Interaction of Fiber Orientation and Direction of Impulse Propagation With Anatomic Barriers in Anisotropic Canine Myocardium

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We developed a computer model of the interaction of impulse propagation with anatomic barriers in uniformly anisotropic tissue. Its predictions were confirmed experimentally by using an in vitro cut to create a 6×1-mm anatomic barrier in 12 canine epicardial strips. The model predicted that long, thin barriers located parallel to the direction of impulse propagation would have little effect in delaying conduction regardless of the arrangement of cardiac fibers. In this situation, the mean experimental ratio of postcut to control conduction times across the barrier was 1.05:1.00 in 10 tissues. When impulses were proceeding perpendicular to an anatomic barrier, significant distal conduction delay was predicted and found to occur only when the conduction from pacing to recording sites was initially longitudinal to fiber orientation (mean experimental ratio, 2.34:1.00 in five tissues) but not transverse to fiber orientation (ratio, 1.08:1.00 in five tissues). We conclude that the direction of initial impulse propagation and the orientation of myocardial fibers have large effects on the degree to which anatomic barriers delay activation in cardiac tissue. These findings may have implications for the participation of anatomic barriers in reentrant circuits. (Circulation 1988;78:1478–1494)

Slow conduction and unidirectional block are requirements for reentrant pathways.1–9 In addition to slow conduction because of a decrease in the rate of rise of the intracellular potential, differences in cell-to-cell coupling and the geometric arrangement of fibers in cardiac tissue may also produce slow conduction.10–15 Spach et al15 have shown that highly anisotropic tissue may produce both the slow conduction and the unidirectional block required to support reentrant impulses. However, most models of reentry require in addition fixed anatomic barriers around which reentrant impulses circulate.

Reentry involving an anatomic barrier does not depend on any particular conduction velocity but rather on an adequate amount of time for a previously activated area to recover before the circulating impulse returns. Thus, a circuitous anatomic pathway defined by fixed areas of block could provide a long enough conduction pathway to allow sufficient time for an impulse conducting at a normal velocity to return to fully recovered cardiac tissue. The extent of increased conduction time distal to anatomic barriers in cardiac tissue has not been extensively investigated. In addition, the consequences of the interrelation of fixed anatomic barriers and tissue anisotropy are unknown. Such activation delay distal to a barrier may have important implications for the participation of a barrier in reentrant circuits.

Therefore, we developed a computer model of the interaction of fixed anatomic barriers with conduction in anisotropic tissue. Our goals were to verify the hypotheses that the direction of impulse propagation and the orientation of fibers relative to a fixed anatomic area of block were crucial in determining the degree of conduction delay and perturbation of activation patterns produced distal to the block. We then validated the predictions of this computer analysis in a simple model of anatomic barrier in canine epicardium produced by a thin surgical cut in an in vitro preparation.

Materials and Methods

Model of Conduction and Anisotropic Tissue

Directional differences in conduction velocity in canine myocardium related to fiber orientation have
been recognized since the 1950s. Several investigators have proposed a variety of different geometric models to predict conduction velocity in various directions in anisotropic tissue. Roberts et al compared an elliptical model of impulse propagation to a more complex model based on voltage potential differences and could not distinguish these experimentally (see "Discussion"). More recently, Roberge et al have developed an equivalent circuit model of conduction in anisotropic tissue in which propagation is elliptical.

We, thus, assume that conduction from a point source in anisotropic tissue can be sufficiently approximated according to an "elliptical" model; that is, conduction along a given direction is given by the magnitude of an ellipse in that direction (the length of the ellipse being normalized such that the minor axis is equal to 1). The ellipse is defined by the equation:

\[(X^2/Z^2) + Y^2 = 1 \] (1)

where \(Z\) is the length of the major axis, and \(X\) and \(Y\) are coordinates.

We note that if we transform coordinates \(X' = X/Z, Y' = Y\), in the transformed coordinate system, conduction is isotropic and isochrones will be circular (conduction velocity will be normalized to 1). Therefore, conduction times can be computed by figuring the lengths in the new coordinate system, and the problem becomes an exercise in simple trigonometry. We write the \(x\) and \(y\) coordinates of the origin of the signal, the recording points; transform coordinates; and use the expression that the length of a line between \(X', Y'\), and \(X'_2Y'_2\) is:

\[\text{Length} = [(X'_1 - X'_2)^2 + (Y'_1 - Y'_2)^2]^{1/2} \] (2)

If we assume uniform fiber orientation and conduction throughout the preparation and a two-dimensional preparation, then the conduction time (CT) between a pacing site and a recording site is the sum of segment times (distances in the transformed coordinates) consisting of the shortest line between the two points. If we assume a barrier of length \(b_1 + b_2\) and thickness \(T\), then there are two possible paths consisting of three separate segments between the pacing and recording sites (Figure 1). The conduction time in the presence of a barrier will then be the minimum of CT1 and CT2 of Equation 3 and Equation 4 below.

\[
\begin{align*}
\text{CT}_1 &= 1/V \left( (a_1 \sin \theta b_1 cos \theta)^2 + V^2 [a_1 \cos \theta b_1 \sin \theta]^2 \right)^{1/2} \\
+ &\left( [a_1 \sin \theta b_1 \cos \theta]^2 + V^2 [a_1 \cos \theta b_1 \sin \theta]^2 + T \sin^2 \theta \right) \\
+ &V^2 \cos^2 \theta \right)^{1/2}
\end{align*}
\] (3)

\[
\begin{align*}
\text{CT}_2 &= 1/V \left( (a_1 \sin \theta b_1 \cos \theta)^2 + V^2 [a_1 \cos \theta b_1 \sin \theta]^2 \right)^{1/2} \\
+ &\left( [a_1 \sin \theta b_1 \cos \theta]^2 + V^2 [a_1 \cos \theta b_1 \sin \theta]^2 \right)^{1/2} + V^2 \sin^2 \theta \right)^{1/2}
\end{align*}
\] (4)

Referring to Figure 1, \(a_1\) is the distance from the pacing site to the beginning of the barrier, \(T\) is the thickness of the barrier, \(a_2\) is the distance from the barrier to the recording site, \(V\) is the ratio of longitudinal to transverse conduction velocities, or the "anisotropic ratio," \(b_1\) is the distance from a line between the pacing electrode and the recording electrode to one end of the barrier, \(b_2\) is this distance to the other end, \(\theta\) is the angle between the barrier and the long axis of cardiac fibers, and \(\psi\) is the angle between a line between the pacing and recording electrodes and a line perpendicular to the barrier (\(\psi = 90°\) in Figure 1). If no barrier is present, conduction occurs in a straight line, and its time is determined by Equation 5:

\[
\begin{align*}
\text{CT without barrier} &= (a_1 + a_2 + T \sec \psi)\left( V^2 \cos \theta + \sin^2 \theta \right)^{1/2}/V
\end{align*}
\] (5)
Thus, the model allows conduction times from a point source to any point distal to a rectangular anatomic barrier to be calculated and describes conduction around such a barrier. We used in vitro epicardial strips to confirm the model’s predictions.

We also used the computer model to generate complete isochronal activation maps to predict activation patterns. Isochronal maps were constructed by using Equations 3–5 to determine activation times at various sites throughout the hypothetical tissue depending on pacing site. We simulated barriers of various lengths at different angles to fiber orientation. In addition, two separate procedures were used to generate isochronal maps. In one, an essentially infinite mapping density was simulated. In the other procedure, data were estimated for discrete mapping sites given distances apart from each other. These separate simulations were used to estimate the effects of mapping density on isochronal activation patterns.

Tissue Preparation

Eight adult mongrel dogs weighing 10–16 kg were used for these experiments. The dogs were anesthetized with sodium pentobarbital (30 mg/kg i.v.), and the chest opened via a left lateral thoracotomy. Tissues approximately 2 cm x 3 cm x 2 mm thick were shaved from the epicardial surface of either the left or right ventricle. They were cut so that the fiber orientation was parallel to the long axis of the tissue. Areas of epicardial fat, blood vessels, or irregular or bending fibers were avoided. We have previously subjected tissues obtained in a similar manner to histological examination to confirm our ability to obtain parallel fiber orientation over the length of the tissue. In addition, the typical elliptical isochronal pattern identified in vitro correlates excellently with the direction of myocardial fibers.

Immediately after removal, tissues were placed in the tissue bath or in an oxygenated Tyrode’s solution at room temperature with the epicardial surface up. Tissues were superfused with Tyrode’s solution containing 1.6 mM calcium and equilibrated with 95% O2-5% CO2 at 37.5° C. Tissues were stimulated with one or more bipolar electrodes consisting of Teflon-coated silver wires. Constant current rectangular pulses, 2 msec in duration and twice-diastolic threshold, were delivered at a cycle length of 1,000 msec. In experiments which premature beats were delivered, eight beats were delivered at a pacing cycle length of 1,000 msec followed by the premature beat and a 2-second pause.

Extracellular and Intracellular Potential Recording

Reference extracellular electrograms were recorded with bipolar Teflon-coated silver electrodes and amplified from 100 to 1,000 times. Tissue mapping was performed with a custom-made bipolar recording electrode containing four 0.1-mm diameter electrodes arranged in two orthogonal pairs. The center-to-center electrode distance was 0.3 mm, and electrograms were filtered at 1 Hz to 1 kHz. This custom-made probe was mounted on a micromanipulator and used to record two bipolar electrograms at each site.

To determine the area of injury caused by the experimental cuts described below, intracellular potentials were recorded around the cut area of the tissue. Recordings were made with standard 3 M potassium-filled microelectrodes. Intracellular and extracellular recordings were displayed on a multiple channel oscilloscope and photographed on 35-mm film. Intracellular potentials were also recorded after further amplification and instantaneous analog differentiation. After the experiment, extracellular electrogram amplitude, duration, and activation time (either the largest peak or baseline crossing) were measured to the nearest millivolt in 0.1 msec with a Hewlett-Packard Model 9836 computer and manual digitizing system. Distances on the surface of the tissue were measured with a two-dimensional ocular micrometer that was visually calibrated and has a resolution of 0.1 mm. Action potential variables that were measured included action potential amplitude, action potential duration at 100% repolarization, maximum rate of depolarization determined by instantaneous differentiation of the analog signal, and resting membrane potential. These characteristics were used to examine cellular action potentials near the area of the cut. Isochronal activation maps were generated with a Hewlett-Packard Model 9836 computer plotting system with the Condot Algorithm of Simons as previously described.

Experimental Protocol

After tissues had stabilized as evidenced by constant conduction times for at least 15 minutes, two pacing electrodes (S1 and S2) were placed on the surface near the edge of the tissue at approximately the middle of two adjacent sides of the tissue (Figure 2). Thirty- to 50-point grid isochronal activation maps of the tissue were performed with an extracellular probe mounted on a micromanipulator and guided by an optical micrometer. In addition, closely spaced extracellular recordings were made (less than 1 mm apart) longitudinal and transverse to fiber orientation (dots in Figure 2) during propagation from one of the pacing electrodes (S1) to determine conduction velocities longitudinal and transverse to fiber orientation in the tissue. After control measurements had been made, a 4–7-mm long, transmural cut was made in the tissue surface with a number 10 surgical blade (solid line in Figure 2). The cut procedure produced no changes in tissue excitability, and conduction times stabilized less than 5 minutes after the cut. After conduction times had stabilized, complete isochronal activation maps at points similar to those obtained in the control situation were performed. In 10 tissues, cuts were made directly longitudinal (five tissues) or directly transverse (five tissues) to fiber orientation.
selected tissues, premature impulses were introduced in 1 msec decrements toward refractoriness, and extracellular electrograms were monitored on each side of the cut. In two additional tissues, cuts were made at 45° to fiber orientation. Although refractory periods were not measured distal to the barrier, the normal intracellular and extracellular electrograms recorded from such areas make such an abnormality extremely unlikely.

We defined criteria in advance for the suitability of inclusion of these tissues in the protocol, including an anisotropic ratio of at least 2 : 1, uniform conduction as evidenced by $R^2$ values of more than 0.95 for distance-versus-time plots, and stability of the tissue with only limited areas of injury after the cut procedure. All tissues studied had anisotropic ratios of more than 2 : 1 and $R^2$ values of distance-versus-time plots of more than 0.985. One tissue in which the cut produced an extensive area of abnormality in conduction and extracellular electrograms was excluded.

Statistics

Conduction velocities were determined by linear regression plots of distance versus time. As indicated, an $R^2$ value of more than 0.95 was required for inclusion and indicated uniform conduction. Comparison of calculated and predicted activation times was performed with linear regression. Comparison of variables between two separate groups was performed with Student’s unpaired $t$ test. Comparison of conduction times in the same tissue before and after interventions was performed with paired $t$ tests. To compare activation times before and after the cut, a single point on the opposite side of the cut from each pacing electrode was chosen ($R_A, R_B$ in Figure 2), and conduction times from the stimulating to recording electrodes ($S_A-R_A$ and $S_B-R_B$) before and after the cut were used for analysis. Thus, in analyzing the experimental data, impulse propagation was either directly parallel ($\Omega=90^\circ$) or directly perpendicular ($\Omega=0^\circ$) to the barrier. Computer simulations and calculations were performed with a Hewlett-Packard Model 9836 computer.

Results

Results of the Model

Our model of elliptical impulse spread in anisotropic tissue quantified our hypothesis that the orientation of a propagating wavefront and the arrangement of cardiac fibers will determine the degree of apparent conduction slowing and disturbance in the pattern of impulse propagation created by a fixed area of block. To evaluate the effects of an anatomic barrier on conduction, we compared conduction time after the insertion of an anatomic barrier to those without the barrier.

Initially, we investigated how the angle of a long, thin barrier relative to impulse propagation would affect conduction independent of fiber orientation. In our model, a barrier (in this simulation, 6 mm long) of essentially no width parallel to the direction of impulse propagation will produce no slowing or perturbation because it would not change the pathway or conduction velocities involved in the propagation between two points. This relatively thin barrier oriented parallel to the direction of propagation would produce little conduction slowing regardless of the arrangement of cardiac fibers. As the barrier is rotated from directly parallel to a line between the pacing and recording electrode to perpendicular to the initial direction of impulse propagation, a progressively greater increase of conduction time would be produced. Figure 3 shows how, when propagation is parallel to fiber orientation, this barrier rotation increases the ratio of conduction time with the barrier to conduction time without the barrier. In this simulation, impulse propagation was parallel to fiber orientation, and the barrier rotated from parallel to the impulse ($\theta=0^\circ, \Omega=0^\circ$) to perpendicular to the impulse ($\theta=90^\circ, \Omega=90^\circ$). The result was a threefold increase in conduction time.

We then evaluated how differing fiber orientation alters the effect of anatomic barriers. We made three simplifying assumptions for the gen-
general Equations 3–5 to ease presentation of the model’s predictions: 1) that barrier thickness was essentially 0; 2) that \( \Omega = 90^\circ \), that is, that propagation is proceeding from the pacing to recording electrodes directly perpendicular to the barrier; and 3) that \( a_1 = a_2 = b_1 = b_2 = a \), that is, that the distance between the pacing and recording sites and the length of the barrier are equal.

Equations 6 and 7 describe conduction times before and after the introduction of the barrier with the above simplifying assumptions:

\[
\text{CT without barrier} = 2a(\sin^2 \theta + V^2 \cos^2 \theta)^{1/2} / V \tag{6}
\]

\[
\text{CT with barrier} = \frac{a}{V} \left\{ \left( 1 + V^2 \right) + \left( 1 - V^2 \sin^2 \theta \right) \frac{1}{V^4} + \left[ (1+V^2) + (V^2-1) \sin^2 \theta \right]^{1/2} \right\} \tag{7}
\]

where \( \theta \) and \( V \) are as in Equation 3, and \( a = \) one half the barrier length = the distance from pacing site to barrier = the distance from the barrier to the secondary site. Because propagation is proceeding perpendicular to the barrier, initial propagation from pacing to recording sites is parallel to fiber orientation when \( \theta = 90^\circ \).

As shown in Figure 4 for the case where no barrier was present (control), conduction times varied between a maximum perpendicular to fiber orientation \( (\theta = 0^\circ) \) and minimum parallel to fiber orientation \( (\theta = 90^\circ) \). Note that at 45°, conduction time was more than twofold that parallel to fiber orientation. After a block 6 mm in length was inserted, conduction times varied by a relatively small percentage regardless of the initial fiber orientation (Figure 4, barrier). This is largely explained by the fact that pathway lengths were equal and that if one part of the total path occurred rapidly and parallel to fiber orientation, the second part would be slow and perpendicular to fiber orientation. After the barrier was inserted, a minimum in conduction time was present at 45° because a pathway that is half parallel and half perpendicular will have a shorter conduction time than a pathway all at 45° (because conduction time at 45° is closer to that transverse than that longitudinal to fiber orientation).

However, the model predicts that the angle of fiber orientation relative to the orientation of an area of block will have a large influence on the degree of conduction time prolongation compared with the barrier-free state produced by the barrier. In particular, if conduction is initially proceeding transverse to fiber orientation and encounters a perpendicular area of block parallel to fiber orientation, it will have little effect on the conduction times \( (\theta = 0^\circ, \text{Figure 4}) \). In contrast, if an impulse is initially proceeding parallel to fiber orientation and encounters a perpendicular area of block transverse to fiber orientation, a large degree of conduction slowing will be produced \( (\theta = 90^\circ, \text{Figure 4}) \).

In addition, as shown in Figure 5, the model predicts that the ratio of the length of the barrier to the distance between the pacing and recording sites will have a major effect on the degree to which the anatomic barrier disturbs and delays conduction. Propagation was initially proceeding parallel to fiber orientation, and a perpendicular cut was present. There was a nearly linear relation between the increase in conduction time produced by the barrier and the length of the barrier.

We also used the computer model to generate complete isochronal activation maps. Figure 6 shows an “infinite density” isochronal map containing a
barrier 6×1 mm at two different orientations to cardiac fibers. In Figure 6, top panel, impulses are proceeding parallel to fiber orientation toward the barrier. The perpendicular barrier produces a perturbation in activation pattern as well as a delay in activation distal to the barrier. In contrast, when impulses are proceeding transverse to fiber orientation (Figure 6, bottom panel) and encounter a perpendicular barrier, little perturbation in the activation pattern is seen. A 6-mm barrier located 7 mm from the pacing site produces only minor perturbation in impulse conduction, even with “infinite density” mapping.

As is the case with transverse barriers (Figure 5), barrier length is a crucial determinant of the degree of the impulse interruption produced. Figure 7 shows a simulation similar to that in Figure 6, bottom panel, with an 18-mm instead of a 6-mm barrier. Note that impulses distal to the barrier now clearly proceed parallel to and identify an area of block producing delay of distal activation.

Mapping density also affects the ability to identify an area of block. Figure 8 shows a 6-mm block similar to that in Figure 6, bottom panel, mapping with interpoint densities of 0.5 and 2 mm. Note that as mapping density increases from 2 to 0.5 mm between points, the subtle area of block produced by the barrier parallel to myocardial fibers becomes easier to identify. Nonetheless, for any given barrier length and mapping density, far more pertur-

**Figure 4.** Upper panel: Plot of control conduction times during propagation at various angles to fiber orientation with the elliptical model of impulse spread in anisotropic tissue (solid line). In this figure, a barrier of no thickness is assumed. In addition, a line between the stimulating and recording electrodes is assumed to be perpendicular to and passing through the middle of the anatomic barrier (Ω=90°). When the angle on the x axis is equal to 0°, propagation is initially proceeding transverse to fiber orientation, and this is associated with the shortest conduction time. Propagation at θ=90° is proceeding parallel to fiber orientation, and the shortest conduction time occurs. At 45°, the elliptical model predicts that conduction will be less than half as fast as that parallel to fiber orientation. The dashed line shows conduction time between pacing and recording electrodes, which are 6 mm apart after a 6-mm long anatomic barrier has been situated 90° to a line between the two points, halfway between them. When the anatomic barrier is situated at either 0° or 90° to fiber orientation, propagation from the stimulating to recording electrodes proceeds at 45° between the stimulating electrode and the edge of the barrier and at 45° from the edge of the barrier to the recording electrode; thus, these two total times are equal. A minimum in postbarrier conduction time is obtained at 45° because propagation proceeds exactly parallel to fiber orientation for half of the distance and exactly perpendicular to fiber orientation for half the distance. Because propagation parallel to fiber orientation is more than twice propagation at 45° to fiber orientation, this conduction time is the least. Lower panel: Plot of the ratio of conduction times after a barrier has been introduced to that present without the barrier. This ratio represents the degree to which the anatomic barrier affects and slows conduction in a given modeled tissue. When the angle between the cut and fibers is 0°, propagation initially proceeding transverse to fiber orientation is caused to go more longitudinal to fiber orientation by the presence of an anatomic barrier, and, thus, the total increase in conduction time is small despite the increase in distance. In contrast when conduction is initially rapidly parallel to fiber orientation (θ or the angle between the cut and fibers equals 90°), propagation must pass transverse to fiber orientation for a large distance to reach the recording electrode unless the conduction time is increased by a large amount. Interestingly, the model predicts that at 45° very little increase in conduction time will be present.
bation of impulse conduction and delay of distal activation is produced when impulses intercept a barrier that is transverse rather than longitudinal to fiber orientation.

Because this computer model allows the simple calculation of conduction times between pacing and recording electrodes before and after the introduction of anatomic barrier, we chose to validate the qualitative and quantitative predictions of the model with a simple in vitro preparation obtained from canine epicardium. A discrete anatomic barrier was created by a surgical cut in the tissue.

**Experimental Results**

We performed experiments in five tissues in which a cut was made parallel to fiber orientation (θ = 0°) and in five tissues in which the cut was made perpendicular to fibers (θ = 90°). Control conduction characteristics of the tissues are shown in Table 1. The tissues were highly anisotropic with a mean longitudinal:transverse conduction velocities ratio of 3.19. Uniform conduction was initially present through the large majority of the tissues as shown by the isochronal activation maps (Figure 9).

Although the cut itself was microscopically narrow, local injury produced a slightly wider effective area of block. Microelectrode impalement showed abnormally depolarized cells with no or only subthreshold depolarization for approximately 0.3 mm on each side of the cut. Abnormally short action potentials with less negative resting membrane potentials and decreased amplitude were present for an additional 0.2 mm on each side of the block. Thus, the total effective thickness of the area of conduction block was approximately 1 mm.

In all tissues, we evaluated propagation proceeding parallel to the area of block (Ω = 0°) after the cut was made and compared it with that occurring before the block (Table 2). In five tissues, the cut was transverse to fiber orientation (θ = 90° cut), and in five other tissues, it was parallel (θ = 0° cut). The mean ratio of conduction times after the cut compared with before the cut was 1.05. Isocronal activation maps during propagation parallel to the cut (Ω = 0°) showed little perturbation in the pattern of impulse spread (regardless of fiber orientation) except an occasional slowing directly over the area of the cut. Postcut conduction times agreed with the model's predictions for Ω = 0°. In addition, the fact that propagation was relatively undisturbed was also in agreement with the model of isochronal activation maps (Figure 10).

**Propagation Perpendicular to the Area of Block (Ω = 90°)**

Unlike propagation parallel to the area of block, we observed that propagation perpendicular to the block produced a marked perturbation in the activation times when propagation began parallel to fiber orientation and the cut was 90° to fiber orientation (θ = 90°, Ω = 90°) (Figure 11). This propagation pattern was the predicted one for propagation around a fixed anatomic area of block (Figure 6, top panel). However, propagation transverse to fiber orientation was associated with slight slowing and little perturbation of the isochronal activation time, even when propagation was occurring perpendicular to the block (Figure 12). Careful analysis of the isochronal activation maps showed small areas of slowing around the area of block (Figure 12). However, the degree of perturbation in activation times was small. These
results are in agreement with the predicted isochronal map shown in Figure 6, bottom panel.

The mean ratio of postconduction to preconduction times when propagation perpendicular to a transverse cut was 2.34 (Table 2). In contrast, even when propagation was perpendicular to the area of block, little conduction delay relative to control conditions was noted when a longitudinal cut was present and propagation in the barrier-free state occurred transverse to fiber orientation. The ratio of postcut to
precut conduction times was 1.01 (p<0.05 vs. longitudinal conduction). This was also as predicted from the computer model (see Figure 4 at 0°).

Additional Experiments

In two tissues, a cut was made 45° to fiber orientation. The propagation was examined when pacing from one side of the cut. The increase of conduction time from control across the barrier was 1.31 and 1.22 in these two tissues and was intermediate between those and cuts that were made at 0° and 90° but closer to the values obtained for cuts parallel to fiber orientation.

In four tissues, (two 0° cut and two 90° cut) ventricular premature beats were introduced to refractoriness while recording both proximal and distal to the cut area. Decremental conduction was present with closely spaced ventricular premature beats, but it was proportionally equal proximal and distal to the area of block, and no block in the area of the barrier was observed.

Discussion

We have developed a geometric model of propagation around anatomic barriers in anisotropic tissue and confirmed its predictions that the importance of a fixed anatomic barrier in an vitro model of block is dependent on factors other than the size of the anatomic barrier. For long, thin barriers, the influence of an area of block on the pattern of impulse propagation is dependent on the angle between the incident wavefront and the anatomic barrier. When an anatomic barrier is situated close to parallel to direction of propagation and is thin, little perturbation of impulse propagation occurs. In addition, even when propagation occurs perpendicular to a fixed area of block, if propagation is initially proceeding transverse to fiber orientation, the barrier is far less "visible" than when impulses are proceeding parallel to fiber orientation. There is far less disturbance of the isochronal activation pattern and delay of conduction distal to the barrier.

Anisotropic Conduction

The anisotropy of cardiac tissue is related to the anatomic arrangement of long, thin fibers so that more relatively high resistance cell-to-cell junctions per unit distance are encountered during propagation transverse versus parallel to fiber orientation, and thus, impulse spread is relatively slowed. Although the three-dimensional arrangement of cardiac fibers may be complex and involve different fiber orientation at different depths and bending fibers, localized areas of epicardial tissue generally contain uniform and parallel fibers. Discontinuities in propagation transverse to fiber orientation may be present on a microscopic or macroscopic scale and have been referred to as nonuniform anisotropy. In human atrial tissue, Spach and Dobler have shown that the degree of nonuniform conduction and ratio of longitudinal to transverse conduction velocities is related to patient age. Several investigators have modeled propagation in anisotropic cardiac tissue in an attempt to account for directional differences in conduction velocity, apparent tissue resistivity, and the shape of transmembrane action potentials. Roberts et al used two different models in an attempt to predict conduction...
velocities at various angles between the maximum (parallel to fibers) and minimum (perpendicular to fibers) conduction velocities. They compared a complex model based on varying tissue resistivity and recorded membrane potentials with that suggested by a simple ellipse and found them experimentally indistinguishable. In addition, their more complex model is based on the assumption that transmembrane potentials during propagation longitudinal and transverse to fiber orientation are identical. Spach

FIGURE 8. Computer simulation of isochronal activation maps obtained with mapping densities of 0.5 mm (top panel) and 2 mm (bottom panel). Tissue characteristics are similar to those in Figure 6, bottom panel, with conduction velocity being threefold more rapid longitudinal than transverse to fiber orientation. Barrier length and location is also identical to that in Figure 6, bottom panel. The 0.5-mm density isochronal activation map in Figure 8, top panel, shows the minor disturbances in activation pattern that were detected in the infinite density activation map in Figure 6, bottom panel. In contrast, the 2-mm mapping density simulation shown in Figure 8, bottom panel, shows little if any disturbance of activation distal to the barrier. Thus, for a barrier of given dimensions, location, and orientation, increasing mapping density increases the ability to identify the barrier. Nonetheless, even with the infinite resolution shown in Figure 6, bottom panel, only the activation of small areas of tissue immediately distal to the barrier is affected by anatomic obstacle.
et al\textsuperscript{13} have demonstrated and we have confirmed in epicardial tissues in our laboratory that this is not so.\textsuperscript{14} We have thus chosen to use a simple elliptical model of impulse spread in anisotropic tissue and demonstrated such an isochronal activation pattern.

**Role of Anatomic Barriers in Cardiac Tissue**

The simplest model of reentry in cardiac tissue initially described by Mines\textsuperscript{1} involves a wavefront circulating around an anatomically defined circuit. By definition, at least a partially excitable gap is present in this model. A variety of other models of reentry in cardiac tissue involves wavefronts circulating around an anatomic barrier with or without other complicating factors.\textsuperscript{23} Only in the leading circle model of reentry described by Allesie et al\textsuperscript{24} are anatomic barriers unimportant. In addition to defining a pathway for reentrant arrhythmias and preventing their termination by short circuiting, anatomic barriers may have another role in the facilitation of the development of a reentrant arrhythmia. The critical factor in the maintenance of reentry around a fixed anatomic barrier is a sufficient conduction time around the "slowly conducting pathway" to allow tissue to recover when the impulse returns around the circuit. It is not a specific conduction velocity but an adequate conduction time relative to tissue refractoriness that allows a circuit to be completed.\textsuperscript{25} Increasing pathway length through the insertion of an anatomic barrier without altering membrane properties could help produce an adequate increase of conduction of time to allow the maintenance of reentry. The presence of a fixed anatomic obstacle in one limb of the reentrant circuit is thus an alternative explanation for the "slow conduction" that may be observed in addition to the more classic explanations related to the magnitude and type of inward current, excitability, and cell-to-cell coupling.

**Visibility' of an Anatomic Barrier**

To determine the effect of an anatomic barrier, conduction times after the introduction of the anatomic barrier were compared in a geometric model and experimental condition with those without the barrier. We found that the perturbation of conduction times and conduction patterns and the slowing of conduction produced by an anatomic barrier of fixed size or the "visibility" of the anatomic barrier was related to several factors. The angle between the propagating wavefront and the orientation of a regular anatomic barrier, the length of the barrier, and mapping density were all important factors.

As might be predicted, when impulses were propagating parallel to a long, thin, anatomic barrier, little slowing of conduction or perturbation of isochronal activation patterns was observed. This result was confirmed by our modeling procedure. Although this result was not surprising, it has probably been underemphasized that fixed anatomic barriers may be unappreciated depending on the direction of impulse propagation.

We hypothesized based on qualitative principles and our geometric model that the angle between fiber orientation and an anatomic barrier would have a crucial influence in determining the importance of the anatomic barrier in affecting conduction. For example, consider conduction initially proceeding slowly transverse to fiber orientation. During such propagation, the introduction of a limited perpendicular anatomic barrier would cause conduction to proceed more longitudinal to fiber orientation and return in a similar direction around the anatomic barrier. This barrier location was predicted and experimentally demonstrated to cause relatively little increase in conduction times or major perturbation of isochronal activation times relative to the barrier free situation (Figure 9, bottom panel). In contrast, propagation longitudinal to fiber orientation that initially is occurring rapidly could be markedly slowed in highly anisotropic tissue by the introduction of a perpendicular barrier. Isochrones indicated propagation occurred directly toward the anatomic barrier at which time it suddenly stopped except around the edges of the barrier at which sites angular propagation around the barrier was noted. Propagation on the distal side of the barrier appeared as if it were generated from two point sources at each end of the barrier producing elliptical isochrones on the distal side of the barrier from each of these points (Figure 11). Such propagation patterns were predicted from our model.

In addition to the orientation of a barrier relative to myocardial fibers, barrier length and mapping density were also important in determining the degree to which the barrier could be observed disturbing conduction. Although a 6-mm barrier oriented parallel to fiber orientation produced small disturbances in conduction relative to a transverse barrier when barrier length was increased from 6 to 18 mm, it interrupted

**TABLE 1. Control Conduction Characteristics of Tissues**

<table>
<thead>
<tr>
<th>Tissue</th>
<th>( CV_L ) (M/sec)</th>
<th>( CV_T ) (M/sec)</th>
<th>( CV_{L/T} )</th>
<th>Cut angle* (°)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.56</td>
<td>0.23</td>
<td>2.44</td>
<td>90°</td>
</tr>
<tr>
<td>2</td>
<td>0.71</td>
<td>0.22</td>
<td>3.23</td>
<td>90°</td>
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\( CV_L \), longitudinal conduction velocity; \( CV_T \), transverse conduction velocity.  
*Angle between cut and fiber orientation.
conduction patterns, and its presence could be detected even with a 2-mm mapping density. In addition, although the 6-mm barrier did not disturb conduction in a major way, its presence could be detected with a mapping density of 0.5 mm. Although mapping density and barrier length affect barrier visibility and the degree of conduction delay produced, for any given barrier length and mapping density, barriers transverse to fiber orientation were far more easily identified than longitudinal barriers.

**FIGURE 9.** Typical isochronal activation maps during propagation over a large distance longitudinal (top panel) and transverse (bottom panel) to fiber orientation obtained by pacing from two different sites (Figure 2) in typical tissue. In the top panel, the pacing site at the left midportion of the tissue is indicated by the 3-msec activation time. In the bottom panel, pacing was begun above the site indicated by 0 msec. Thick arrow indicates the direction of fiber orientation. Computer-generated isochronal maps demonstrate acute angles along the line of propagation longitudinal to fiber orientation, which are artifacts of the extrapolation process. Note that aside from these acute angles, there is a generally elliptical nature of impulse spread parallel to fiber orientation. Observe also that conduction is relatively uniform throughout the tissue.
Validation of Model

Several assumptions of our model were borne out by the experimental results. The elliptical pattern of impulse spread in uniformly anisotropic tissue was grossly confirmed by the patterns of activation as shown in Figure 9, top panel. The isochrones remained elliptical except for an area of disruption during propagation longitudinal to fiber orientation (Figure 11). Distal to the area of block, impulses grossly proceeded as if two ellipses were emanating from the edges of the block. Apparent barrier width suggested by the isochronal activation map was small. In addition to qualitatively relating the simple geometric model of elliptical impulse spread to the patterns of activation that we observed, there was an excellent quantitative agreement between the predicted and actual conduction times measured before and after the creation of a cut between pacing and recording sites ($R^2=0.89$, Table 3). Thus, over a range of different cut angles, pacing and recording sites, and barrier lengths, there was good agreement between the model and measured experimental results.

The concordance in results between the computer model and our findings indicates that the model that we developed describing perturbations introduced by a localized area of fixed anatomic barrier in anisotropic tissue was borne out in this simple model of canine epicardium.

Functional Block Produced by Limited Barriers

Spach et al.\(^{13}\) have previously shown that in anisotropic tissue, premature impulses are more likely to block longitudinal rather than transverse to fiber orientation. By changing the direction of propagation relative to fiber orientation, the introduction of an anatomic barrier could also affect the development of unidirectional block and the contralateral limb of a reentrant circuit. One would expect that if propagation were caused by the anatomic barrier to occur more parallel to fiber orientation that a more closely coupled premature beat would be more likely to block. We performed only a limited number of experiments in which propagation block was placed either parallel or perpendicular to fiber orientation and found no evidence of differential block. In such situations, impulses are proceeding both on the proximal and distal side of the block of approximately 45° to fiber orientation, and we would not have expected to find preferential block on one or the other side of the barrier. On the other hand, if a barrier were placed at 45° to fiber orientation depending on which side the barrier is approached, differential block might be expected to develop.

Application of Model to Reentry In Vivo

Conduction times through one limb of a possible reentrant circuit in anisotropic tissue while being initially dependent on fiber orientation could be increased by varying degrees by an anatomic barrier, depending on the initial angle of fiber orientation (Figure 13). Based on our experimental and modeling results, if fiber orientation through one of these limbs was perpendicular to the direction of propagation, the introduction of a limited additional anatomic barrier would have little effect on conduction times. In contrast, if propagation was initially proceeding through a long, thin area of parallel fibers, the introduction of an anatomic barrier could have major effects on conduction time and poten-
FIGURE 10. Computer simulation and actual recorded isochronal activation map during propagation parallel to a longitudinal barrier. Top panel: Computer simulation of a tissue with conduction velocity of 0.6 m/sec longitudinally to fiber orientation and 0.2 mm/sec transverse to fiber orientation is shown. The resolution of this map is close to infinite, and a 6×1-mm barrier is located parallel to fiber orientation parallel to the angle of impulse conduction. Only small deviations immediately distal to the barrier in the isochronal activation pattern are evident, even in this high resolution map. Bottom panel: Typical isochronal activation map obtained during propagation parallel to fiber orientation is shown. Thick arrow indicates direction of myocardial fibers; thin rectangle, the location of the anatomic barrier; activation time 3 msec, the pacing site. Note that like in the computer simulation, there is little disturbance in the isochronal activation pattern caused by the cut.

Isochrones at 5

Visually allow the perpetuation of a reentrant circuit by creating further conduction slowing (see Figure 13 for details).

A long, thin cut in a two-dimensional layer of anisotropic tissue in vitro may be an oversimplification of some relevant clinical or experimental situations involving reentrant arrhythmias. However, some physiological situations may involve two-dimensional conduction, and the principles involved and the geometric model will be applicable
to more complex situations. For example, atrial tissue is highly anisotropic with the ratio of longitudinal to transverse propagation velocities of up to 10:1. In addition, Spach et al have demonstrated that this anisotropy in the propensity of propagation longitudinal to fiber orientation to develop unidirectional block can provide appropriate substrates for reentry in atrial sheets. Atrial tissue is generally thin with uniform fiber orientation, and the surfaces of both atria are frequently interrupted by fixed

**Figure 11.** Isochronal activation map showing the effect of propagation across a barrier ($\Omega=90^\circ$) when propagation is initially proceeding parallel to fiber orientation. When propagation is initially proceeding parallel to fiber orientation, elliptical isochrones are present on the proximal side of the block as shown in Figure 9. As expected, the computer extrapolated closely spaced isochrones indicating either slow conduction or block at the area of the cut. Propagation proceeds uniformly around the area of cut perpendicular to the isochrones and resumes with elliptical isochrones appearing to emanate from both ends of the block (activation times, 29 and 44 msec) to activate areas on the distal side of the block. The smooth elliptical isochrones proximal to the block, the $45^\circ$ impulse spread around the area of the block, and the resumption of elliptical spread distal to the area of the block confirmed predictions of our model.

**Figure 12.** Isochronal activation map of propagation initially proceeding transverse to fiber orientation. Despite the presence of a block perpendicular to the direction of impulse propagation, little perturbation of the general pattern of impulse spread is noted. A small degree of slowing of conduction indicated by more closely spaced isochrones may be present around the area of the cut, but the effect is minimal when compared with acute perpendicular to fibers and initial propagation longitudinal to fiber orientation. This figure qualitatively demonstrates what was quantitatively predicted from our computer model.
anatomic barriers such as blood vessels. Several models of reentry in the atria involve some of these blood vessels as fixed anatomic barriers, and others of such vessels may also serve to slow conduction in one limb of a potential reentrant circuit. The anatomic relation of atrial fibers to such barriers may have a relevance to create potential sites of slow conduction and potential reentrant circuits in atrial myocardium.

The pathology of surviving border zones of human myocardial infarction has recently been investigated in some detail. Areas of surviving fibers interspersed with areas of fibrosis similar to those demonstrated in a variety of experimental models of myocardial infarction have been found to be present. Certain surviving subendocardial regions may resemble a two-dimensional sheet. Thin fibrous septa may provide discontinuous conduction that produces slow conduction and fractionated electrograms in surviving myocardial infarction as indicated above; however, thick areas of fibrosis may

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a₁, distance from pacing electrode to barrier (mm); a₂, distance from barrier to recording electrode (mm).

FIGURE 13. Schematic diagram showing how the angle between cardiac fibers and an anatomic barrier can have major effects on the ability of this anatomic barrier to participate in an idealized reentrant circuit. A: Reentrant circuit superimposed on anisotropic tissue is shown. Fibers are oriented directly vertically in this figure. In the right-hand limb of the reentrant circuit, an area of unidirectional block indicated by the light shading is present, and elliptical patterns of isochronal impulse spread similar to those we and others have previously demonstrated are shown beginning at the entrance to this idealized reentrant circuit. As impulses proceed around the reentrant circuit, their relation of impulse direction spread to fiber orientation changes, and this accounts for the difference in the spacing between isochrones at various portions of the reentrant circuit. For the purposes of this example, we have assumed that the area of unidirectional block has a functional refractory period of 180 msec. Because the time from initial penetration of the area of the unidirectional block until impulses circulate around the other pathway of the reentrant circuit is less than the functional refractory period (150 vs. 180 msec), a reentrant impulse is unable to propagate in the presence of only a fixed circular anatomic barrier in the center of the circuit. B: The addition of a long thin tongue to the central barrier is shown. The barrier is present perpendicular to fiber orientation in an area where impulses are propagating longitudinal to fiber orientation. As we have shown in our computer model and validated experimentally, impulses require a longer time to propagate around the barrier because they are beginning to proceed transverse to fiber orientation and there is effective "slow conduction" as impulses proceed around the left hand portion of the idealized reentrant circuit. The conduction time around the left-hand limb of the circuit is now more (200 vs. 180 msec) than the functional refractory period of the area of unidirectional block and allows a reentrant impulse to occur. C: An anatomic barrier tongue is extended parallel to fiber orientation. Again, as we have shown in our computer model and validated experimentally, little increase in conduction time is produced by this anatomic barrier located in a region where propagation is already occurring transverse to fiber orientation, and thus, only a minimal increase in conduction time is produced. Conduction time around the left-hand portion of the circuit is still less than the functional refractory period of the area of unidirectional block, and reentry is not possible.
provide fixed anatomic barriers around which impulses must spread. The anatomic arrangement of remaining fibers may be somewhat preserved, at least in experimental models, and thus the relation of those areas of fibrosis to fiber orientation may be extremely important as well in defining reentrant circuits in chronic myocardial infarction tissue.

The concepts derived from this computer model in simple anisotropic tissue may prove useful in analyzing more complex and nonuniform areas of conduction present in reentrant circuits in which the relation of conduction velocity to fiber orientation is preserved.

Limitations

The objective of our study was to define the fundamental mechanisms determining conduction patterns in anisotropic myocardium during interaction with an anatomic barrier with an elemental mathematical model and in vitro preparation. To facilitate the analyses, certain simplifying assumptions and experimental confines were required. Thus, the study was confined to a two-dimensional system that has some direct clinical relevance (see above) but also allows for verification of the model’s predictions in vitro. Thus, generalization of the principles developed will require additional adjustments.

The importance of late activation of an area distal to a fixed anatomic barrier will vary depending on details of propagation and the anatomy of a given situation. For example, if a uniform wavefront of large width is proceeding through an area of tissue, a relatively limited anatomic barrier may produce localized delay of activation distal to the area of block but not delay activation of areas far away from the block. In addition, our finding that barriers parallel to the direction of impulse propagation lack “visibility” is strictly true only for delays in conduction time. If such barriers were long enough and situated in an appropriate arrangement, they could provide the longitudinal dissociation necessary to create two pathways for a reentrant circuit.

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Key Words • anisotropy • arrhythmias • conduction velocity • anatomic barriers
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