Slow Conduction in the Infarcted Human Heart

‘Zigzag’ Course of Activation

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Background. Ventricular tachycardias occurring in the chronic phase of myocardial infarction are caused by reentry. Areas of slow conduction, facilitating reentry, are often found in the infarcted zone. The purpose of this study was to elucidate the mechanism of slow conduction in the chronic infarcted human heart.

Methods and Results. Spread of activation was studied in infarcted papillary muscles from hearts of patients who underwent heart transplantation because of infarction. Recordings were carried out on 10 papillary muscles that were superfused in a tissue bath. High-resolution mapping was performed in areas revealing slow conduction. Activation delay between sites perpendicular to the fiber direction and 1.4 mm apart could be as long as 45 milliseconds. Analysis of activation times revealed that activation spread in tracts parallel to the fiber direction. Conduction velocity in the tracts was between 0.6 and 1 m/s. Although tracts were separated from each other over distances up to 8 mm, they often connected with each other at one or more sites, forming a complex network of connected tracts. In this network, wave fronts could travel perpendicular to the fiber direction. Separation of tracts was due to collagenous septa. At sites where tracts were interconnected, the collagenous barriers were interrupted.

Conclusions. Slow conduction perpendicular to the fiber direction in infarcted myocardial tissue is caused by a “zigzag” course of activation at high speed. Activation proceeds along pathways lengthened by branching and merging bundles of surviving myocytes ensheathed by collagenous septa. (Circulation. 1993;88:915-926.)

Key Words • tachycardia • reentry • septa

Clinical as well as experimental data provide convincing evidence for reentry as the underlying mechanism of postinfarction ventricular tachycardia in humans. Zones of slow conduction have been demonstrated in the infarcted human heart. Slow conduction facilitates reentry because it generates enough time for the tissue in the circuit to recover its excitability, allowing the excitation wave front to reenter.

In uniformly anisotropic cardiac tissue, the resistance to current flow is higher in the direction perpendicular to fiber orientation and therefore conduction velocity is slow in contrast to that parallel to fiber direction. In infarcted myocardium, fibrosis causes an increase in the distance between fibers as the infarct heals. The resulting reduction of the number of gap junctions, which occurs predominantly in a side-to-side apposition, enhances axial resistivity in the transverse direction and further slows conduction. However, if proliferation of fibrous tissue results in a complete separation of bundles over long distances, circuitous conduction through the bundles via interconnections at distant sites can occur.

To investigate the hypothesis of slow conduction via circuitous routes in infarcted myocardium, we studied conduction in and histology of infarcted human papillary muscles. The infarcted papillary muscle was chosen because bundles of viable myocardial cells that survive in the subendocardial rim remain parallel in orientation. In infarcted myocardium, the parallel orientation of the surviving fibers often is not preserved and the surviving fibers appear to course in different directions. Methods

Ten papillary muscles were resected from the left ventricle of seven patients. Preparations were excised from the hearts of patients who underwent heart transplantation because of extensive infarction. In three patients the location of the infarct was anteroseptal, and in one patient the location was anterolateral. The infarct was restricted to the inferior wall in two patients and to the inferoposterior in one patient. The ejection fraction of the hearts, measured before transplantation, ranged from 10 to 19.

Before removal, the hearts were perfused with a cardioplegic solution. After removal, they were immersed in a modified Tyrode's solution of 0°C. The solution contained (in mmol/L): Na+ 156.5, K+ 4.7, Ca2+ 1.5, H2PO4− 0.5, Cl− 137, HCO3− 28, and glucose 20. The hearts were transported to the experimental laboratory in the cold Tyrode's solution gassed with 95% O2 and 5% CO2.
In Vitro Recordings

The papillary muscles were pinned to the base of a tissue bath and superfused with oxygenated Tyrode's solution at 37°C. Preparations were allowed to recover in the tissue bath for at least 45 minutes, until spread of activation during basic stimulation was stable. They were stimulated (at twice threshold) at a basic cycle length of 600 milliseconds through a bipolar electrode. The poles of this electrode—500 μm apart—were the cut ends of two isolated silver wires 200 μm in diameter.

Recording Technique

High-resolution mapping of the electrical activity was carried out with a compound electrode comprising 8 modified bipolar electrodes arranged in a line. Each electrode was composed of two silver wires with a diameter of 100 μm that were insulated except at the tips, which were electrolytically coated with a silver chloride layer. One of the leads made contact with the tissue and the other was clipped so that its position was about 2 mm above the surface of the tissue. By recording signals in this way, 50-Hz interference was reduced while unipolar characteristics were preserved. The peak-to-peak input noise of the amplifiers was typically 10 μV.

Signals from each bipolar electrode were fed into AC differential amplifiers with gain settings of 2000. Signals were band pass filtered between 0.1 Hz and 2 kHz (3 dB points).

Amplified and filtered signals were recorded with an 8-channel data acquisition system. The system included a 12-bit AD converter that sampled data with a frequency of 4 kHz per channel. Data were stored on a 100-megabyte hard disk.

The compound electrode was mounted in a micromanipulator and positioned with electrodes 1 to 8 perpendicular to the fiber direction (Fig 1). The electrode was moved in steps of 200 μm along the papillary muscle over a distance ranging from 3.4 to 10.2 mm. Recordings were made at every position of the compound electrode, yielding grids that consisted of 144 to 416 recording sites. All grids had 8 rows, determined by the 8 terminals of the compound electrode, and 18 to 52 columns, determined by the number of positions of the compound electrode along the papillary muscle. Recording sites were named according to their column and row numbers.

A solitary extracellular electrode, positioned a few millimeters from the site of stimulation, was used to monitor constancy of the activation. Only those recordings with identical reference signals were analyzed.

After the electrophysiological measurements, fine needles were used to mark the tissue at the site of stimulation and at the first and last positions of the compound electrode.

Signal Analysis

Virtually all extracellular electrograms revealed multiple deflections (fractionated electrograms). Individual signals thus could have more than one activation time. The amplitude, the maximally negative derivative, and the activation time of each deflection in the electrograms were determined. Because our recording mode was unipolar, the instant(s) of steepest negative deflection between a maximum and the ensuing minimum were used as the activation time. Deflections with an amplitude >2.5 times the peak-to-peak noise level were included in the analysis.

Activation times were determined in an interactive way. Starting at the first electrogram, a computer algorithm determined the activation times of all deflections in a signal. Then, the signal and the computer-selected activation times were displayed on a monitor. Computer-generated activation times were excluded when they were obviously unauthentic, and missing activation times could be supplied with a mouse-driven cursor. The new value thus added was subsequently replaced by that of the nearest maximally negative deflection, which was calculated by a computer algorithm. This procedure was followed because the exact time of steepest negative deflection is difficult to indicate with a mouse. The amplitude and maximally negative derivative of the deflection corresponding to the computed activation time were calculated and stored. This procedure was used for all signals.

Construction of Tracts of Activation

Activation times of signals recorded from every site in a row (parallel to the long axis of the papillary muscle) were used to construct a map depicting spread of activation along that row. Electrode positions (column numbers) were plotted on the horizontal axis; activation time(s) were plotted along the vertical axis (Fig 2a). Such maps were constructed for all eight rows. If the activation times of two adjacent points in a map differed less than 1 millisecond, it was assumed that activation progressed from one point to the other, and the points were connected. This yielded lines (activation lines) indicating spread of activation along a row. Activation moving to the base of the papillary muscle resulted in
ascending lines; activation moving toward the tip resulted in descending lines. The slope of the lines reflected the conduction velocity.

Deflections in the signals resulted either from activation waves running through bundles directly beneath the recording electrode or from activity in more distant bundles. Because bundles were oriented parallel to the long axis of the papillary muscle, remote components were expected to arise mainly in signals recorded at positions along a column, ie, perpendicular to the fiber direction. The remote components of the eight signals in a column could be readily recognized because they yielded virtually identical activation times. These components were identified by selecting deflections with activation times within ±0.25 milliseconds of each other. The deflection with the greatest negative derivative was interpreted as being caused by local activity. Concurrent deflections in the other traces were rejected because they were considered to be the result of remote activity.

The results of this procedure are illustrated in Fig 3. All deflections in signals 2 to 8, occurring in concert with the vertical line, had the same activation time and were preselected. The deflection of signal 5, however, had the greatest negative derivative and was selected as the local deflection (dot marked as 20.0 milliseconds). All other deflections along the line were regarded as being remote and therefore were excluded. Note that the amplitude of the deflections decreases for signals recorded increasingly farther away from row 5.

After eliminating the remote components, the individual maps, derived from the signals in each of the eight rows, were combined in a single map. Points in this compound map were indicated by the row number of the recording electrode from which the activation originated (Fig 2b). Activation lines were constructed by
initial activation time and were connected vertically at the sites where the corresponding activation lines connected.

**Relation Between Row Numbers and Tracts**

The relation between row numbers and tracts is indicated by vertical line segments at the left of Figs 2, 4, and 5. The numbers next to the line segments indicate the row numbers that correspond to the tract(s) located between the upper and lower end points of the segments. A line segment may enclose more than one tract, for instance, when several small bundles give rise to multiple local deflections in the signals recorded from the electrodes in one row. This is clearly illustrated in Fig 5, where all of the line segments cover several tracts.

Line segments overlap when one (or more) separated tracts with different row numbers are in line. This occurs in Fig 5 for segments 6 and 7; the tract with activation times of 14.5 to 14.0 milliseconds is derived from electrograms in row 6, whereas the tract with activation times 16.8 to 15.5 milliseconds results from signals in row 7. Overlap may also occur when tracts and rows are not exactly parallel to each other. In that case, the row number of an electrode located over a tract may change, and different parts of the tract may have different row numbers, resulting in an overlap of the line segments.

A line segment may also have more than one row number. This happens when the diameter of a bundle is wide, exceeding 0.2 mm. In that case, more than one electrode in a column is positioned over that bundle, and all signals of the electrodes located over the bundle have the same activation time. However, only the deflection of the signal that generates the greatest negative derivative is selected as being local. This deflection may originate from the signal of another electrode located over the bundle if we proceed along the row because the diameter of the bundle changes or rows and bundles are not exactly parallel. Line segments having more than one row number occur in Fig 4.

**Histological Methods**

Histological investigations were carried out on seven papillary muscles. Immediately after the experiment, the preparations were fixed with formaldehyde. Sections were taken from at least three sites: the first and last positions of the compound electrode and a site exactly in between. Sections were 5 or 10 μm thick and cut perpendicular to the long axis of the papillary muscle. Staining was performed with sirius red to discriminate connective tissue from surviving myocytes.

**Results**

**Characteristics of Extracellular Electrograms**

Electrograms were fractionated in virtually all preparations. Deflections were sometimes separated by an isoelectric interval, but in the majority of electrograms the next deflection started before the preceding one had returned to the baseline. The maximal number of deflections in the signals ranged from 3 to 14. Duration of the fractionated electrograms ranged from 2 to 36.5 milliseconds. The maximum delay between deflections in signals recorded from the extreme terminals of the compound electrode (distance, 1.4 mm) was between 6 and 45 milliseconds (mean, 15 milliseconds).
Fig 4. Tracts A through D of the papillary muscle from Fig 6. Tracts A and B are electrically isolated over a distance of 5.4 mm but merge at a site along column 29. Tracts C and D originate from tract B at sites located along column 28 and 24, respectively. The marker indicates the site of stimulation. Numbers in the tracts are activation times measured with respect to the stimulus. Arrows show spread of activation in the tracts. Numbers next to the vertical line segments at the left are the row numbers of the signals from which the local activation times in the tracts were determined. The activation times in tracts C and D are derived from signals recorded at electrodes in rows 6 and 7, respectively, whereas the activation times of tract B originate from signals in rows 2 and 5. Activation times in tract A originate from signals recorded from electrodes in rows 2 to 5.

Characteristics of Tracts of Activation

In all papillary muscles, tracts were parallel to the fiber direction; there were no tracts running in a vertical direction. Activation proceeded toward the tip of the papillary muscle in part of the tracts and toward the base in the others. This was true irrespective of the site of stimulation. The conduction velocity in the tracts was uniform. The number of isolated tracts was found to be between 2 and 35 (mean, 12), depending on the fractionation of the signals. Most tracts were interconnected with neighboring tracts at one or more sites. Tracts without any connection to neighboring tracts were found sporadically.

Preparations With Mildly Fractionated Signals (Group 1)

Spread of activation within the tracts. In 3 preparations, the recorded electrograms possessed fewer than 5 deflections (group 1). The number of tracts in this group was between 2 and 4 (tract length >0.4 mm), and the tracts were separated from each other over distances up to 5.2 mm before interconnecting with adjacent tracts.

A schematic drawing of one of these papillary muscles is shown in Fig 6a. The preparation was stimulated at the site marked, near the tip of the papillary muscle, and registrations were made between the site of stimulation and the base of the papillary muscle (distance, 5.8 mm). Figure 6c depicts the 8 signals recorded with the compound electrode positioned at column 1 (panel b), close to the site of stimulation. Dots located along column 1 indicate the recording sites. Each tracing in panel c consists of 2 deflections separated by an isoelectric interval. The amplitude of the first component increases progressively from signal 1 to 8, whereas the amplitude of the second component decreases. This observation suggests that the signals originate from 2 wave fronts running in tracts that are separated by an inexcitable barrier. Activation running in one of the tracts gives rise to remote components in signals recorded at sites located over the other tract.

Fig 6d depicts 7 tracings recorded from sites located along row 6 (panel b). Dots along row 6 indicate the electrode positions. Tracings exhibit 1 to 3 deflections. Activation of the first component is earliest in tracing 24 and gradually becomes later for signals recorded from sites closer to the base (tracing 30). The first deflections are generated by an activation front running from the site of stimulation toward the base of the papillary muscle. A second deflection is present in signals 24 to 29. This deflection is earliest in signal 29 and gradually becomes later in signals recorded farther away from the base. These deflections are generated by a second activation front that moves from the site where signal 29 was recorded toward the tip of the papillary muscle. The point of inflection in signal 29 (lower arrow) indicates that this wave front emerges from the first wave front at the recording site of signal 29. The second deflection in tracing 26 also has a point of inflection (upper arrow), indicating the genesis of a third component. A third component is also present in the signals 27, 28, and 29, and their sequence indicates that a third wave front emerges from the second wave front at the site where signal 26 was recorded. The third front again moves from tip to base.

Histological examination. Histological investigations were carried out on 3 preparations from group 1. Sections revealed that more than 60% of the total tissue area consisted of surviving myocardium. Zones of collagen were found throughout the intramural area. Major vessels were often surrounded by dense areas of collagen. Collagenous septa divided the surviving subendocardial rim in several electrically isolated zones. Septa that traversed the subendocardial rim often merged intramurally with compact zones of fibrous tissue. The thickness of the collagenous septa that traversed the subendocardial rim varied markedly but could reach values of 100 μm.
FIG 5. Facing page: Tracts along which activation proceeded in the papillary muscle of Fig 3. The papillary muscle was stimulated at the lower left corner ( , stimulation marker). Numbers in the tracts indicate activation times measured with respect to the stimulus. Vertical line segments at the left indicate the relation between rows and tracts. All tracts located between the upper and lower end points of a line segment are derived from signals recorded at electrode positions along the row indicated by the number next to the segment. For a discussion about the overlap of line segments, see "Methods." A and B mark the two tracts having the largest intertract distance, yet they are joined via interconnected tracts. See text for discussion.

Fig 7 shows the histological appearance of the papillary muscle from Fig 6. Dark areas indicate fibrous tissue; light areas indicate surviving myocytes. Panel a is the section made at column 15, halfway between the tip and the base of the papillary muscle, and illustrates that the subendocardial zone of myocardial tissue is divided by collagenous septa into several areas. Panel b is an enlargement of the area marked in panel a, showing a broad strand of fibrous tissue (arrow) penetrating into the subendocardial layer and separating it into two zones (A and B) corresponding with tracts A and B in Fig 4. Panel c shows that the fibrous strand has decreased in width and length and is interrupted at a point 220 μm beneath the endocardium. By way of the 300- to 600-μm subendocardial rim of tissue that survives dur-

FIG 6. Panel a: Schematic drawing of a papillary muscle in which recordings revealed minor fractionation. The preparation was stimulated near the tip (marked site). Recordings were made with the compound electrode from 30 positions (rectangle). Panel b: Recording area. Solid circles indicate the recording sites of the tracings in panels c and d. Panel c: Recordings made with the compound electrode positioned along column 30. All tracings comprise two deflections separated by an isoelectric interval, indicating that activation runs in two electrically isolated tracts. Panel d: Recordings made at 7 sites located along row 6 (stim indicates stimulation artifact). See text for discussion.
FIG 7. Photomicrographs of sections of the papillary muscle of Fig 6 made perpendicular to the long axis. The section of panel a is taken halfway between the tip and the base (column 15) and shows that strands of fibrous tissue (dark areas) separate the viable subendocardial rim into several isolated zones. Panel b is an enlargement of the area marked in panel a and shows the broad strand of fibrous tissue (arrow) that separates tracts A and B in Fig 4. Panel c shows the section near the base of the papillary muscle (column 29 in Fig 6) and illustrates that the fibrous strand (arrow) has decreased in width and length. At this site, tracts A and B merge, and activation can cross the barrier. Panel d is the section made 300 μm away from that of panel c toward the base of the papillary muscle and illustrates reappearance of the fibrous strand (arrow), again separating the subendocardium into two isolated zones.

**Preparations With Highly Fractionated Signals (Group 2)**

In 7 preparations, fractionated signals exhibited between 5 and 14 deflections (group 2). The number of tracts in this group ranged from 7 to 35 (tract length >0.4 mm). Fig 3a is a schematic drawing of one of these papillary muscles. The preparation was stimulated from the lower left corner of the recording grid, and the compound electrode was moved toward the base over a total distance of 3.6 mm. In panel b, the 8 signals recorded at column 13 (vertical line in panel a) are depicted and illustrate extensive fractionation in all signals.

Dots in the tracings indicate local activation times. These are used, together with local activation times of recordings in other locations, to construct the tracts of Fig 5. The activation times at the dot locations in Fig 3 are given in milliseconds next to the signals. The values are listed in the same sequence as the dots and correspond to the activation times noted in the tracts in column 13 (Fig 5).

A and B mark the two tracts that have the largest intertract distance and are nevertheless joined via interconnecting tracts. The earliest activation in tract A (at column 1) occurs 10.7 milliseconds after the stimulus. The latest activation in tract B (at column 19) occurs 39 milliseconds later. Activation delay between earliest activation in tracts A (10.7 milliseconds) and B (47.2 milliseconds) that is perpendicular to the fiber direction is 36.5 milliseconds. This delay takes place over a distance of 1.2 mm, which is the distance between row 1 and 7.

Several tracts uninterruptedly traversed the entire distance between the first and last recording sites parallel to the fiber direction. Between A and B, all except two tracts were connected with a neighboring tract at one or more sites. Some tracts that interconnected with adjacent tracts at one end did not do so at the other end.

Activity in the tracts ran either toward the site of stimulation or away from it. Activation running toward
the site of stimulation was observed in about 30% of the total length of the tracts (Fig 8a).

Activity starting in tract A at column 1 could reach tract B at column 3 via the tortuous but continuous path indicated by the bold line in Fig 8b. Delay between adjacent electrode positions along this path nowhere exceeded 1.0 millisecond. The length of the path is 25.2 mm; in contrast, the shortest distance between tracts A and B is only 1.2 mm. Thus, the separation of bundles by collagenous septa was responsible for increasing the activation route by a factor of 18.

**Histological examination.** Histological investigations were carried out on four papillary muscles from group 2 with highly fractionated signals. In all preparations of this group, myocardial tissue comprised less than 30% of the area of the section. In three preparations, a core of dense connective tissue was surrounded by a thin subendocardial rim of surviving muscle fibers. Within the rim, clusters of myocytes were surrounded by fibrous septa. The number of myocytes within a cluster varied markedly. One preparation from group 2 contained large areas of fatty tissue that divided the surviving rim into several isolated zones.

A section of the papillary muscle from Fig 3 is illustrated in Fig 9. Panel a is a section made at column 1 near the site of stimulation and illustrates the scarcity of surviving myocardium that mainly occupies the thin rim. Electrode positions of column 1 were located along the endocardium within the marked area. Panel b is an enlargement of the area marked in panel a and shows the surviving rim of myocardial bundles sheathed by collagenous septa.

**Conduction Velocity**

For every preparation, four conduction velocities were determined.

**Conduction velocity perpendicular to fiber direction (V1).** The activation delay was determined between the two recording sites in the same column for which the longest continuous path of activation could be con-
In the Table, the calculated conduction velocities are shown. The Table shows that conduction velocity parallel to the fiber direction (V2) is fast compared with the velocity perpendicular to the fiber direction (V1). There was no significant difference between the velocity for activation running toward or away from the site of stimulation. The conduction velocity within the tortuous routes (V3) was slightly lower than the velocity parallel to fiber direction (V2). The conduction velocity at sites where tracts interconnected (V4) was lower than that parallel to the fiber direction (V2).

These observations show that the main contribution to activation delay perpendicular to fiber orientation is the result of the increasing length of the route along which activation has to travel. The velocity at the sites of interconnection suggests that an additional although minor activation delay occurs at these sites.

**Discussion**

**Conditions for Reentry**

Both clinical and experimental data most strongly support the concept of reentry as the underlying mechanism of ventricular tachycardias in the healed phase of myocardial infarction.1-7 Circus movement in an anatomically defined pathway and circus movement in the absence of an anatomic obstacle have been observed in infarcted human hearts. To initiate reentrant activation, unidirectional conduction block must occur in some part of the circuit. For maintaining reentrant activation, the circuit length must be long enough to enable tissue in each part of the circuit to restore its excitability sufficiently to respond to the next impulse. This means that at least one wavelength (the product of conduction velocity and refractory period) must fit within the circuit.1 The dimensions of the human heart are sufficiently large to meet this requirement even when the conduction velocity and refractory period are normal; a conduction velocity of 0.3 m/s and a refractory period of 200 milliseconds require a circuit length of 6 cm. Inexcitable regions caused by infarction in the human heart may have a circumference of that length.3

Although slow conduction is not a prerequisite per se for reentry in the infarcted human heart, it reduces the minimal length of reentrant circuits and therefore enhances the likelihood that a circuit can be contained within an area of myocardial scar. Activation sequence mapping has demonstrated areas of slow conduction during ventricular tachycardia in canine models and human hearts.8-11

**Abnormal membrane characteristics.** The propagation velocity in ventricular myocardium is determined by the active membrane processes as well as the passive electrical properties of the tissues. Reduction of the amplitude and upstroke velocity of the action potential, which occurs in acute ischemia, may reduce the conduction velocity,17-20 thereby leading to ventricular tachycardia and fibrillation.21,22

Intracellular recordings from surviving myocytes in infarcted human myocardium have yielded normal as well as abnormal action potentials.3,6,16,23-29 The proportion of cells with relatively normal action potential upstrokes increases as the infarct ages.6,18,24,25 In addition, we have observed that the refractory period of surviving cells with abnormal action potentials were invariably long. This makes them unlikely candidates
Conduction Velocities in the Papillary Muscles in Meters per Second

<table>
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<th>Papillary muscle</th>
<th>V1</th>
<th>V2</th>
<th>V3</th>
<th>V4</th>
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<td>0.83</td>
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</tbody>
</table>

Mean value 0.07 0.79 0.68 0.49

V1 indicates conduction velocity perpendicular to fiber direction; V2, conduction velocity parallel to fiber direction; V3, conduction velocity within the tortuous route; and V4, conduction velocity at the bifurcation of tracts.

for generating rapid rhythms. Therefore, abnormal membrane characteristics are improbable as the cause of slow conduction in healed infarcts.

Coupling resistance between cells. Because conduction depends on local current circuits, its velocity is determined by the coupling resistance between cells. Conduction velocity decreases with increasing coupling resistance.12,27,28 Progressive interstitial fibrosis during aging in atrial tissue results in loss of electrical coupling.29 Similar proliferation of fibrotic tissue in healed infarctions has been suggested as the cause for changes in side-to-side cell connections.30 Therefore, activation delays in our preparations could have been caused by an increase of the coupling resistance between the cells. Our recordings were analyzed under the assumption that an activation delay >1 millisecond between two adjacent recording sites was not caused by conduction between the sites. An activation delay >1 millisecond between two sites in adjacent but separate bundles caused by slow impulse conduction across high-resistance barriers would therefore not show up in our maps as a connection between the tracts. However, it would betray itself in the second bundle, where activation could be expected to start at an unconnected site and, at least occasionally, to spread from there in both directions along the tract. The latter was never observed.

Several investigators have shown that in compromised areas, the connections of cells in side-to-side apposition were reduced, whereas end-to-end connections were virtually unaffected.13,14 This is compatible with our finding that conduction velocity parallel to the fiber direction was normal.

Disruption of side-to-side connections may increase path length and the number of intercellular junctions traversed by a wave front moving in the transverse direction. In papillary muscles, proliferation of fibrous tissue resulted in longitudinally oriented shells of connective tissue, insulating adjacent groups of myocardial fibers. Side-to-side electrical coupling among these fibers was absent over distances of several millimeters, so that interconnections farther away transferred the activation to neighboring bundles.

At the sites of interconnection, activation was slightly delayed. The reason for this may be a reduced number of gap junctions at these sites, resulting in slow conduction transmission across high-resistance junctions or barriers.12,27,31,32

Activation delay has also been observed in normal myocardium at sites where an activation front proceeds from a small strand into a larger structure.12,27 In these cases, activation delay occurred because of the difference between the current supply of the small source and the current requirement of the large sink, leading to activation delay and providing an alternative explanation of slow conduction at sites where bundles interconnect.

Infarct Structure

Investigations carried out in superfused epicardial preparations from infarcted canine hearts have shown that fibrosis increases with time.9 During the first weeks of infarction, the muscle fibers of the epicardial border zone were parallel, with little connective tissue separating individual bundles. In this stage, little fractionation of the electrograms was observed. After 8 weeks, the muscle bundles were widely separated and had fewer side-to-side connections, although bundles were still arranged in parallel. After several months, the muscle fibers were not only separated by large amounts of connective tissue, but they were no longer oriented in parallel in some regions. We did not observe this loss of orientation in the papillary muscles. It is likely, however, that loss of orientation of the bundles in other infarcted areas increases the complexity of the tracts and enhances activation delay.

Fractionated Activity

Fractionated electrograms are a common finding in animal models of infarction as well as in infarcted human hearts.33 In superfused epicardial preparations of infarcted dog hearts, the duration of fractionated complexes was between 10 and 70 milliseconds.34 In the infarcted human heart, durations of more than 133 milliseconds for fractionated electrograms have been documented.35 These values are not entirely compatible with our results (2- to 36.5-millisecond fractionation). The reason for this may be related to the size of the recording electrodes and the distance between poles. In the animal study, bipolar recording electrodes were used. The catheter electrodes in clinical studies usually have 10-mm distances between the poles, and the electrodes themselves have large surface areas.

Limitations of the Recording Technique

Activation spreading out with a conduction velocity of 1 m/s results in a time difference of 0.2 millisecond in signals recorded 0.2 mm apart. This is compatible with the time resolution of our recording system (sample interval, 0.25 milliseconds). The peak-to-peak noise level of our recording system was about 10 µV. Spach and Dolber29 have calculated that the signal of a recording electrode at a distance of 250 µm from a bundle with a radius of 25 µm would have an amplitude of 35 µV. Because about 300 µm of subendocardial tissue survives in superfused preparations,66 the activation in bundles with a diameter of 25 µm should be detectable. Activation in smaller bundles at distances >250 µm are undetectable, and this could explain that a number of tracts seem to end without connecting with neighboring
tracts (Fig 5). We cannot, however, rule out that such tracts indeed constitute dead-end pathways.

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