current flow, a relatively steep fall-off in $V_m$ (i.e., Bessel function) is expected, which is most apparent at distances less than 0.3 $\lambda$ from the current electrode.\(^28,39\) This result was not obtained in the present experiments.

Of possible concern is the 1-hour period of equilibration that preceded the electrophysiological studies. It is well known that SPFs surviving in 24-hour myocardial infarctions undergo progressive changes in electrical activity during continuous superfusion in vitro after their excision.\(^3,6\) Initially, on placement in the tissue bath, the SPF preparations became spontaneously active and could not be paced. This rapid spontaneous activity gradually disappeared during the first hour of superfusion, and the resting potential recovered toward more negative values. After an hour of superfusion, the resting potential and the shape of the action potential remained reasonably stable, and the cable measurements were begun by using current injection at a fixed time during diastole. The SPF preparations were allowed to stabilize for 1 hour before study 1) to simplify the analysis of cable properties by avoiding the complication of time- and voltage-dependent changes in membrane resistance that would occur in gradually recovering, spontaneously active preparations and 2) to facilitate comparisons with previous studies on the mechanisms of arrhythmogenesis in this model, in which a 1-hour period of equilibration was also used before in vitro analysis (e.g., see References 2, 6, and 13). Although this approach may miss possible contributions by labile factors that “wash out” during superfusion, the results will nevertheless be relevant to the more persistent changes in electrical activity, for example, increased action potential duration.

**Statistical Analysis**

Data were analyzed by calculating means, standard deviations, and standard errors of the mean. Approximation of the data to a normal distribution was confirmed by the Kolmogorov-Smirnov one-sample test, and outliers (i.e., data values >2 SD from the mean) were eliminated before testing for significance. Comparisons between groups were performed by a two-sample Student’s $t$ test, with $p<0.05$ indicating a significant difference. Data are presented as the mean±SEM.
Results

Action Potential Characteristics

Complete sets of action potential and cable measurements were obtained in 21 normal and 19 infarcted SPF preparations. Action potentials recorded in SPFs from normal hearts during steady pacing at a basic cycle length of 630 msec had maximum diastolic potentials of $-87.2 \pm 1.8$ mV and durations measured at 90% repolarization of $301 \pm 40$ msec ($n = 21$). Maximum diastolic potentials in SPF preparations taken from regions of day-old infarction were significantly reduced ($-79.8 \pm 5.1$ mV), and action potentials were prolonged (396$\pm$23 msec) compared with noninfarcted controls ($n = 19$), as illustrated in Figure 1. $\theta$ at this cycle length was similar in both normal (2.3$\pm$0.2 m/sec) and infarcted (2.0$\pm$0.2 m/sec) preparations and comparable with that recorded in free-running strands. Upstroke velocity was not measured in these experiments. As previously reported, action potentials characteristic of SPFs could generally be recorded from two to four consecutive cell layers in normal hearts and from one to two consecutive cell layers in infarcted hearts. In normal hearts, further advancement of the microelectrode revealed action potentials characteristic of ventricular muscle, whereas in infarcted tissue, no electrical activity could be recorded from deeper cell layers. Representative tracings are shown in Figure 2.

Electrical Coupling Between SPFs and Ventricular Myocardium

The extent of electrical coupling between adjacent layers of SPFs and between SPFs and neighboring ventricular myocardium was assessed by examining the decrement in electrotonic potential at various sites during current injection, as shown in Figure 3. In the majority of SPF preparations from normal hearts (20/21), electrotonic potentials could not be recorded in ventricular myocardium when the current electrode was placed at a superficial SPF site. Similarly, current injected into ventricular myocardium did not produce measurable electrotonus in the SPF strand. A simpler situation was obtained in...
infarcted preparations, in which the underlying ventricular myocardium was electrically silent and no evidence of coupling could be obtained. In both cases, however, cells generating action potentials within the SPF strand appeared to be well coupled in both longitudinal and radial directions.

Length Constant Determinations

The absence of significant electrical coupling between SPFs and adjacent ventricular myocardium suggests that current spread within the SPF strand may occur in one dimension. This was tested in normal hearts by examining the longitudinal decrement in membrane potential produced by current pulses injected at one end of the SPF strand. Voltage recordings were made as close to the current electrode as possible; in practice, it was difficult to achieve interelectrode distances of less than 500 μm without jeopardizing the impalements. As predicted by one-dimensional cable theory, the steady-state voltage distribution was well fitted by a single-exponential function. λ measured in normal SPFs was 1.2±0.1 mm (n=21). Similar values for λ were obtained in SPFs from infarcted hearts (1.2±0.1 mm, n=19).

Although these results appear to be consistent with one-dimensional cable behavior, the possibility of two-dimensional current spread cannot be entirely excluded, since the steady-state voltage distribution for a two-dimensional cable (i.e., Bessel function) will approximate a single-exponential function at distances greater than 0.3 λ from the site of current injection. The more complex nature of two-dimensional current flow will thus become most apparent in the vicinity of the current passing electrode (i.e., x<0.3 λ). To improve the resolution of the voltage response at these close distances, experiments were performed in solutions containing 1 mM BaCl₂ to decrease membrane conductance and consequently increase λ. In the experiment illustrated in Figure 4, addition of BaCl₂ to the normal Tyrode's solution increased λ from 1.8 to 3.0 mm.
Despite this twofold increase in $\lambda$, which reduced the shortest interelectrode distance to approximately 0.15 $\lambda$, the voltage distribution remained exponential, providing additional support for the assumption of one-dimensional cable behavior in these preparations. Similar results were obtained in two other experiments.

**Cable Properties of SPFs From Normal and Infarcted Hearts**

Passive electrical properties were determined for both normal and infarcted SPF preparations on the assumption of one-dimensional cable behavior. In normal SPF strands, $R_m$ averaged 67.4±7.4 K$\Omega$ ($n=20$), yielding calculated $r_m$ and $r_i$ values of 8.2±0.7 K$\Omega$-cm ($n=21$) and 0.52±0.06 M$\Omega$-cm ($n=19$), respectively. $\tau_m$ in these experiments was 7.3±0.8 msec ($n=21$), and $\tau_{AP}$ averaged 118±7 $\mu$sec ($n=20$). The DC membrane capacitance ($C_m$) was determined to be 960±102 nF/cm ($n=21$), and $C_{AP}$ was 340±65 nF/cm ($n=19$). The $C_m/C_{AP}$ ratio was 3.4±0.6 ($n=19$), indicating that the action potential charges only a fraction (~30%) of the total SPF preparation membrane.

Table 1 compares the electrical properties of the SPFs obtained in the present study with published values from similar experiments in other cardiac Purkinje fiber and ventricular muscle preparations. Included are estimates for the specific $R_m$ and $R_s$ and the specific $C_m$ which assume that SPF strands approximate right cylinders with a radius of 100 $\mu$m. In general, the results are similar to values reported for free-running Purkinje fiber bundles from canine, sheep, and rabbit ventricle and intact ventricular myocardium, as well as more recent data obtained in single ventricular Purkinje fiber myocytes.

Table 1. Passive Electrical Properties of Subendocardial Purkinje Fibers: Comparison With Other Cardiac Preparations

<table>
<thead>
<tr>
<th>Preparation</th>
<th>$\lambda$ (mm)</th>
<th>$\tau_m$ (msec)</th>
<th>$\tau_{AP}$ (msec)</th>
<th>$\theta$ (m/sec)</th>
<th>$R_m$ (K$\Omega$-cm$^2$)</th>
<th>$R_s$ (K$\Omega$-cm$^2$)</th>
<th>$C_m$ (nF/cm$^2$)</th>
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$\lambda$, membrane length constant; $\tau_m$, membrane time constant; $\tau_{AP}$, time constant of the foot of the action potential; $\theta$, conduction velocity; $R_m$, membrane resistance; $R_s$, axial resistance; $C_m$, membrane capacitance; $C_{AP}$, capacitance charged during the foot of the action potential; SPFs, subendocardial Purkinje fibers; PF, free running Purkinje fiber; VM, ventricular muscle.

*Assumed value.

Discussion

The results obtained in this study support previous reports in suggesting that few electrical connections exist between SPF strands and the neighboring ventricular myocardium, whereas cells within the SPF strand are well coupled in both longitudinal and radial directions. As a result, current within the long unbranched sections of SPF selected for analysis in the present set of experiments flows largely in one dimension; thus, conventional one-dimensional cable theory in the determination of passive electrical properties can be applied. The data further indicate that the electrical properties of SPFs surviving 1-day-old experimental myocardial infarctions are altered in a fairly specific manner; that is, roughly parallel increases in both $r_m$ and $r_i$ and a corresponding decrease in $c_m$ leave $\theta$, $\lambda$, and $\tau_m$ relatively unaltered in the infarcted SPF cells.

**Coupling Between Subendocardial Purkinje Fibers and Myocardium**

The apparent lack of electrical coupling between SPF and adjacent myocardium is in substantial agreement with previous reports by several investigators. Lathrop and Bailey found little, if any, functional interactions between the proximal bundle branch and myocardium in canine heart. In those experiments, direct activation of either the bundle branch or the

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<td>Dog SPFs</td>
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<td>7.3</td>
<td>118</td>
<td>2.3</td>
<td>0.5</td>
<td>164</td>
<td>13.0</td>
<td>5.4</td>
<td>This study</td>
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<td>Dog PF</td>
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<td>47.6</td>
<td>...</td>
<td>...</td>
<td>4.1</td>
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<td>...</td>
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<td>135</td>
<td>2.7</td>
<td>1.7</td>
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<td>12.8</td>
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<td>...</td>
<td>...</td>
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<td>6.5</td>
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<td>3.3</td>
<td>1,130</td>
<td>0.7</td>
<td>4.0</td>
<td>100*</td>
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<td>0.8</td>
<td>9.1</td>
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<td>0.8</td>
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<td>Isolated myocytes</td>
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<td>7.0</td>
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<td>2.8</td>
<td>...</td>
<td>2.7</td>
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<tr>
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<td>3.0</td>
<td>...</td>
<td>...</td>
<td>3.2</td>
<td>...</td>
<td>2.0</td>
<td>...</td>
<td>43</td>
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<tr>
<td>Rat VM</td>
<td>0.5</td>
<td>16.2</td>
<td>...</td>
<td>...</td>
<td>2.8</td>
<td>605</td>
<td>...</td>
<td>5.0</td>
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neighboring myocardium using suprathreshold stimuli failed to produce changes in the electrical activity of the adjacent tissue. Similar results were obtained by Myerburg et al. who identified discrete, inhomogeneously distributed sites of coupling between myocardium and the diffuse SPF network overlying the apical papillary muscle. These sites allow action potentials to propagate from Purkinje fiber to myocardium and also electrically load the superficial Purkinje fiber layers to reduce \( \theta \) and alter the shape of the action potential. They may also form a substrate for unidirectional block and reentrant excitation.44

Comparison of Passive Electrical Properties in Other Cardiac Cells

A comparison of the passive electrical properties obtained in the present experiments from noninfarcted SPFs with published values in other Purkinje fiber and canine myocardial preparations reveals several similarities. For example, \( \theta \) measured in canine SPFs (2.3 m/sec) is comparable with that in sheep Purkinje fibers (2.7 m/sec). The value obtained for \( r_1 \) is comparable with that seen in dog and sheep Purkinje fibers but less than that obtained in rabbit Purkinje fibers, possibly reflecting differences between these species in the density of myoplasmic contents (e.g., myofibrils) or in the frequency and/or conductance of the gap junctions, or both.9 The value for \( r_m \) (0.5 K\( \Omega \) cm\(^2\)) is somewhat lower than that reported for intact Purkinje fibers from sheep (1.7 K\( \Omega \) cm\(^2\)), dog (1.4–4.1 K\( \Omega \) cm\(^2\)), and rabbit (1.32 K\( \Omega \) cm\(^2\)) on the assumption that the multicellular preparations can be treated as smooth right cylinders. If one were to correct for additional surface area within the SPF strand, which may exist either as sarcolemmal infoldings or membranes facing intercellular spaces, the value of \( r_m \) obtained would be greater by a factor of twofold to sixfold or more. For free-running canine Purkinje strands 250–350 \( \mu m \) in diameter, a surface-to-volume ratio of 0.137 \( \mu m^{-1} \) has been reported.66 This value is 13-fold greater than expected for a right cylinder of the same dimensions. Using this ratio to correct for total surface area, we obtain \( r_m = 106 \) K\( \Omega \) cm\(^2\) and \( c_m = 1 \mu F/cm^2 \). \( r_m \), a property of the membrane that should be relatively independent of fiber geometry, is very similar to that recorded in single myocytes isolated from rat ventricle (8 msec) and dog Purkinje fiber bundles (7.6 msec). The difference observed between the values of \( c_m \) and \( c_{\lambda P} \) in the SPFs suggests that, as in ungulate Purkinje fibers, only a fraction (30%) of the total membrane of the SPFs in charged during the foot of the action potential.

**Table 2. Passive Electrical Properties of Canine Subendocardial Purkinje Fibers From Normal Hearts and Regions of 1-Day-Old Infarction**

<table>
<thead>
<tr>
<th></th>
<th>Normal</th>
<th>Infarcted</th>
<th>%Δ</th>
</tr>
</thead>
<tbody>
<tr>
<td>( R_m ) (K( \Omega ))</td>
<td>67.4±7.4 (20)</td>
<td>94.7±7.5* (19)</td>
<td>+40.5</td>
</tr>
<tr>
<td>( \lambda ) (mm)</td>
<td>1.2±0.1 (20)</td>
<td>1.2±0.1 (19)</td>
<td>0.0</td>
</tr>
<tr>
<td>( \theta ) (m/sec)</td>
<td>2.3±0.2 (20)</td>
<td>2.0±0.2 (18)</td>
<td>-13.0</td>
</tr>
<tr>
<td>( \tau_m ) (msec)</td>
<td>7.3±0.8 (21)</td>
<td>7.4±0.9 (18)</td>
<td>-1.4</td>
</tr>
<tr>
<td>( \tau_{AP} ) (msec)</td>
<td>118±7 (20)</td>
<td>106±6 (19)</td>
<td>-10.2</td>
</tr>
<tr>
<td>( r_m ) (K( \Omega ) cm)</td>
<td>8.2±0.7 (21)</td>
<td>11.8±1.5* (18)</td>
<td>+43.9</td>
</tr>
<tr>
<td>( r_1 ) (M( \Omega ) cm)</td>
<td>0.52±0.06 (19)</td>
<td>0.77±0.08* (19)</td>
<td>+47.5</td>
</tr>
<tr>
<td>( c_m ) (nF/cm)</td>
<td>960±102 (21)</td>
<td>727±114* (18)</td>
<td>-24.3</td>
</tr>
<tr>
<td>( c_{\lambda P} ) (nF/cm)</td>
<td>340±65 (19)</td>
<td>355±48 (18)</td>
<td>+4.4</td>
</tr>
</tbody>
</table>

Values are mean±SEM. Number in parentheses represents number of normal or infarcted subendocardial Purkinje fiber preparations. %Δ, percent change in infarcted preparations compared with normal preparations; \( R_m \), input resistance; \( \lambda \), membrane length constant; \( \theta \), conduction velocity; \( \tau_m \), membrane time constant; \( \tau_{AP} \), time constant for the foot of the action potential; \( r_m \), membrane resistance; \( r_1 \), axial resistance; \( c_m \), membrane capacitance; \( c_{\lambda P} \), capacitance charged during the foot of the action potential.

* \( p < 0.05 \) by two-sample \( t \) test.
Effects of 24-Hour Ligation on Electrical Activity

As previously described, ligation of the left anterior descending coronary artery results in the eventual death of the myocardial cells and obvious changes in the electrical activity of Purkinje fibers in the zone of infarction. Similar to other investigators, we found a significant prolongation of the SPF action potential and a reduction in diastolic membrane potential 24 hours after complete coronary ligation. However, was essentially unchanged in the SPFs, despite the abnormalities in action potential configuration; this finding was consistent with the observed lack of change in \( \lambda \). Sugii et al. similarly report no significant difference in conduction time of basic impulses in canine Purkinje fibers from the infarcted region of the right ventricle after coronary occlusion. These findings in Purkinje fibers, however, are in sharp contrast to observations in chronically infarcted ventricular myocardium, in which distinct regions of slow conduction and reduced \( \lambda \) can be identified.

Although \( V_{\text{max}} \) was not measured in the present study, other investigators using similar 24-hour infarction models have reported little change in this parameter in surviving SPFs having relatively normal resting potentials. Reductions in \( V_{\text{max}} \) when they occur, appear to be associated with reductions in maximal diastolic potential, consistent with an increase in the amount of resting inactivation for the excitable sodium channel just before initiation of the action potential. Allen et al. found no differences in \( V_{\text{max}} \) between normal and infarcted zone SPF preparations with maximal diastolic potentials greater than \(-73 \) mV (group 1 fibers), whereas significant reductions in \( V_{\text{max}} \) were noted in fibers with maximal diastolic potentials less than \(-73 \) mV (group 2 fibers). Significant reductions in \( V_{\text{max}} \) have been reported when data from relatively well-polarized as well as more severely depressed surviving SPF preparations are included in the analysis. However, much larger effects on \( V_{\text{max}} \) are seen in epicardial muscle surviving 24 hours after infarction, even though maximal diastolic potential may not be dramatically reduced. For example, Spear at al. reported an average decrease in \( V_{\text{max}} \) from 113 to 50 V/sec in uniformly conducting epicardial fibers, despite a relatively modest reduction in resting potential (from \(-83 \) to \(-75 \) mV). The reason for this apparent difference is unclear but may possibly involve changes in the voltage dependence of sodium channel gating, in combination with a lower margin of safety (i.e., lesser degree of nonlinearity in the \( V_{\text{max}} \)-sodium channel conduction relation) for excitation and conduction in the epicardial cells.

In the present set of experiments, since neither \( \theta \) nor \( r_{\text{AP}} \) were significantly reduced in SPFs after infarction and since the SPFs remained fairly well polarized, with characteristics similar to group 1 fibers, dramatic decreases in \( V_{\text{max}} \) would not be expected to have occurred. However, given the square root relation between \( \dot{V}_{\text{max}} \) and \( \theta \) (\( \theta = \dot{V}_{\text{max}}^{-0.5} \)), which can be derived by cable theory and which has been demonstrated experimentally in cardiac Purkinje fiber preparations, reductions in \( V_{\text{max}} \) of at least 30% would be required to produce a 10% decrease in \( \theta \). Thus, possible effects on \( V_{\text{max}} \) in the present study, although considered to be unlikely, cannot be entirely excluded by the available data.

Possible Basis for Observed Changes in Electrical Properties

It has been reported that lysophosphoglycerides accumulate in the ischemic myocardium and contribute to the genesis of arrhythmias. Application of exogenous LPC to cardiac tissue in vitro can induce marked electrophysiological changes, including a decrease in resting membrane potential, a depression of \( V_{\text{max}} \) and membrane responsiveness, a slowing of \( \theta \), and the induction of spontaneous repetitive firing. Voltage-clamp studies have revealed that the depolarization induced by LPC is the result of a decrease in resting membrane conductance associated with a linearization of the background potassium current \( I_{\text{Kt}} \) and a reduction in single \( I_{\text{Km}} \) channel conductance. Consistent with these results, Arnsdorf and Sawicki found by using cable analysis that low concentrations of exogenous LPC significantly increased resting \( r_{\text{m}} (+41.7\%) \) and \( r_{\text{i}} (+14.1\%) \) in sheep Purkinje fibers, with concomitant increases in \( R_{\text{m}} (+22.8\%) \), \( \lambda (+9.8\%) \), and \( \tau_{\text{m}} (+29.7\%) \). In these experiments was unchanged.

In the present study, \( r_{\text{m}} \) and \( r_{\text{i}} \) were both significantly increased in the SPF networks taken from the region of infarction. Although the observed increase in \( r_{\text{m}} (+43.9\%) \) was remarkably similar to that reported by Arnsdorf and Sawicki and might therefore be consistent with an accumulation of LPC in these cells, the magnitude of the change in \( r_{\text{i}} \) was considerably greater in the infarcted preparations (+47.5%); these findings suggest that additional factors (such as cell uncoupling) must contribute to the observed alterations in the electrical structure of SPFs in the infarcted heart.

Several investigators have examined the effects of hypoxia on \( r_{\text{i}} \) in various cardiac muscle preparations. Ikeda and Hiraoka found in canine ventricle that hypoxia in the presence of glucose produced a modest but significant reduction (-13.6%) in \( \lambda \) which resulted primarily from an increase (+23.7%) in \( r_{\text{i}} \), \( c_{\text{m}} \) and \( \tau_{\text{m}} \) were unchanged. The increase in \( r_{\text{i}} \) induced by hypoxia became even more dramatic (+57 to 80%) when glucose was omitted from the bathing solution. Wojtczak found that hypoxia in the absence of glucose increased internal resistance by 300% in cow ventricular muscle and attributed this entirely to the electrical uncoupling (due to calcium overload) of cells within the bundle. More recently, Kleber et al. have reported a similar threefold increase in \( r_{\text{i}} \) in isolated arterially perfused rabbit papillary muscle during ischemia.
The large increases in $r_m$ and $r_1$ seen in the present study may, therefore, be the result of cell uncoupling in combination with effects on membrane potassium channels produced by the accumulation of lysophospholipids. However, the observed decrease (-24%) in $c_m$ of the SPF preparations is not readily explained by either of these mechanisms. Neither exposure of normal Purkinje fibers to exogenous LPC$^2$0 or to hypoxia$^{12}$ have been reported to decrease $c_m$. Moreover, the absence of any change in $c_{AP}$ argues against a fundamental change in membrane dielectric produced by ischemia.

The data also argue against the possibility that depolarization per se is responsible for the increase in $r_m$. Hellam and Studt$^{51}$ found that small changes in membrane potential over the range -70 to -100 mV produced by application of external current in sheep Purkinje fibers could increase $r_m$ by amounts (50-60%) comparable with that seen in the present study. However, the increase in $r_m$ observed during current injection was accompanied by concurrent increases in $\lambda$ and $c_m$, while in the present study $\lambda$ remained constant and $c_m$ decreased. Thus, it appears unlikely that simple changes in slope conductance secondary to depolarization can explain the differences between normal and infarcted zone SPFs.

One possible alternative explanation consistent with all the data is that ischemia simply changes the electrical structure of the SPF network by completely uncoupling some cells within the strands, without changing the passive electrical properties of the individual myocytes that remain coupled. Friedman et al$^1$ found that action potentials could be recorded from only one to two cell layers of SPFs, in contrast to the two to four layers usually accessed in noninfarcted preparations. Similar results were reported by Sugi et al$^8$ after right coronary artery occlusion. We have also seen a "thinning" of the infarcted zone SPF layer in the present set of experiments; the number of electrophysiologically observable layers was reduced from two to four in normal hearts to only one or two in the zone of infarction. Although no histological or morphometric correlation with electrophysiologically data was performed, this observation could be explained if infarction caused some cells to be electrophysiologically isolated and perhaps depolarized as well.

Calculations based on the hypothesis of complete uncoupling of some cells can explain the changes in passive electrical properties of the cable we observed after infarction. Using the values for the membrane resistance ($r_m^*$) and membrane capacitance ($c_m^*$) of single canine Purkinje myocytes as determined by Sheets et al$^{44}$ one can calculate the effective values of $r_m$, $r_1$, and $c_m$ that would be measured for different geometric arrangements of cells. As a simple first approximation, one may assume that the individual SPF myocytes are electrically well coupled and connected in parallel to form the multicellular bundle. In this array, the measured $r_m$ would be given by $r_m = r_m^* / n$ and the measured $c_m$ by $c_m = n c_m^*$, where $n$ is the total number of cells in the bundle. From the single cell data, $r_m^* = 248$ K$\Omega$cm and $c_m^* = 29$ nF/cm. The total number of cells calculated in this model is 28 or 30, based on measurements of $c_m$ or $r_m$ respectively. Since approximately one third of the membrane is charged during an action potential ($c_m / c_{AP} = 3.4$), we can assume that nine cells (0.3 x 29) are superficial and that the remainder (n=20) are electrically "buried" within the bundle. If one assumes that six of the deeper cells are completely uncoupled and lost from the cable after coronary occlusion, with no change in electrical properties of the remaining cells, then values of $r_m = 10.7$ K$\Omega$cm, $c_m = 661$ nF/cm, and the ratio $c_m / c_{AP} = 2.6$ can be predicted, which compare favorably with the experimentally measured values of 11.8 K$\Omega$cm, 727 nF/cm, and 2.4, respectively.

The decrease in total number of coupled cells would also serve to reduce the effective electrical diameter of the SPF bundle and consequently increase the effective $r_1$. It is assumed that cell dimensions for the Purkinje myocytes remain constant; therefore, bundle cross-sectional area in the present model would effectively decrease from $262 \times 10^{-6}$ cm$^2$ to $208 \times 10^{-6}$ cm$^2$. Thus, the measured $r_1$ is increased by a factor of 1.59, whereas an increase of 1.48 was actually measured. One can also predict the $R_m$ expected after infarction (96.8 K$\Omega$), which also compares favorably with that measured (94.7 K$\Omega$). Thus, the assumption that some cells within the SPF bundle become electrically uncoupled during ischemia, with no change in specific resistance or capacitance of the remaining well-coupled cells, appears to be sufficient to explain all of the observed changes in the measured passive electrical properties.

Evidence for the heterogeneous pattern of cell injury we hypothesize for canine SPFs has been demonstrated in the subepicardial borderzone of ischemically injured rat hearts by use of fluorescent antymyosin antibodies.52 Injured cells stained by the antibody and histologically normal cells without antibody staining were seen adjacent to each other and separated by intercalated discs. Antibody staining indicates membrane defects large enough to allow passage of macromolecules, which would presumably be associated with loss of membrane potential and equilibration with the extracellular calcium concentration that would uncouple cells. The heterogeneity of cell injury means that cells escaping this severe injury may remain viable. Although similar techniques have not been used to study SPFs, these fibers do represent a borderzone in the canine infarct after 24 hours. Electrically viable Purkinje cells are adjacent to depolarized myocardial cells in deeper layers, and the decrease in the apparent number of Purkinje cell layers suggests heterogeneous drop out of Purkinje cells.

Possible Directions for Future Study

The description of the passive electrical properties of the SPF strands from both normal and infarcted regions of the canine myocardium suggests that they
behave electrically as one-dimensional cables. Thus, it should be possible to shorten the preparations by dissection to lengths (1–2 mm) permitting application of the two-microelectrode voltage-clamp technique. Unfortunately, this approach may be limited by an inability to adequately control membrane potential in the deeper-lying membranes, as well as by a possible loss of control if the preparations contained discrete regions of electrical coupling between SPFVs and myocardium. It would also be important to determine, by histological or biochemical techniques, whether loss of cell-to-cell coupling or localized cell death occurs within SPFV strands surviving in the infarction zone, as suggested by these experiments. Regions of heterogeneity in cell coupling within the SPFV strand could provide a substrate for microentry and possibly contribute to the production of arrhythmias arising in the SPFV's 24 hours after coronary ligation.

References
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51. Hellam DC, Studt JW: Linear analysis of membrane conductance and capacitance in cardiac Purkinje fibers. J Physiol (Lond) 1974;243:661–694


KEY WORDS • subendocardial Purkinje fibers • myocardial infarction • cable analysis • passive electrical properties • electrophysiology
Electrical properties of canine subendocardial Purkinje fibers surviving in 1-day-old experimental myocardial infarction.

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