Multiplexing Studies of Effects of Rapid Atrial Pacing on the Area of Slow Conduction During Atrial Flutter in Canine Pericarditis Model

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Background. We report that rapid atrial pacing interrupts atrial flutter when the orthodromic wave front from the pacing impulse is blocked in an area of slow conduction in the reentry circuit. To characterize the area of slow conduction during atrial flutter and rapid pacing, we studied 11 episodes of induced atrial flutter, mean cycle length 157±20 msec, in eight dogs with sterile pericarditis.

Methods and Results. Atrial electrograms were recorded simultaneously from 95 pairs of right atrial electrodes during the interruption of atrial flutter by rapid atrial pacing, mean cycle length 139±21 msec. Areas of slow conduction during atrial flutter were demonstrated at one to three sites in the reentry circuit. After rapid pacing captured the reentry circuit, one area of slow conduction either disappeared (10 episodes) or the degree of slow conduction in an area of slow conduction decreased (one episode). Both changes were in association with activation of the region by a wave front from the pacing impulse that arrived from a direction different than that during the induced atrial flutter. Interruption of atrial flutter during rapid pacing occurred when the orthodromic wave front from the pacing impulse blocked in an area of slow conduction that had either newly evolved during rapid pacing (seven episodes) or that was previously present (four episodes).

Conclusions. Areas of slow conduction present during atrial flutter and rapid pacing of atrial flutter are functional and depend on both the atrial rate and the direction of the circulating wave fronts. Interruption of atrial flutter by rapid pacing results from block of the orthodromic wave front from the pacing impulse in an area of slow conduction in the reentry circuit. (Circulation 1991;83:983−994)

We previously demonstrated that atrial flutter in our canine pericarditis model results from reentry in the free wall of the right atrium.\textsuperscript{1,2} Our previous studies have also shown that this atrial flutter could be entrained and interrupted with rapid atrial pacing.\textsuperscript{3} However, those studies were performed using techniques that included sequential site atrial mapping. Our recent studies using multiplexing techniques to record electrograms simultaneously from 190 sites during the onset of induced atrial flutter\textsuperscript{4} indicated the importance of the development of areas of slow conduction in the initiation and maintenance of atrial flutter.

The present study is an extension of these previous studies. In this study, we used multiplexing techniques to examine the effects of rapid atrial pacing on the area of slow conduction to understand better why and where these areas of slow conduction occur, and what happens to them during interruption of atrial flutter. This also permitted us to test the hypothesis of the third criterion of transient entrainment,\textsuperscript{5,6} which states that during pacing at a constant rate faster than the rate of a spontaneous tachycardia, interruption of the tachycardia is associated with the demonstration of localized conduction block to a site or sites for one beat followed by activation of that site or sites by the next paced beat from a different direction and with a shorter conduction time.
Methods

Eleven episodes of induced atrial flutter were studied in eight adult mongrel dogs (weight, 18–25 kg) after creation of sterile pericarditis. All of the studies were performed in accordance with the guidelines of the Institutional Animal Care and Use Committee.

Creation of Model

Atrial flutter was induced in our canine model using our previously described techniques. Using sterile technique, each dog was submitted to a right thoracotomy at the fourth intercostal space under general anesthesia (thiamylal sodium, 3–5 mg/kg body wt i.v. supplemented with halothane). With the use of standard surgical techniques, the heart was exposed and cradled in the pericardium. Three pairs of stainless-steel wire electrodes coated with FEP polymer except for the tip (0 Flexon, Davis and Geck, Puerto Rico) were sutured on the following three epicardial atrial sites: the sulcus terminalis of the right atrium; the interatrial band, known as Bachmann’s bundle; and the posteroinferior left atrium close to the proximal portion of the coronary sinus. The interelectrode distance of each electrode pair was approximately 5 mm. These wire electrodes were brought out through the chest wall and exteriorized posteriorly in the neck near the midline. In five dogs, the electrodes were not placed in the sulcus terminalis site (for ease in subsequent placement of the electrode array for later multiplexing studies in the open-chest state). The surfaces of both atria were then generously dusted with sterile talcum powder. A single layer of gauze was then put on the right and left atrial free walls, and the pericardiectomy was closed. The chest was then closed in standard fashion. The dogs were given antibiotics and analgesics and allowed to recover.

Studies in the Conscious, Nonsedated State

Before performing studies in the open-chest state, it was necessary to make certain that the atrial flutter could be induced. Therefore, beginning on the second or third postoperative day, induction of atrial flutter was attempted in the conscious, nonsedated state using the epicardial wire electrodes placed during the initial surgery in all study dogs.

Induction of atrial flutter was attempted by pacing performed from one of the electrode sites (sulcus terminalis, Bachmann’s bundle region, or posteroinferior left atrium). A modified Medtronic 5325 programmable stimulator (Medtronic Inc., Minneapolis, Minn.) with a pulse width of 1.8 msec was used for all pacing studies. Pacing modes included introduction of one or two premature atrial beats after a train of eight paced atrial beats at cycle lengths of 400, 300, or 200 msec or rapid atrial pacing for a period of 1–10 seconds. Both pacing methods were performed using stimuli of twice diastolic threshold.

During these studies, electrocardiographic leads I, II, andIII were recorded simultaneously with bipolar electrograms from the sulcus terminalis, the Bachmann’s bundle region, and the posteroinferior left atrium. The electrocardiograms were filtered between a band pass of 0.1 and 500 Hz, and the epicardial electrograms were filtered between 30 and 500 Hz. All data were monitored on an oscilloscope and recorded on photographic paper at a speed of 100 mm/sec using a switched-beam oscilloscopic recorder (model VR-16, Electronics for Medicine, White Plains, N.Y.). The data were also recorded simultaneously on FM tape using a Honeywell 101 FM tape recorder (Honeywell Inc., Denver, Colo.) for later playback and analysis.

Multiplexing Studies in Open-Chest State

On the third or fourth postoperative day, the open-chest study was performed. The dogs were anesthetized with pentobarbital (30 mg/kg body wt i.v.) and mechanically ventilated using a Harvard respirator (Harvard Apparatus, Natick, Mass.). The body temperature of the dog was kept within the normal physiological range throughout the study by using a heating pad. The chest was opened through a median sternotomy. The heart was exposed, the epicardium was gently separated from the adherent pericardium, and the heart was then suspended in a pericardial cradle. After removing the gauze strips from both atria, the talcum powder that had become encrusted was carefully peeled off. The stainless-steel wire electrodes previously sutured onto the sulcus terminalis were removed to permit placement of the epicardial electrode array in the three dogs with electrodes at this site. A new reference bipolar electrode was sutured on the tip of the right atrial appendage in all dogs.

Placement of the electrode array. After opening the chest, the right atrial electrode array containing 190 electrodes was secured with a Velcro belt (Figure 1). The patch was constructed of a sheet of Dacron-
reinforced Silastic into which fine silver wire electrodes (diameter, 0.25 mm) were embedded and fixed at room temperature with a vulcanizing silicon rubber adhesive. The interelectrode distance was 1.5 mm, and the distance between the center of each electrode pair was 4.2 mm diagonally and 6.0 mm perpendicularly. These distances were used to calculate approximate conduction velocity of the wave front in areas of slow conduction.

**Induction of atrial flutter.** The same pacing protocol as used during the closed-chest state was used to induce atrial flutter in the open-chest state. The only difference was that because the sulcus terminalis electrode pair was removed, it was not used as one of the pacing sites. In its place, the pair of electrodes placed at the tip of the right atrial appendage was used.

After sustained atrial flutter was induced, rapid atrial pacing was initiated at a rate of 5–10 beats/min faster than the spontaneous rate, continued for as long as 10 seconds, and terminated abruptly. If atrial flutter was not interrupted, rapid atrial pacing was again initiated but with an increment in rate of 5–10 beats/min. This procedure was repeated until the atrial flutter was interrupted.

**Data acquisition.** Before, during, and after the interruption of 11 episodes of atrial flutter in eight dogs, electrograms were recorded simultaneously from 190 electrodes distributed over the right atrial free wall (Figure 2) along with electrocardiographic lead II. Data recording and processing were performed using a cardiac mapping system designed at Case Western Reserve University. Data were individually amplified, filtered between a band width of 1 and 500 Hz, sampled at 1,000 Hz, and digitized with a 12-bit analog-to-digital converter. The data were then transferred to a 68020 coprocessor with 4 Mbytes of memory via optoisolators. Data collection and processing were performed using this coprocessor, which is resident to a Sperry IT PC host system (IBM AT compatible). An SGT PEPPER (Number Nine Computer Corp., Cambridge, Mass.) graphic processor was used to display raw and processed data. Data were archived on either a floppy or a hard disk, both being resident to the host system.

**Data analysis.** Analysis of data consisted of selecting activation times and drawing isochronous maps with a minimum resolution of 1 msec. Data were filtered in software with a low cutoff frequency (high-pass filter) of 10 Hz before analysis to avoid baseline drift in the electrograms. A 600-msec analysis window was chosen from within 4 seconds of stored data. A time reference signal was arbitrarily selected from one of the 95 pairs of electrode sites and used to depict zero activation time. The stimulus artifact during atrial pacing or the electrode pair site activated at the earliest time during each spontaneous beat was chosen as a time reference for each beat. The electrograms recorded at each site during the time window were displayed on a graphics screen, and selection of activation time was done manually with a cursor.
Figure 3. Panel A: Schematics of 10-msec isochronous maps during pacing interruption of atrial flutter. Numbers in each map show activation time for that isochrone. Arrows show main direction of activation wavefront. Dashed line represents region of functional block. Upper left schematic shows atrial flutter at a cycle length of 142 msec resulting from clockwise rotation of the circulating reentry wavefront. A, B, and C indicate sites of electrode pairs in panels B, C, and D and are pairs 80, 58, and 67, respectively, in Figure 2. Upper right, lower left, and lower right schematics show isochronous maps for fifth (S5), sixth (S6), and seventh (S7) paced beats, respectively, during rapid pacing at a cycle length of 125 msec delivered from right atrial appendage. Square wave indicates right atrial appendage pacing site. Open arrow during S5 and S6 represents orthodromic activation wavefront of previous pacing impulse. Numbers in parentheses are activation times measured from previous stimulus artifact. In lower left schematic, thick black line represents block of orthodromic activation wavefront of S6 pacing impulse; this is associated with interruption of atrial flutter. S7 is first paced beat immediately after interruption of atrial flutter. (See text for discussion.) Panel B: Recording of electrocardiographic lead II simultaneous with electrograms from electrode pair sites A, B, and C, shown in panel A, during atrial flutter (cycle length, 142 msec) before initiation of rapid atrial pacing. Arrows indicate relative sequence of activation at electrode sites. Activation times were 57 msec from A to B, 39 msec from B to C, and 46 msec from C to A. (See text for discussion.) Panel C: Recording of rapid atrial pacing at a cycle length of 125 msec during same atrial flutter shown in panels A and B. S3 to S9 are respective stimulus artifacts for third through ninth stimuli. S6 (denoted by solid arrow) is same beat shown in lower left schematic in panel A. Numbers indicate activation times from B to C, from C to A, and, after interruption of atrial flutter, from B to A. Activation times between B and C were 30, 20, 14, 12, 12, and 12 msec during beats S2, S3, S4, S5, S6, S7, and S8, respectively. Activation times between C and A were 47, 60, 65, and 68 msec during beats S2, S3, S4, and S5, respectively. Activation times from B to A were 36 and 45 msec during beats S7 and S8, respectively. Block of activation wavefront occurred between electrode pairs B and C. (See text for discussion.)
The moment of activation at each site was taken as the peak of the rapid deflection in a predominant monophasic recording or as the time when the first rapid deflection crossed the baseline in a predominantly biphasic recording. The activation time at sites at which polyphasic waveforms were recorded was assigned to the major deflection (highest amplitude or fastest downstroke). If there were two discrete deflections for one atrial complex in the electrocardiogram (i.e., a so-called double potential), the activation time at these sites was assigned to the deflection with the highest amplitude or the more rapid deflection as it crossed the baseline.

Because of the differences in size of the right atrium among dogs, anatomical landmarks were identified on the grid (electrode array) by visual inspection. For each atrial beat, activation time at each site was placed on an anatomical grid representing activation at each bipolar recording site (Figure 3, and isochronous lines at 10-msec intervals were drawn manually. The center of the reentry circuit was defined by analyzing the isochronous lines. In the present study, slow conduction was defined as conduction velocity of less than 0.2 m/sec.

**Results**

We studied 11 episodes of atrial flutter (mean cycle length, 157±20 msec; range, 135–198 msec) in eight dogs with sterile pericarditis. Atrial flutter resulted from clockwise circus movement in the right atrial free wall in seven episodes and counterclockwise circus movement in the right atrial free wall in four episodes. The mean cycle length of rapid atrial pacing that interrupted atrial flutter was 139±21 msec (range, 109–181 msec). The atrial pacing sites during interruption of atrial flutter were the right atrial appendage in seven episodes and the posteroinferior left atrium in four episodes.

| Table 1. Characteristics of Atrial Flutter Reentry Circuit During Atrial Flutter, Rapid Atrial Pacing of Atrial Flutter, and Interruption of Atrial Flutter |
|---|---|---|---|---|---|---|---|
| Dog | CL (msec) | Dir | ASC | Site | CL (msec) | ASC | ASC | Site | Velocity (m/sec) | Block |
| 1 | 140 | CW | HRA | PLA | 109 | HRA | PM | PM | 0.75→0.12 |
| 2A | 142 | CW | HRA, PM | RAA | 125 | PM | LRA | LRA | 0.26→0.10 |
| 2B | 147 | CW | LRA, PM | PLA | 128 | LRA | HRA | HRA | 0.50→0.05 |
| 3A | 145 | CW | HRA, LRA | PLA | 126 | LRA | PM | PM | 0.35→0.20 |
| 3B | 169 | CW | HRA, LRA | PLA | 151 | LRA | PM | PM | 0.43→0.18 |
| 3C | 155 | CW | HRA, LRA | RAA | 133 | HRA | PM | PM | 0.23→0.06 |
| 4 | 198 | CCW | HRA, LRA | RAA | 181 | HRA | PM | PM | 0.27→0.14 |
| 5 | 150 | CCW | HRA, LRA, PM | RAA | 141 | HRA | PM | PM | 0.14→0.10 |
| 6 | 188 | CCW | HRA, LRA, PM | RAA | 171 | HRA | LRA | LRA | 0.11→0.07 |
| 7 | 135 | CW | HRA, LRA | RAA | 126 | HRA | LRA | LRA | 0.12→0.10 |
| 8 | 160 | CCW | HRA, LRA, PM | RAA | 141 | HRA- | PM | PM | 0.19→0.09 |

Block, block of orthodromic wave front of pacing impulse that resulted in interruption of atrial flutter; CL, cycle length; Dir, direction of rotation of reentry circuit; ASC, area of slow conduction during atrial flutter before atrial pacing; ASC, new area of slow conduction that disappeared during rapid atrial pacing; ASC, new area of slow conduction that developed during rapid atrial pacing; CW, clockwise rotation; CCW, counterclockwise rotation; HRA, high right atrium in sulcus terminalis; PM, pectinate muscle region; LRA, low right atrium in sulcus terminalis; PLA, posterior inferior left atrium; RAA, right atrial appendage; HRA-*, degree of slow conduction decreased in this area of slow conduction.

Velocity (m/sec) represents conduction velocity; this measurement was made at site where orthodromic activation wave front was blocked; left side of velocity column is conduction velocity in that ASC site during atrial flutter; right side of velocity column is conduction velocity in that ASC site during beat immediately before occurrence of block.
Table 1 lists the characteristics of atrial flutter interrupted by rapid atrial pacing.

** Interruption of Atrial Flutter During Rapid Atrial Pacing by Block at a Newly Formed Area of Slow Conduction **

Figures 3A–3D show one representative episode of the interruption of atrial flutter by rapid atrial pacing. The cycle length of atrial flutter before rapid atrial pacing was 142 msec. The atrial flutter reentrant wave front circulated in the free wall of the right atrium in a clockwise direction around an area of apparent functional block, which is represented by dashed lines (Figure 3A, upper left map). A, B, and C in panel A indicate the location of bipolar electrogram recording sites shown in Figures 3B–3D. As noted from the bipolar electrograms recorded during atrial flutter before rapid pacing (Figure 3B), activation time was 57 msec from site A to site B, 39 msec from site B to site C, and 46 msec from site C to site A. As indicated by crowding of the 10-msec isochronous lines (Figure 3A, upper left map), an area of slow conduction was present at the high right atrium close to the superior vena cava (close to site B) and in the region of the pectinate muscles (close to site C). Thus, areas of slow conduction were present between A and B and between B and C.

Rapid atrial pacing at a cycle length of 125 msec was then performed from the right atrial appendage. After the wave front from the pacing impulse captured (entrained) the reentry circuit, the area close to the pacing site (i.e., the atrial appendage) was activated by the wave front from the pacing impulse. However, the antidromic activation wave front from the pacing impulse collided with the orthodromic wave front of the previous beat in the high right atrium close to the superior vena cava. Nevertheless, the orthodromic activation wave front of the same pacing impulse captured the reentry circuit, circulating in a clockwise direction around the area of functional block. This is illustrated in Figure 3A, upper right panel. During the fifth pacing stimulus, the antidromic activation wave front from this pacing impulse collided with the orthodromic activation wave front of the previous beat (S4) in the high right atrium. However, the orthodromic activation wave front of S5 circulated in a clockwise direction around the area of functional block.

Note that during pacing, the area of slow conduction between electrode pairs B and C, which was present during atrial flutter, disappeared, and a new area of slow conduction appeared in the inferior right atrium in the region of the sulcus terminalis between electrode pairs C and A. It is of interest that this new area of slow conduction developed at a pivot point in the reentrant circuit. Actually, comparison of the isochronous map during atrial flutter and beat S5 suggests that this new area of slow conduction could be considered to represent development of an increase in conduction time through an area of previous minimal slow conduction present during spontaneous atrial flutter. Note also that the orthodromic activation wave front from the S5 pacing impulse traveled across this new area of slow conduction. Therefore, activation time between B and C, which was 39 msec during atrial flutter before initiation of rapid atrial pacing, decreased, changing to 30, 20, 14, and 12 msec with beats S2, S3, S4, and S5, respectively (Figure 3C). That activation time between these sites gradually decreased even though the atrial rate was faster than that of atrial flutter is in part related to the disappearance of the area of slow conduction previously present between these two sites and in part to the influence of the change in the direction of activation of site C caused by the orthodromic wave front of the pacing impulse (Figure 3A). Note, however, that activation time between C and A, (46 msec during atrial flutter before rapid atrial pacing) increased to 47, 60, 67, and 68 msec during beats S2, S3, S4, and S5, respectively (Figure 3C). Thus, activation time gradually prolonged as a new long but localized area of slow conduction developed in the area of the sulcus terminalis close to the inferior vena cava (Figure 3A).

During beat S6, the antidromic wave front from the pacing impulse collided with the orthodromic wave front of the previous beat, S5. In addition, now the orthodromic wave front from the S6 pacing impulse blocked in the area of slow conduction close to the inferior vena cava (Figure 3A, lower left panel). Thus, each orthodromic activation wave front from the pacing impulse developed increasing conduction delay in the new area of slow conduction until block of the orthodromic wave front of S6 finally occurred between electrode pairs C and A (Figure 3C). Note also that the area activated by the orthodromic wave front of the previous beat, S5, was not activated by the orthodromic wave front of S6. In fact, this area, which included site A, was not activated by either the orthodromic or the antidromic wave front of the S6 pacing impulse. Thus, there was localized conduction block to this area for one beat (Figures 3C and 3A, lower left panel), as predicted by the third criterion of transient entrainment.

The combination of collision of the antidromic wave front and of block of the orthodromic wave front led to termination of circus movement. During the next beat, S7, there was no longer any circus movement, so that atrial flutter was no longer present. Instead, there was radial activation of the right atrial free wall from the pacing site (Figure 3A, lower right panel). Also, note that the area of localized conduction block (i.e., the area that was not activated by beat S6) was now activated by a wave front from S7 but in large part from a different direction and with a shorter conduction time, as predicted by the third criterion of transient entrainment. As electrode site A was in the area of localized conduction block, note that this electrode site was activated from a different direction (via site C in S5 versus site B in
S7) and with a shorter activation time (80 msec in S5 versus 36 msec in S7) (Figure 3C). Sinus rhythm resumed after termination of pacing, which was continued to paced beat S14 (Figure 3D). During rapid atrial pacing to interrupt atrial flutter, disappearance of an area of slow conduction in the reentry circuit occurred in 10 of 11 episodes studied, and interruption of atrial flutter occurred with block of the orthodromic wave front from the pacing impulse in a newly developed area of slow conduction in the reentry wave front in seven of the 11 episodes.

**Interruption of Atrial Flutter During Atrial Pacing by Block at an Existing Area of Slow Conduction**

A representative episode in another dog is demonstrated in Figure 4. The upper map of Figure 4A shows atrial flutter at a cycle length of 150 msec before initiating rapid atrial pacing. The activation wave front circulated in a counterclockwise direction around an area of apparent functional block, represented by a dashed line (Figure 4, top map). Three small areas of slow conduction were present: one in the high right atrium in the region of the sulcus terminalis, one in the low right atrium in the region of the sulcus terminalis, and one in the pectinate muscle region. In this example, rapid pacing was performed from the right atrial appendage at a cycle length of 141 msec. As shown in the middle map of Figure 4A, with the eighth stimulus, S8, the antidromic wave front from this pacing impulse collided with the orthodromic wave front of the previous beat (white arrow), S7. The orthodromic activation wave front of this pacing impulse circulated in a counterclockwise direction around the area of functional block, as occurred with the previous pacing impulses. However, although the previous orthodromic wave fronts from the pacing impulse traveled across both the area of slow conduction near the inferior vena cava and the area in the pectinate muscle region to collide with the antidromic wave front of the next pacing impulse, this time the orthodromic activation wave front from the S8 pacing impulse blocked in the area of slow conduction in the pectinate muscle region. Note also that the area of slow conduction at the high right atrial portion of the sulcus terminalis present during atrial flutter before rapid pacing disappeared during rapid pacing.

Bipolar electrograms recorded from sites A through D (Figure 4A, top map) close to the area of slow conduction in the high right atrium near the superior vena cava during atrial flutter and during atrial pacing are shown in Figures 4B and 4C, respectively, along with electrocardiographic lead II. Activation time between sites A and D during atrial flutter before rapid pacing was 50 msec, and the duration of fractionated electrograms recorded from the electrode pair at site B was 82 msec (Figure 4B). After capture of the reentry circuit during rapid pacing at a cycle length of 141 msec, activation time between A and D decreased to 38, 29, and 22 msec with beats S6, S7, and S8, respectively (Figure 4C), which was associated with disappearance of the area of slow conduction in the upper portion of the sulcus terminalis. Note also that the duration of the fractionated electrogram recorded from site B decreased from 82 msec during atrial flutter before rapid pacing to 49 msec with paced beat S8 and to 24 msec during paced beat S10.

With block of the orthodromic activation wave front from the pacing impulse during beat S8 (Figure 4A, middle map), the reentrant circuit was interrupted. This was associated with a further decrease in activation time between sites A and D to 12 msec and complete disappearance of fractionated electrograms at site B (Figure 4C).

Figure 4D shows electrocardiographic lead II and bipolar electrogram from sites A, E, and F in the reentrant circuit (Figure 4A, middle map) during the period of spontaneous atrial flutter. Sites E and F straddle an area of slow conduction. Figure 4E shows bipolar electrograms from sites A, E, and F during rapid pacing at which time the orthodromic activation wave front of the S8 pacing impulse blocked, resulting in interruption of the atrial flutter. Activation time from site E to site F, a distance of 4.2 mm, was 37, 40, 42, and 52 msec during pacing impulses S4, S5, S6, and S7, respectively. Each orthodromic wave front from the pacing impulse developed increasing conduction delay in this area of slow conduction that had been present before rapid atrial pacing, and block of the orthodromic wave front finally occurred in an area between sites E and F. Site F was not activated by a wave front from S8 (localized conduction block for one beat); it was activated by a wave front from S9 but from a different direction (via site E during S7 versus via site A during S9) and with a shorter activation time (166 msec in S7 versus 78 msec in S9), as predicted by the third criterion of transient entrainment.5,6 In addition, fractionated electrograms recorded from sites E and F disappeared after the interruption of the reentry circuit (S9; Figure 4E). Sinus rhythm resumed after termination of pacing, which was continued to paced beat S19 (Figure 4F).

**Summary of Data From All 11 Episodes of Pacing Interruption of Atrial Flutter**

Table 1 indicates the areas of slow conduction that 1) were present during atrial flutter, 2) disappeared with rapid atrial pacing, 3) developed during rapid atrial pacing, and 4) developed block of the orthodromic wave front from the pacing impulse. In all 11 episodes of atrial flutter, an area of slow conduction was demonstrated at one to three sites: the high and/or low right atrium in the region of the sulcus terminalis and/or in the pectinate muscle region (Figure 5A). In all instances, the area of slow conduction was present where the activation wave front crossed perpendicularly to the longitudinal orientation of atrial muscle fibers.7 After rapid atrial pacing captured the reentry circuit, one area of slow con-
duction disappeared in 11 episodes, including one episode that demonstrated a decrease of slow conduc-
tion in an area of slow conduction (Figure 5B). In
addition, in seven of these episodes, a new area of
slow conduction developed at sites indicated in Fig-
ure 5B, right panel. All former areas of slow conduc-
tion were activated by a wave front from the pacing
impulse from a somewhat different direction than
that during atrial flutter before rapid atrial pacing
(Figures 3A and 4A). All other areas of slow conduc-
tion that were activated identically during atrial
pacing and atrial flutter remained until atrial flutter
was interrupted.

Before interruption of the atrial flutter by rapid
atrial pacing, each orthodromic wave front from the
pacing impulse developed increasing conduction de-
lay in an area of slow conduction until block of the
orthodromic activation wave front finally occurred.
(Figure 5C), resulting in termination of circus movement. The block was in a new area of slow conduction produced by rapid atrial pacing in seven episodes (Figure 3) and in an area of slow conduction that had been present before rapid atrial pacing in four episodes (Figure 4).

Discussion

We recently demonstrated the importance of an area of slow conduction and block for the initiation of atrial flutter in our canine pericarditis model. The presence of one or more areas of slow conduction in
That there is usually more than one area of slow conduction in the reentry circuit and that these areas occur where the circulating wave front travels perpendicularly to the longitudinal orientation of the atrial muscle fibers suggest the importance of anisotropic conduction for their development and maintenance. It is also of interest that these areas of slow conduction are usually at the pivot points of the circulating atrial flutter wave front, similar to that previously noted by Allessie's group in a rabbit model of reentrant ventricular tachycardia.

**Effects of Rapid Pacing on Area of Slow Conduction**

It is of interest that the areas of slow conduction in the reentry circuit often changed during rapid pacing. The fact that a previous area of slow conduction disappeared and a new area of slow conduction appeared, associated with both a change in direction of circulating wave fronts and an increase in rate, emphasizes the importance of both of these factors in the development of areas of slow conduction. Also, this has potential implications for the study of atrial flutter in patients. Recently, there have been several reports of catheter ablation used to treat (i.e., cure) atrial flutter. Identification of a critical area of slow conduction is central to application of the ablation techniques and depends in part on pacing techniques (entrainment) to confirm that an area of slow conduction identified by fractionated electrograms is in the reentry circuit. If one can extrapolate the data from the present study to patients in atrial flutter, then the location of the pacing site during atrial flutter in patients will be quite important: it must be such that during pacing the direction of propagation through the area of slow conduction must remain the same as during atrial flutter.

**Confirmation of the Third Criterion of Transient Entrainment**

The transient entrainment hypothesis for reentrant rhythms with an excitable gap holds that during transient entrainment of the tachycardia, the antidromic wave front of each pacing impulse collides with the orthodromic wave front of the previous beat, but that the orthodromic wave front of each pacing impulse captures the reentry circuit, thereby increasing the tachycardia to the pacing rate. This was demonstrated during rapid pacing of atrial flutter in the present study. The third criterion of transient entrainment holds that interruption of the tachycardia by rapid pacing occurs when the antidromic and orthodromic wave fronts of the same pacing impulse block during the same paced beat. Furthermore, it holds that the orthodromic wave front from the pacing impulse blocks in the area of slow conduction. This, too, was confirmed by the present study. Finally, it holds that there is localized conduction block for one beat followed by activation of that blocked area by the next pacing impulse from a different direction and with a shorter conduction time. This also was confirmed by the present study.

The reentrant circuit demonstrated in the present study during sustained atrial flutter also indicates the importance of these areas, not only for the initiation of atrial flutter but also for its maintenance.
Relation of Anisotropic Conduction to Interruption of Atrial Flutter by Rapid Pacing

A much more difficult observation to explain is why the orthodromic wave front from the pacing impulse that finally interrupts atrial flutter always blocked in an area of slow conduction. If conduction in this area is slow due to anisotropy, it follows that the so-called “safety factor for conduction” should not favor the occurrence of block in one of these areas of wave fronts propagating transverse to the local fiber orientation.7 But that is what happened. An explanation based on data from the present study can only be speculative.

Success or failure of propagation of an activation wave front results from factors that determine local source-sink relations. These include fiber orientation relative to the direction of spread of wave front, the electrophysiological state of the membrane (i.e., its excitability, refractoriness, or both).14,15 The presence or absence of branching of the muscle fibers and other abrupt changes in load, and, in this model, probably the effects of inflammation. Clearly, the data from this study do not permit all of these possibilities to be directly addressed and their effects to be separated. However, a possible explanation consistent with what is known about anisotropic conduction may be found in the observation that the block often occurs in an area of slow conduction at the pivot point in the reentry circuit.8,16 Thus, a transverse wave front traveling slowly because of anisotropy suddenly turns to travel along the fiber axis, experiencing an abrupt increase in load and reduced safety factor for conduction, resulting in block. This possible explanation, although tenable, must be further tested. Also, it is not clear what role is played by the beat-to-beat increase in activation time across the area of slow conduction in which the block subsequently occurs.

Nevertheless, not all block that occurred in the area of slow conduction during rapid pacing occurred at a pivot point. In the present study, in seven of the 11 episodes, block did not occur at a pivot point. Thus, although the observations are clear and one would like to explain them by what we presently understand with regard to anisotropic conduction, there clearly are more studies required for a fuller explanation.

Recording of Fractionated Electrograms

Fractionated electrograms have been recorded from ventricular myocardium after acute myocardial infarction,17 from chronically infarcted tissue in experimental models18–21 and humans,22,23 and most recently during atrial flutter in experimental models2,4,7,24 and humans.11–14,25–27 A generally accepted explanation of fractionated electrograms is that they reflect nonsynchronized activation of nearby muscle bundles.21,26 The recording of fractionated electrograms from electrode sites in the area of slow conduction in the present study provides additional evidence that these electrograms reflect slow conduction. The fact that these electrograms disappeared despite rapid pacing for several beats from the same pacing site after interruption of atrial flutter associated with a change in the direction of activation emphasizes the many factors required to generate this signal. It is probable that rate (either resulting from the tachycardia itself or pacing), duration of the rapid rate, and direction of the wave front are among the important factors.

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References


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