Circus Movement Atrial Flutter in Canine Sterile Pericarditis Model

Activation Patterns During Entrainment and Termination of Single-Loop Reentry In Vivo

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Background. Recently, we used a custom designed “jacket” electrode with 127 bipolar electrodes in a flexible nylon matrix to map the total atrial epicardial surface in the in situ canine heart. Atrial flutter in dogs with sterile pericarditis was shown to be due to a single wave front circulating around a combined functional/anatomic obstacle, with the arc of functional conduction block contiguous with one or more of the atrial vessels.

Methods and Results. In the present study, this model was used to analyze the activation pattern during pacing-induced entrainment and termination of single reentrant loops in a syncytium without anatomically predetermined pathways. Sustained atrial flutter was induced in five dogs with 3–5-day-old sterile pericarditis. Atrial pacing at a cycle length 5–30 msec shorter than the spontaneous cycle length entrained the arrhythmia and could result in a “classical” activation pattern, characterized by an antidromic stimulated wave that collided with the reentrant orthodromic wave front of the previous beat at a constant site. However, two variations of this classical activation pattern were also observed: 1) Pacing at short cycle lengths could lead to localized conduction block in antidromic direction, forcing a change in the pathway of the antidromic wave front. This could prevent the expected shift of the site of collision in antidromic direction. 2) The stimulated orthodromic wave front could also use a pathway different from that of the original reentrant impulse, so that a different circuit was active during the pacing period. Termination of atrial flutter by rapid atrial stimulation was associated with progressive slowing and finally blocking of the paced orthodromic wave front and a progressive shift of the site of collision in antidromic direction. The occurrence of conduction block was determined by the cycle length of stimulation and the number of stimulated beats. A longer train at the critical cycle length or the critical number of beats at a shorter cycle length could induce the same reentrant circuit or a different reentrant circuit, respectively, during stimulated cycles following the beat that terminated reentry.

Conclusions. The epicardial activation sequence during entrainment of reentrant arrhythmias does not necessarily follow a standard activation pattern. Instead, the stimulated orthodromic as well as the antidromic wave front might use a pathway different from that of the original reentrant wave front. The mechanisms of termination, failure of termination, and reinitiation of single-loop reentry are similar to those in the “figure-eight” reentrant circuit. (Circulation 1991;83:1716–1730)

In 1977, Waldo et al demonstrated that failure to interrupt atrial flutter with rapid atrial pacing at rates faster than the atrial flutter rate was due to transient entrainment of the arrhythmia. They defined entrainment of a tachycardia by rapid pacing as “an increase in the rate of all tissue of the chamber being paced to a faster rate than the tachycardia, with resumption of the intrinsic rate of the tachycardia upon either abrupt cessation of pacing or slowing of the pacing rate below the intrinsic rate of the
tachycardia.” They also described three criteria, any of which, if present, established transient entrainment of a tachycardia and suggested reentry as the most likely underlying mechanism: 1) the demonstration of constant fusion, except for the last transiently entrained beat, 2) progressive fusion, that is, different degrees of constant fusion at different pacing rates, and 3) interruption of a tachyarrhythmia by rapid pacing associated with localized conduction block to a site, followed by activation of that site from a different direction and with shorter conduction time by the next pacing impulse. Clinical interest in the entrainment phenomenon and these criteria arose from their implications for antitachycardia pacing, their value in identifying and understanding reentrant arrhythmias, and their possible role in identifying the critical site for ablative interventions in the nonpharmacological treatment of reentrant arrhythmias. However, the entrainment concept has been developed largely by deductive analysis, based on the surface electrocardiogram and a limited number of intracardial recordings. Only a few attempts have been made to actually document the activation sequence during entrainment and termination of ventricular or supraventricular tachyarrhythmias. In fact, the spread of activation during entrainment and termination of circus movement atrial flutter in a functional model of reentry has never been shown. We have recently described a technique for epicardial mapping of the total atrial surface in the in situ canine heart. Using this approach in dogs with sterile pericarditis, we could demonstrate the epicardial activation sequence during induction, spontaneous termination, and sustenance of circus movement atrial flutter in a synchytium without anatomically predetermined pathways. The present study was conducted to analyze the epicardial activation sequence during pacing-induced entrainment, termination, and failure of termination of reentrant atrial flutter in this animal model.

Methods
Details of the model preparation, the recording techniques, and the methods for constructing isochronal maps have previously been described. Studies were performed in five mongrel dogs (15–20 kg) with sterile pericarditis and inducible sustained atrial flutter. Sterile pericarditis was created by generously dusting the epicardial surface of both atria with talcum powder. After recovery, induction of atrial flutter by rapid atrial pacing was attempted daily with the dogs in the conscious, nonsedated state. Mapping studies were performed on the day following induction of sustained atrial flutter (3–5 days after the initial surgery). The chest was reopened, and a specially designed electrode array was placed on the epicardial surface of both atria. This atrial “jacket” contained 111 bipolar recording electrodes with an interpolar distance of 1–2 mm in a flexible nylon mesh. The interelectrode distance ranged from 3 mm to 5 mm but could reach 5–8 mm in certain areas (e.g., the atrial appendages) when the nylon mesh was stretched. Five small Teflon patches containing two to five electrode pairs provided 16 additional bipolar recordings from the area between the pulmonary veins, the area below the inferior vena cava, and the anterior aspect of the atrial appendages. Data were stored and analyzed using a 128-channel computer-ized multiplexer recording system. Activation times were marked manually after review of each individual recording. In electrograms showing a sharp intrinsic deflection, the maximum first derivative was taken as the moment of activation. In multiphasic electrograms, a contribution of the ventricular activation or the stimulus artifact to the recorded signal was excluded by comparing the timing of the electrogram components with the surface electrocardiogram and other epicardial recordings. The peak of the major deflection was then chosen as the moment of activation. From these activation times, isochronal epicardial activation maps were constructed manually at 10-msec intervals. During the mapping experiments, electrocardiographic lead II, a left or right atrial electrogram, and aortic blood pressure were continuously monitored on a VR 12 recorder (Electronics for Medicine, Lenexa, Kan.).

Study Protocol
After placement of the jacket electrode, several spontaneous beats were recorded to confirm a normal sinus activation. If necessary, the electrode array was repositioned to assure adequate recordings from all 16 patch electrodes and at least 90% of the electrodes on the jacket. Induction of atrial flutter was then attempted either by rapid burst pacing or by critically timed premature stimuli, provided by a DTU-101 digital stimulator (Bloom, Reading, Pa.). Once sustained atrial flutter was induced, recordings from all 127 electrode sites were obtained. The cycle length and electrocardiographic morphology were observed over a time course of at least 30 minutes to confirm the stability of the arrhythmia. Atrial pacing was then applied through an electrode pair on the jacket electrode. Rectangular impulses of four times diastolic threshold strength assured atrial capture at rapid rates. The stimulation protocol started with a single beat at a cycle length 5 msec shorter than the average cycle length of the induced arrhythmia. The number of stimuli was increased in steps of one to a maximum of 15 beats without a change in cycle length. The above sequence was then repeated at progressively shorter cycle lengths (in steps of 5 msec) until 1:1 atrial capture was no longer achieved. If a stimulation protocol terminated the arrhythmia, atrial flutter was reinduced. The stimulation sequence was completed if the reinduced episode of atrial flutter had an identical cycle length and activation sequence. Otherwise, the sequence was started again.
Figure 1. Epicardial activation map (left panel) and selected electrograms (right panel) during an episode of sustained atrial flutter. Heavy black dots in map indicate position of selected electrode sites (A–K). Representative examples for each isochronal area and site of stimulation were chosen for demonstration. Heavy solid lines denote arcs of functional conduction block. Arrows outline general direction of major activation wave front. Numbers in electrogram recordings reflect interval between consecutive activations in milliseconds.

Statistical Methods

Data are expressed as mean±SD.

Results

All five dogs had inducible sustained atrial flutter with a mean cycle length of 139±21 msec (110–170 msec) in the open-chest state. During the arrhythmia, the atrial electrogram morphology was uniform, and the beat-to-beat interval variation was less than 10 msec. Epicardial activation maps revealed single reentrant loops in the left (n=1) or right (n=4) atrium, with the circumference of one or more of the atrial vessels and an arc of functional conduction block forming a combined functional/anatomic obstacle. Subsequent episodes in the same dog had the same activation sequence and a similar average cycle length (±5 msec). In one dog, however, the reentrant wave front proceeded either clockwise or counterclockwise around a similar functional/anatomic obstacle in the left atrium. Respective episodes differed in cycle length by 15 msec and were analyzed separately.

Entrainment of the induced arrhythmia(s) could be demonstrated in all five dogs during stimulation with up to three (2±0.9) different cycle lengths 5–30 msec shorter than the cycle length of the sustained atrial flutter. The term “entrainment” was only used if the observed activation pattern was stable from beat to beat even with long drive trains. The shortest pacing cycle that successfully entrained the arrhythmia was 20±9 msec shorter than the cycle length of the spontaneous tachycardia. Of the six different tachycardias induced in the five dogs, two tachycardias could be entrained within 25 msec, whereas entrainment was possible within 5, 15, 20, and 30 msec in one episode for the other four tachycardias. Repeated attempts to entrain a tachycardia at the same paced cycle length resulted in the same activation pattern. Termination was always possible at a stimulated cycle length of 10–35 msec (25±9 msec) shorter than that of the induced arrhythmia. The epicardial activation pattern during 22 different episodes of entrainment and termination was critically analyzed, and representative examples are presented.

Classical Entrainment of Single-Loop Reentry

Figure 1 shows the epicardial activation map (left panel) and selected electrograms (right panel) during an undisturbed episode of sustained atrial flutter at a cycle length of 140 msec. The epicardial atrial surface in this as well as in all subsequent figures is displayed in a planar projection as if the atria were separated from the ventricles along the atrioventricular (AV) ring and as if the inferior bodies of the atrial appendages were incised from the AV ring to their tips and unfolded. The heavy black dots indicate the position of the selected recording electrodes. A single reentrant loop was oriented around an arc of block (the heavy solid line) extending from the proximity of the superior vena cava to one of the right pulmonary veins. Conduction within the free right atrial wall was very slow, especially in the area between the central obstacle and the superior vena cava. The right panel of Figure 1 depicts representative electrograms from each isochronal area within the reentrant circuit and from the future site of stimulation (site G). Here and in subsequent figures, electrograms are presented to underline the stability and regularity of the described activation pattern, and respective sites were chosen on the basis of the quality of the recording. The double potentials recorded at electrode sites I and K were interpreted as local activation and an electrotonic potential reflecting activation at an adjacent...
Atrial stimulation at a cycle length of 130 msec increased the rate of the tachycardia to the paced rate, with resumption of the spontaneous rate (140 msec) after cessation of pacing. Representative epicardial activation maps and selected atrial electrograms are demonstrated in Figure 2. Because the epicardial activation pattern was constant during the pacing period, maps of only two stimulated beats ($S_{11}$ and $S_{15}$) are shown (Figure 2, top panel). Stimulation was applied to a site in the posteroinferior aspect of the left atrium, outside the reentrant circuit. The time of stimulation was chosen as the time reference. The stimulated wave front proceeded within the original reentrant pathway in orthodromic (i.e., in the direction of the original reentrant wave front) as well as in antidromic (i.e., opposite the original reentrant wave front) direction. The stimulated antidromic wave front collided after 50 msec at a constant site with the reentrant orthodromic wave front of the beat preceding $S_{11}$ and $S_{15}$ ($S_{10}$ and $S_{14}$, respectively). This collision blocked further spread of
either impulse. The stimulated orthodromic wave front, however, advanced undisturbed and reset the tachycardia by 10 msec. Selected electrograms (Figure 2, bottom panel) illustrate the stability of this activation pattern. Different from the spontaneous tachycardia (Figure 1), activation at site G preceded that at site F during the pacing period, and the electrogram morphology at site F had changed, indicating activation from a different direction. Because S15 was the last stimulated beat, the reentrant S15 orthodromic wave front did not encounter an antidromic wave front with which to collide. Instead, activation continued to proceed within the original reentrant pathway. During A1 (Figure 2), the spread of activation up to electrode site D was identical to the activation pattern during paced beats. Respective electrodes (A–D) were, therefore, reactivated after 130 msec. As the A1 reentrant wave front continued within the circuit pathway, electrode sites that had previously been reset by the stimulated wave front were now activated by this reentrant impulse at their original coupling interval of 140 msec. Thus, the A1 activation was entrained to the paced cycle up to the previous site of collision. The coupling interval returned to 140 msec at all electrode sites during the following beat (A2).

**Classical Termination of Single-Loop Reentry**

Further shortening of the cycle length of stimulation to 120 msec terminated the arrhythmia after a train of nine stimuli. Epicardial activation maps of four stimulated beats (S7–S10) and selected atrial electrograms are shown in Figure 3. Up to S6, only local capture was achieved, and the original activation sequence was basically undisturbed. Accordingly, there was no change in cycle length other than at site G (bottom panel). At the time of the S7 stimulation, the reentrant orthodromic wave front of the preceding beat (S6) had reached site C (top panel). There was an “incomplete” collision in the area below the inferior vena cava (note the change in the electrogram morphology and the shortening of the coupling interval at site F in the bottom panel). The remaining electrode sites within the circuit were activated at their original coupling interval (140 msec). When S8 was introduced (top panel), the S7 orthodromic activation had only reached site A. This allowed further advancement of the antidromic wave front elicited by S8, until both impulses collided in the proximity of electrode site E. Accordingly, the electrogram morphology at site E changed (bottom panel). The stimulated orthodromic wave front of S8 arrived at the entrance to the slow zone of the reentrant circuit (site H) only 130 msec after the S7 activation had passed this site, resulting in further slowing of conduction (illustrated by the increasing isoelectric interval between the two components of electrogram I in the bottom panel). Thus, the orthodromic wave front of S6 had only reached the area between electrode sites J and K at the time of initiation of S8 (top panel). Again, the activation wave front induced by S8 could now advance even further in antidromic direction, before collision occurred near site D. In orthodromic direction, site H was reactivated after only 120 msec. This interval was probably not sufficient for the tissue distal to site I to recover excitability, resulting in conduction block to sites J, K, and A. Figure 3, bottom panel, documents not only the absence of an activation potential at electrode sites J, K, and A during S8 but also the absence of the second deflection in electrogram I. During S10 (top panel), the complete atrial surface was activated exclusively by the activation wave front induced by this very stimulus, with a more or less radial spread of activation from the site of stimulation and a relatively short total atrial activation time (80 msec). Sites A, K, and J (marked by stars in the bottom panel) were now activated from a different direction (note the change in the electrogram morphology and the activation sequence in the bottom panel) and at a shorter coupling interval. Activation at site J preceded activation at site I, which is reflected by reversal of the double potential in electrogram I. Continuation of pacing at a cycle length of 120 msec restored the original conduction block, as indicated by the activation sequence and electrogram morphology (bottom panel) during the beat following S10.

**Entrainment With a Change in the Reentrant Pathway**

In another dog with sustained atrial flutter, the epicardial activation map revealed the activation pattern illustrated in Figure 4A (left). A single reentrant wave front circulated around a large functional/anatomic obstacle that included the inferior vena cava, the right pulmonary veins, and an arc of
Figure 4. Panel A: Epicardial activation sequence (left) and selected electrograms (right) during episode of sustained atrial flutter at cycle length of 140 msec. A–L are electrode sites. Panel B: Epicardial activation sequence and selected atrial electrograms during entrainment of tachycardia shown in panel A (sustained atrial flutter) at cycle length of 130 msec. Again, the moment of stimulation (S) is chosen as the time reference. Shaded area represents tissue activated by reentrant orthodromic wave front of preceding beat; dotted area contains site of collision with stimulated antidromic impulse. Panel C: Epicardial activation sequence and selected electrocardiograms during entrainment of tachycardia shown in panel A (sustained atrial flutter) at a cycle length of 120 msec. Site of collision has shifted in antidromic direction (electrode site K). Note change in pathway of orthodromic wave front. (See Figure 1 for explanation of activation maps.)
functional conduction block. The slow conducting zone of this reentrant circuit was located in the lower right atrium and in the isthmus between the inferior vena cava and the nearby AV ring. As demonstrated by the selected electrograms (Figure 4A, right), this activation sequence repeated itself regularly at a cycle length of 140 msec.

Atrial stimulation at a cycle length of 130 msec entrained the arrhythmia to the paced rate. The selected electrograms (Figure 4B, right) illustrate the stability of the activation pattern during the pacing period. Thus, the epicardial activation map of only one stimulated beat is shown (Figure 4B, left). Stimulation was applied to a site in the left atrial appendage, outside the reentrant circuit (electrode site G). At the time of stimulation, the orthodromic wave front of the preceding impulse had constantly reached the area below the inferior vena cava, and this orthodromic wave front collided with the stimulated antidromic wave front in the left atrium close to electrode site I. The stimulated wave front also proceeded in orthodromic direction within the reentrant pathway and reset the tachycardia by 10 msec. Due to the relative prematurity of the stimulated wave front, conduction was now slower than during the spontaneous tachycardia, so that electrode sites F and C were separated by six isochrones (as opposed to three isochrones in Figure 4A). This constant activation pattern was similar to the one in the previous example of transient entrainment (Figure 2) in demonstrating advancement of both stimulated wave fronts within the original reentrant pathway and constant collision of the stimulated antidromic wave front with the reentrant orthodromic wave front of the preceding beat.

Atrial stimulation at a cycle length of 120 msec, however, resulted in a different activation pattern (Figure 4C). The selected electrograms (right) show that the tachycardia was actually entrained to the paced cycle of 120 msec and that the activation sequence was constant during the pacing period. Compared with the original activation sequence (Figure 4A), electrode sites G–K were now activated in reverse order, with G recording the earliest activation (note the change in the electrogram morphology at sites G, H, I, and J). During the preceding entrainment period at 130 msec (Figure 4B, right), these changes had only involved sites G–I. Thus, the two pacing cycles resulted in different sites of collision, indicating different degrees of constant fusion at different cycle lengths (i.e., progressive fusion). The epicardial activation map (Figure 4C, left) demonstrated that the site of collision had shifted to the area below the inferior vena cava, further away from the site of stimulation. However, the early arrival of the stimulated orthodromic wave front at electrode site E had resulted in an extension of the arc of block across the free right atrial wall to the proximity of the AV ring. Therefore, the stimulated orthodromic wave front could no longer proceed within the reentrant pathway that had been active during the spontaneous tachycardia. Instead, entrainment of the tachycardia to the paced rate created a different orthodromic reentrant path, and only on cessation of pacing did the reentrant wave front resume the original activation pattern. This latter phenomenon was probably due to the fact that the reentrant wave front of the first nonstimulated beat arrived later at electrode site E than the stimulated orthodromic wave front during the preceding entrainment period.

In Figure 5, top panel, epicardial activation maps during another episode of sustained atrial flutter and entrainment of the arrhythmia at stimulated cycle lengths of 115 and 105 msec are shown. The sustained arrhythmia was due to a single reentrant loop around a combined functional/anatomic obstacle in primarily the left atrium (Figure 5, top panel, left map). An arc of functional conduction block extended across the free left atrial wall to the proximity of the AV ring, where conduction was slower than in the remaining part of the circuit. The reentrant impulse had a revolution time of 125 msec and activated electrodes A–E in the free left atrial wall consecutively (Figure 5, bottom left panel, top electrograms).

Atrial stimulation at a cycle length of 115 msec entrained the arrhythmia to the paced cycle and created the expected activation pattern (Figure 5, top panel, middle map). The site of stimulation was located within the reentrant circuit, close to electrode site E. Collision of the reentrant orthodromic wave front of the preceding impulse with the stimulated antidromic wave front occurred after 40 msec between sites C and D. Orthodromically, the stimulated wave front entered the original reentrant pathway, where slowing of conduction resulted from the prematurity of the impulse. Selected electrograms (Figure 5, bottom left panel, middle electrograms) confirm that site E was now activated earlier than site D and that the electrogram morphology at sites D and E had changed. Sites A–C were still activated consecutively.

Entrainment of the tachycardia to a shorter paced cycle length (105 msec) resulted in an activation pattern similar to that during the preceding entrainment period (Figure 5, top panel, right map). The electrogram morphology at electrode sites A–E did not change significantly (Figure 5, bottom left panel, bottom electrograms). However, site D was now activated 45 msec after site E. This was interpreted to indicate conduction block rather than marked slowing of conduction between the two sites, based on the absence of fragmented, long-duration electrograms, a hypothetical conduction velocity of 0.09 m/sec, and our previous findings on high resolution recordings in this model.9 The stimulated wave front proceeded toward the inferior pulmonary veins, where it turned medially to enter the orthodromic reentrant pathway and laterally to reach the free left atrial wall. As a result of this delay in the spread of the stimulated antidromic wave front, the reentrant orthodromic wave front of the preceding impulse could activate sites A–C before it coalesced.
with the stimulated antidromic wave front to activate site D. Had electrode site D been activated exclusively by the reentrant orthodromic wave front, an electrogram morphology similar to that during the original tachycardia (Figure 5, bottom left panel, top electrograms) would have been expected. Collision seemed to occur in the same area as during stimulation at the longer (115-msec) cycle. Thus, entrainment at a shorter cycle length was associated with a change in the pathway of the stimulated antidromic wave front, which prevented a shift of the site of collision in antidromic direction (i.e., progressive fusion).

**Termination at Two Different Sites**

The epicardial activation maps shown in Figure 6 were obtained from an experiment in which sus-
tained atrial flutter at a cycle length of 150 msec was interrupted by a train of four stimulated beats at a coupling interval of 115 msec. During the sustained arrhythmia (Aₙ), the reentrant activation proceeded as a single loop around a large functional/anatomic obstacle in the right atrium. A long arc of functional conduction block extended from the circumference of the superior vena cava to the lower right atrium. There it was paralleled by a shorter arc that reached the AV ring. Conduction in the area bounded by these two arcs, as well as in the isthmus between the superior vena cava and the nearby AV ring, was considerably slower than in the remaining part of the circuit. Slow conduction and conduction block was also evident in the lateral right atrial wall, although this area was not part of the reentrant pathway. Stimulation was applied to a site near the tip of the right atrial appendage. Introduction of a train of four paced beats at a cycle length of 115 msec resulted in progressively deeper penetration of the stimulated wave front in antidromic direction and progressively slower conduction in orthodromic direction. This progressive conduction delay was due to further slowing of conduction primarily within the area between the superior vena cava and the nearby AV ring, which acted like a “buffer” for the second slow zone of the reentrant circuit in the free right atrial wall. Thus, despite the coupling interval of 115 msec, the stimulated orthodromic wave front of S₁ and S₃ arrived in the lower right atrium 140 msec after the preceding activation. During S₄ the stimulated antidromic wave front finally encountered an arc of conduction block between the superior vena cava and the AV ring, while the stimulated antidromic wave front was extinguished after collision with the reentrant orthodromic wave front of S₁. After a pause of 230 msec, sinus rhythm resumed (N₁).

Termination of the tachycardia was also attempted with seven stimulated beats at a cycle length of 115 msec (Figure 7). The reinduced arrhythmia had the same cycle length and activation sequence as in the previous example (Aₙ of Figures 6 and 7). Once again, with each stimulated beat the site of collision shifted further in antidromic direction, while the spread of the stimulated orthodromic wave front was progressively delayed. However, different from the previous example (Figure 6), the conduction delay around the superior vena cava was less pronounced and did not compensate for the prematurity of the stimulated beats. As a result, the stimulated orthodromic wave front of S₁ and S₃ reactivated the lower right atrium with a coupling interval of 120 msec. Whereas S₄ was further delayed in this second slow zone of the reentrant circuit, conduction failed on
arrival of the stimulated orthodromic wave front of $S_4$. This conduction block in the lower right atrium terminated the underlying arrhythmia, as indicated by the collision of the stimulated antidromic with the stimulated orthodromic wave front of $S_5$ during the following cycle.

Table 1 summarizes data from multiple attempts at pacing termination obtained during the experiment shown in Figures 6 and 7. The data underline the significance of the cycle length of stimulation and the number of stimulated beats. Atrial stimulation at cycle lengths of 135 and 145 msec entrained the arrhythmia. Thus, by definition, termination could not be achieved, irrespective of the number of stimulated beats. Pacing cycles of 105 msec and shorter, on the other hand, no longer resulted in regular atrial
capture. Within these margins, the minimum number of stimulated beats required for tachycardia termination was directly related to the cycle length of stimulation, so that at least six beats at a cycle length of 125 msec or four beats at a cycle length of 115 msec had to be applied. Figure 6 illustrates why less than four beats at 115 msec were unable to interrupt the arrhythmia. Only repeated activation of the orthodromic pathway at the pacing rate produced the progressive slowing of conduction that culminated in conduction block during $S_6$.

**Termination Followed by Induction of a Different Reentrant Circuit**

Failure of overdrive pacing to terminate atrial flutter was not only the result of entrainment of the arrhythmia but could also be due to induction of a different reentrant circuit or reinitiation of the original tachycardia. As shown in Figure 6, atrial pacing at a cycle length of 115 msec terminated the underlying arrhythmia after a train of four beats. During a train of seven beats at the same cycle length (Figure 7), it was again the stimulated orthodromic wave front of $S_4$ that encountered conduction block, although this time at a different site. During $S_5$ and $S_6$, the stimulated orthodromic and antidromic wave fronts simply proceeded around both ends of the central obstacle and collided with each other on the opposite side of the arc. Both stimulated wave fronts were blocked during $S_5$. Thus, the original reentrant circuit could not have been active on cessation of pacing. However, the pacing train was followed by a self-terminating run of three reentrant beats. There was an area on the base of the right atrial appendage, outside the actual reentrant pathway, that showed various degrees of conduction block during the pacing period. Although this area was not activated during $S_5$ and $S_6$, it was finally reached by $S_6$. $S_6$ reinduced an arc of block in this area, parallel to and cranially contiguous with the AV ring. The $S_7$-stimulated wave front could, therefore, only proceed around the free end of this arc of block, where it coalesced with the reentrant antidromic wave front of $S_5$. A common wave front then proceeded cranially, parallel to the AV ring. Because conduction in the isthmus between the arc of block and the AV ring was very slow and because no further stimulation was applied, the tissue on the proximal side of the arc of block was able to recover excitability. Activation continued as a single reentrant wave front around a functional arc of block parallel to the AV ring ($A_1$). Although the initial revolution time was 160 msec, conduction across the free right atrial wall improved during the following beat. Thus, this cycle was completed after 140 msec ($A_2$). During $A_3$, conduction failed within the slow zone of the reentrant circuit. The following beat showed a normal sinus activation.

**Termination Followed by Reinitiation of the Original Reentrant Circuit**

The activation sequence shown in Figure 8 was recorded in a dog in which the reentrant wave front circulated either clockwise (Figure 8) or counterclockwise (Figure 5) around a similar, yet not identical, functional/anatomic obstacle in the left atrium. The right atrial tissue seemed to be severely compromised and exhibited various degrees of conduction block. Counterclockwise reentrant activation ($A_{n-1}$) had a revolution time of 115 msec, with slowing of conduction in the isthmus between the arc of block and the AV ring. The arrhythmia could be entrained to a cycle length of 110 msec and was terminated by a train of six stimulated beats at a cycle length of 105 msec, with $S_6$ being the critical beat (data not shown). Figure 8 illustrates an attempt with six stimulated beats at a cycle length of 100 msec. Stimulation was applied to a site between the pulmonary veins.

Up to $S_5$ (Figure 8), the stimulated wave front progressively advanced in antidromic direction with each beat. Conduction block near the site of stimulation forced a change in the pathway of the stimulated orthodromic wave front during $S_6$. The length of this new pathway compensated for the prematurity of the stimulus, so that the free left atrial wall was still activated at a coupling interval of 110 msec. This interval shortened to 100 msec during $S_7$. As a result, the stimulated orthodromic wave front of $S_7$ was blocked at the entrance to the slow zone along the AV ring. During $S_4$ and $S_5$, the impulse proceeded in both directions around the remainder of the central obstacle before the orthodromic wave front collided with the antidromic wave front of the same stimulus in the free left atrial wall. Block of the stimulated antidromic wave front and delayed conduction of the stimulated orthodromic wave front of $S_6$ allowed the latter impulse to reexcite the tissue in the upper left atrium. Thus, on cessation of pacing, the original reentrant tachycardia resumed ($A_{n+1}$).
Discussion

The present study demonstrates epicardial activation patterns during entrainment and termination of circus movement atrial flutter in the canine sterile pericarditis model. It is shown that entrainment of the arrhythmia does not necessarily result in a standard activation pattern. Variations of the classical activation pattern during pacing-induced termination of circus movement atrial flutter are also presented.

Comparison With Previous Studies

Transient entrainment of a tachycardia was first described during rapid pacing of atrial flutter and then during ventricular tachycardia, but the mechanism was not initially understood. Subsequent studies on transient entrainment and interruption of the AV bypass type of paroxysmal atrial tachycardia led to a mechanistic concept, based on deductive analysis of the surface electrocardiogram and a limited number of intracardiac recordings. Mapping studies during entrainment of reentrant atrial arrhythmias have used the isolated, perfused canine heart. In this model, a surgically induced lesion forced the reentrant activation to proceed as a single wave front in the supravalvular anulus of the tricuspid ring. Because the reentrant pathway, and thus the pathway of any stimulated wave front, is anatomically predetermined and because the propagating impulse encounters only normal atrial tissue, the demonstrated activation sequence during entrainment of this arrhythmia is not likely to reflect the clinical situation. Atrial flutter in the canine sterile pericarditis model, on the other hand, seems to closely resemble its clinical counterpart. The reentrant pathway is, at least in part, determined by the functional properties of the atrial tissue, which is inhomogeneously affected by the underlying inflammation. Epicardial mapping in the in situ canine heart, as opposed to the endocardial approach in an isolated heart preparation, is not limited by possible mechanical alterations of the atria, hemodynamic changes, and the absence of humoral and autonomic influences. On the other hand, the in vivo mapping method is unable to map atrial septal activation. It seems, however, that at least the major portion and the crucial components of the reentrant circuits in the canine sterile pericarditis model are located in the free atrial wall. The atrial septal tissue, which is not involved in the inflammatory reaction, is not expected to exhibit slow conduction or functional conduction block. Thus, even though our epicardial activation maps might not always reflect the actual activation path for the total length of the reentrant pathway, the possible involvement of the interatrial septum is not likely to produce an essentially different activation pattern.

Although the isochronal maps were constructed manually, it is very unlikely that the changes in the reentrant pathway were due to errors in the measurement of activation times. Not only were the observed changes in the activation sequence profound but so were the changes in local electrogram configurations.

Entrainment of Atrial Flutter: Epicardial Activation Sequence

Our study has demonstrated classical activation patterns for both entrainment and termination of atrial flutter and has lent credence to previously proposed electrocardiographic criteria. The presence of fusion beats in the surface electrocardiogram has been explained as the result of a collision between the reentrant and the stimulated wave fronts, with constant fusion being represented by a constant site of collision for each paced beat. We have shown classical entrainment to be associated with antidromic and orthodromic propagation of the stimulated wave front within the original reentrant pathway, where the orthodromic activation sequence was similar to that during the spontaneous tachycardia. The last stimulated beat was entrained up to the previous site of collision, while its reentrant orthodromic wave front did not longer encounter an antidromic wave front with which to collide. During entrainment at faster pacing rates, the site of collision could shift in an antidromic direction. Termination of the arrhythmia was associated with progressive slowing of the orthodromic wave front and, thus, a progressive shift of the site of collision in an antidromic direction. When the orthodromic impulse was finally blocked, the tissue between the site of this block and the site of collision was not activated. This area was subsequently activated directly by the stimulated wave front of the following beat after a relatively short conduction time. Conduction block to a site in the reentrant pathway was followed by activation of that site from a different direction and with a shorter coupling interval.

Two variations of the classical activation pattern were observed: 1) The orthodromic wave front no longer proceeded within the original reentrant pathway (Figure 4), although the electrocardiographic criteria of progressive fusion suggested classical entrainment. This observation has several implications. First, it emphasizes the limitations of a small number of recording sites when interpreting a complex activation pattern. Second, it raises the question whether the term entrainment, as it has been defined, is applicable to a situation in which a different reentrant pathway is used during the pacing period. And third, it suggests a limited specificity of the criteria proposed for identification of classical entrainment, if the term "entrainment" is inappropriate for this situation. 2) Conduction block in antidromic direction forced a change in the pathway of the antidromic wave front so that entrainment of the arrhythmia to a higher pacing rate did not result in a shift of the site of collision. It has been suggested that the ability or inability to demonstrate the entrainment criteria at different pacing sites can be used to locate the slow zones of a reentrant circuit. However, as shown in Figure 5, the location of the pacing site relative to the slow zone of a reentrant circuit is not necessarily the
critical factor for the inability to demonstrate progressive fusion. Previous investigators have also noted that the extent of the antidromic shift during subsequent entrainment episodes is not proportional to the decrease in the pacing cycle length. The classical entrainment concept was derived from electrocardiographic findings in patients with the AV bypass type of paroxysmal atrial tachycardia, and the suggested activation pattern was confirmed previously in a model of reentry with anatomically predetermined pathways. It is likely that the variations in the classical entrainment pattern that we measured

Figure 8. Epicardial activation maps showing introduction of six stimulated beats at cycle length of 100 msec during atrial flutter at cycle length of 115 msec with termination (S₃) and reinduction (S₆) of original tachycardia. Last tachycardiac beat before initiation of pacing (Aₙ), six stimulated beats (S₁–S₆), and first spontaneous beat after cessation of pacing (Aₙ₊₁) are shown. (See Figure 1 for explanation of activation maps.)
are characteristic of a functional model of reentry and not a fixed reentrant circuit.

Termination and Reinitiation of Circus Movement Atrial Flutter

The mechanisms of termination of circus movement atrial flutter by programmed electrical stimulation were similar to those demonstrated for figure-eight reentrant tachycardias in the ventricle. With every stimulated beat, the increasing conduction delay in the slow zone shortened the interval at which consecutive stimulated orthodromic wave fronts arrived at this critical area. It can be assumed that the tissue with the longest refractoriness within the slow zone was finally reached by the stimulated wave front before its refractoriness expired, resulting in conduction block. However, different from the figure-eight reentrant circuit, there could be more than one critical site for termination within the single loop (Figures 6 and 7).

Continuation of pacing beyond tachycardia termination could result in reinitiation of the same circuit or induction of a different, potentially faster reentrant rhythm. The latter phenomenon is one of the limitations of antitachycardia pacing in the treatment of reentrant arrhythmias. In our study, this was always due to termination of the underlying arrhythmia with the first few stimulated beats, followed by initiation of a different circuit by subsequent stimuli. Similar observations have been previously reported during termination of figure-eight reentrant tachycardias by programmed electrical stimulation and during the initiation of reentrant ventricular arrhythmias by burst pacing.

Clinical Implications

Failure of rapid pacing to terminate atrial flutter despite atrial capture may involve the following mechanisms: 1) entrainment of the arrhythmia, 2) stimulation with less than the critical number of beats, and 3) stimulation with more than the critical number of beats, resulting in either reinitiation of the same or induction of a different reentrant circuit. The fact that single reentrant loops in the atria may involve more than one critical site for termination might have implications for ablative interventions, because it offers the possibility of choosing the more suitable site for respective procedures.

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